IN THE UNITED STATES DISTRICT COURT
FOR THE EASTERN DISTRICT OF TEXAS
MARSHALL DIVISION

PROSTRAKAN, INC. and STRAKAN INTERNATIONAL S.á.r.l.,

Plaintiffs,

v.

ACTAVIS LABORATORIES UT, INC.

Defendant.

Case No: 2-16-CV-0044-RWS-RSP

CLAIM CONSTRUCTION MEMORANDUM OPINION AND ORDER

Before the Court is the opening claim construction brief of Prostrakan, Inc. and Strakan, International S.á.r.l. ("Plaintiffs") (Dkt. No. 50, filed on May 4, 2017),[1] the responsive claim construction brief of Actavis Laboratories UT, Inc. ("Defendant") (Dkt. 53, filed May 18, 2017), and the reply of Plaintiffs (Dkt. No. 57, filed May 25, 2017). The Court held a hearing on the issues of claim construction and claim definiteness on June 22, 2017. Having considered the arguments and evidence presented by the parties at the hearing and in their briefing, the Court issues this Order.

[1] Citations to the parties' filings are to the filing's number in the docket (Dkt. No.) and pin cites are to the pages assigned through ECF.

I. BACKGROUND

A. Defendant's Abbreviated New Drug Application No. 208726

This patent infringement action arises from Defendant's efforts to obtain Federal Drug Administration ("FDA") regulatory approval for Abbreviated New Drug Application ("ANDA") No. 208726, which would allow them to market a generic version of Plaintiffs' SANCUSO® product (granisetron[2] extended release transdermal film, 3.1 mg/24 hr). SANCUSO® is an adhesive patch marketed and sold in the United States pursuant to New Drug Application ("NDA") No. 022198,[3] which was approved by the FDA in September 2008 for use in the prevention of nausea and vomiting in patients receiving moderately and/or highly emetogenic chemotherapy for up to 5 consecutive days. As marketed, the SANCUSO® transdermal film comprises a 52 cm^2 acrylic adhesive patch containing 34.3 mg of granisetron in an acrylate-vinylacetate copolymer.

Under the *Food, Drug, and Cosmetic Act*, Pub. L. No. 52–675, 52 Stat. 1040 (1938) (the "FDCA"), as amended by the Hatch–Waxman Act (the "Act") (21 U.S.C. §§ 301 *et. seq*. (1994)), a pharmaceutical manufacturer may submit an ANDA to seek expedited FDA approval of a generic version of an originator drug product previously approved by the FDA. *See* 21 U.S.C. § 355(j). An ANDA may be approved if the proposed generic drug product is comparable to the previously approved originator drug product in dosage form, strength, route of administration, quality, performance characteristics, and intended use. *See* 21 U.S.C. § 355(j)(2)(A)(iv).

Because originator drugs are often the subject of patent protection[4], upon submission of an ANDA, a generic manufacturer must certify that the referenced originator drug product is either:

[2] 1-methyl-N-[(1S,5R)-9-methyl-9-azabicyclo[3.3.1]nonan-3-yl]indazole-3-carboxamide.
[3] Prostrakan, Inc. is the holder of the NDA.
[4] Pharmaceutical-related patents covering the innovator drug compound, specific formulations of the drug, or methods of treating certain diseases by administering the drug as approved in the NDA

(I) not protected by a patent; (II) was protected by a patent, but the patent has expired; (III) is protected by a patent, but the generic manufacturer is seeking an approval date for the ANDA which is after the expiration date of the patent; or (IV) the patent is invalid and/or will not be infringed by the manufacture, use, or sale of the generic drug product. 21 U.S.C. § 355(j)(2)(A)(vii)(I)-(IV). A certification under 21 U.S.C. § 355(j)(2)(A)(vii)(IV) is commonly referred to as a "Paragraph IV" certification.

In association with its NDA, Prostrakan, Inc. has identified U.S. Patent No. 7,608,282[5] (the "'282 patent"), titled "Transdermal Granisetron," in the Orange Book as encompassing SANCUSO®. In the ANDA filing to the FDA, Defendant has included a Paragraph IV certification that the claims of the '282 patent are invalid, unenforceable, and/or would not be infringed by the manufacture, use, importation, sale, or offer for sale of Defendant's proposed generic product.

Pursuant to 35 U.S.C. § 271(e)(2)(a), a certification under Paragraph IV is considered an act of patent infringement, and as part of the ANDA application process, the ANDA applicant must notify the patent holder and NDA holder of the Paragraph IV certification. *See* 21 U.S.C. § 355(j)(2)(B). Once notified, the NDA holder and patent holder have 45 days to file a lawsuit claiming the generic offering will infringe the Orange Book listed patent. *See* 21 U.S.C. § 355(j)(5)(B)(iii). If a lawsuit is filed within this period, the approval of the ANDA is automatically stayed for 30 months, allowing time for an infringement determination to be made. *See Id.*

On December 1, 2015, Defendant notified Plaintiffs that they had filed ANDA 2087260, with a Paragraph IV certification that the generic product did not infringe the '282 patent. On

---

are listed along with the NDA in the FDA publication *Approved Drug Products with Therapeutic Equivalence Evaluations* (commonly referred to as the "Orange Book").

[5] Prostrakan, Inc. is the exclusive licensee of the '282 patent, which is owned by Strakan S.á.r.l.

January 13, 2016, Plaintiffs commenced this action for relief from Defendant's alleged infringement of the '282 patent, asserting 22 claims—claims 1, 2, 4-8, 10-15, 18-23, and 26-28.

B. The '282 Patent

The '282 patent is titled "Transdermal Granisetron" and was filed in the United States as a 35 U.S.C. § 371 national stage entry of International Application No. PCT/GB2004/000403, filed on February 5, 2004, and which claimed priority to Great Britain Application No. GB 0302662.2, filed on February 5, 2003. The '282 patent was granted on October 27, 2009, and is scheduled to expire on January 22, 2025. The inventors of the '282 patent are identified as Peter Altenschöpfer and Adam Charles Watkinson.

In general, the '282 patent is directed to acrylic adhesive patches for the transdermal administration of granisetron. Granisetron is effective at reducing nausea and vomiting caused by the use of certain chemotherapeutic drugs during cancer treatments. The use of cytotoxic chemotherapeutic drugs is thought to cause the release of serotonin from certain cells of the small intestine. Serotonin stimulates the vagal afferent nerves through the serotonin 5-hydroxytryptamine$_3$ (5-HT$_3$)-receptor, resulting in the stimulation of the vomiting reflux. Granisetron is thought to work as a 5-HT$_3$-receptor antagonist that prevents serotonin's interaction with the 5-HT$_3$-receptor and blocks the vomiting reflex. ('282 patent at 1:11-27.)

According to the specification, 5-HT$_3$-receptor antagonists such as granisetron were traditionally administered via oral, intravenous, or rectal routes, which all have inherent disadvantages (*see id*. at 1:28-45), thus necessitating the need for a non-oral drug delivery system capable of maintaining constant levels of the agent over extended periods of time (*see id*. at 1:46-51). According to the specification, prior attempts at transdermal delivery of 5-HT$_3$-receptor antagonists required excessively large transdermal patches and permeation enhancers or the use of

high-loading "reservoir patches" that contained high volumes of solvents such as ethanol or propylene glycol, resulting in bulky patches that irritated the skin. (*Id*. at 2:27-60.)

Furthermore, according to the specification, attempts at using smaller, "matrix patches," which have the ability to better adhere to the skin and contain the drug within the adhesive matrix, were beset by stability issues and the inability to deliver high amounts of drug. (*See id*. at 2:66-3:35.) In addition, the use of acrylic adhesives containing nucleophilic moieties such as hydroxyl moieties was taught against because of potential cross-linking of the adhesive with the drug due to the basic nature of the drug, resulting in reduced delivery of the drug. (*See id*. at 3:24-35.)

The specification teaches that the problems in the prior art with transdermal delivery of 5-HT_3-receptor agonists can be overcome by using acrylic adhesives that include monomers having non-acidic hydroxyl moieties. (*Id*. at 3:36-46.) According to the specification, the use of non-acidic hydroxyl moieties enhances the permeation or flux of granisetron across the skin (*see id*. at 3:39-42), reducing the need for irritating plasticizers or permeation enhancers (*see id*. at 4:32-39). Furthermore, according to the specification, the use of non-acidic hydroxyl moieties increases stability of granisetron within the patch. (*See id*. at 9:58-65).

The claims of the '282 patent are directed to an adhesive patch, and use thereof, having an effective amount of granisetron in an acrylic adhesive which incorporates monomers having non-acidic hydroxyl moieties. (*See id* at 12:51-14:33.)

II. DISCUSSION

Claim construction begins with the language of the claims. *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312-1314 (Fed. Cir. 2005) (en banc); *Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1582 (Fed. Cir. 1996). Claim terms are generally given their plain and ordinary meaning to

one of ordinary skill in the art[6] when read in the context of the specification and prosecution history. *See Phillips,* 415 F.3d at 1313. When interpreting claim language, courts consult the intrinsic record, which includes the specification and prosecution history. *Id.* at 1315-17. The specification is "the single best guide to the meaning of a disputed term." *Id.* (citation omitted). After considering the intrinsic record, a court may consider extrinsic evidence if there is "genuine ambiguity" in the claims. *Vitronics, Inc.*, 90 F.3d at 1584.

A. Construction of Disputed Terms

Three terms are at issue in this claim construction dispute. The disputed terms are underlined below:

> 1. An adhesive patch suitable for the transdermal administration of granisetron to a subject in need thereof, said patch comprising:
>
> an acrylic adhesive consisting essentially of:
>
> 50 to 98% w/w of a primary acrylate monomer wherein said primary acrylate monomer is either 2-ethylhexyl acrylate or butyl acrylate, and
>
> 0.5 to 20% w/w of a monomer containing non-acidic hydroxyl moieties, and
>
> a physiologically effective amount of granisetron loaded in the acrylic adhesive,
>
> wherein the granisetron content of said patch remains substantially unchanged when stored at 25° C for six weeks.
>
> 22. A patch according to claim 1, incorporating no plasticizers or permeation enhancers.

('282 patent at 12:51-65; 14:13-14.)

[6] Defendant has proposed a person of skill in the art is one with the requisite education, training, knowledge, and experience in formulating and designing acrylic adhesives for use in transdermal patches. (Dkt. No. 53 at 17.) Plaintiffs, in their briefing, did not define the person of skill in the art.

1. "Consisting essentially of"

Plaintiffs' Proposed Construction	Defendant's Proposed Construction
Prostrakan disagrees with Actavis's proposal that this term is indefinite, and submits that this term is a well-developed transitional phrase in patent law and should accordingly have its plain and ordinary meaning. If the Court believes this term requires construction, the Court should construe this term to mean "including the listed ingredients and open to unlisted ingredients that do not materially affect the basic and novel properties of the invention.	The term is indefinite because it does not inform a person of ordinary skill with reasonable certainty of what is claimed. Alternatively, to the extent this term can be construed, it should be construed as: "the acrylic adhesive includes the expressly recited monomers and any other components that do not materially affect the basic and novel properties of the acrylic adhesive, the basic and novel properties being the adhesion, shear resistance, and tack of the adhesive." The claim is nevertheless indefinite because the '282 patent fails to provide reasonable certainty to one of ordinary skill in the art as to the identities of the basic and novel properties of the acrylic adhesive and the bases on which to determine whether an additional ingredient would materially affect any of those basic and novel properties.

Court's Construction: *The term "consisting essentially of" means "including the listed ingredients and open to unlisted ingredients that do not materially affect the basic and novel properties of the invention, the basic and novel properties of the invention being 1) increased transdermal delivery of granisetron, 2) granisetron stability in the patch, and 3) the complete release of granisetron from the patch.*

Both parties agree that the term "consisting essentially of" is a well-developed transitional phrase that "signals that the invention necessarily includes the listed ingredients and is open to unlisted ingredients that do not materially affect the basic and novel properties of the invention," citing *PPG Indus. V. Guardian Indus. Corp.*, 156 F.3d 1351, 1354 (Fed. Cir. 1998). (Dkt. No. 50

at 19; Dkt No. 53 at 17.) The dispute between the parties centers on whether the "basic and novel properties" analysis is directed to the entirety of the claim, i.e. the claimed adhesive patch for transdermal delivery of granisetron as Plaintiffs contend (Dkt. No. 50 at 19-23), or more narrowly focused to the specific claim limitation modified by the transitional phrase, i.e. the acrylic adhesive as the Defendant contends (Dkt. No. 53 at 18-23). Nonetheless, Defendant maintains that the use of the transitional phrase in this case renders the claim indefinite under 35 U.S.C. § 112, ¶ 2[7] for failing to convey with reasonable certainty the scope of the claimed invention.

When asked to construe "consisting essentially of," courts have generally declined to provide any further construction beyond the well-established legal meaning of the term. *Horizon Pharma Ir., Ltd. v. Actavis Labs., UT, Inc.*, 2016 U.S. Dist. LEXIS 109068, *15 (D.N.J. Aug. 17, 2016) (internal citations omitted). When, however, the "basic and novel properties" themselves are in dispute, courts have construed the term in order to define the "basic and novel properties" to delineate what must be shown for the purposes of infringement or invalidity. *Id.* *15-16 (citing *AK Steel Corp. v. Sollac & Ugine*, 344 F.3d 1234, 1239-40 (Fed. Cir. 2003) (determining the basic and novel property of the invention by referring to the specification); *L'Oréal S.A. v. Johnson & Johnson Consumer Cos., Inc.*, 2014 U.S. Dist. LEXIS 190268, *4 (D. Del. Nov. 5, 2014) ("As with claim construction, the court determines the basic and novel properties of an invention as a matter of law, while resorting to the same sources of evidence used for claim construction.").

Accordingly, the Court will construe "consisting essentially of" in accordance with its well-established legal meaning, which is: "including the listed ingredients and open to unlisted ingredients that do not materially affect the basic and novel properties of the invention." Because

[7] The Court refers to the pre-America Invents Act (AIA) version of § 112 which the '282 patent, granted prior to implementation of the AIA, is subject to.

the parties dispute what those basic and novel properties are, the Court finds it necessary to further construe them.

Plaintiffs have identified three basic and novel properties for the claimed invention: 1) increased transdermal delivery of granisetron, 2) granisetron stability in the patch, and 3) the complete release of granisetron from the patch. (Dkt. No. 50 at 20.) Conversely, Defendant argues that the basic and novel properties of the acrylic adhesive, not the adhesive patch, are at issue because the transitional phrase "consisting essentially of" precedes and applies to the acrylic adhesive claim element. (Dkt. No. 53 at 21.) Defendant argues that, because the '282 patent fails to identify the basic and novel properties of the acrylic adhesive, the basic and novel properties of the acrylic adhesive are those most commonly referenced by a person of skill in the art, those being 1) adhesion, 2) shear resistance, and 3) tack. ((Dkt. No. 53 at 23.) Nonetheless, the Defendant argues that the '282 patent fails to identify which unlisted ingredients would material affect the adhesion, shear resistance, and tack of the acrylic polymer, rendering the claims indefinite. (Dkt. No. 53 at 21.)

Plaintiffs point to *AK Steel Corp.*, 344 F. 3d 1234, as controlling in this instance. (Dkt. No. 57 at 4-5.) In *AK Steel*, the Federal Circuit examined a claim generally directed to hot-dipped aluminum coated steel, and particularly to a ferrous base ferritic strip comprising a metal strip including at least 6% by weight chromium and a coating metal "consisting essentially of" aluminum.[8] 344 F.3d at 1237. Hot-dipped aluminum steel has desirable resistance to corrosion

[8] The claim at issue in AK Steel provided:
1. A ferrous base ferritic strip continuously hot dip coated with a coating metal, comprising:
the strip including at least 6% by weight chromium,
the coating metal consisting essentially of aluminum,
the coating layer on said strip being substantially free of uncoated areas and formed without a thick brittle Fe-Al alloy inner layer,

and high-temperature oxidation, making it a particularly useful component for use in automotive exhaust systems and combustion equipment. *See id*. at 1236. According to the Federal Circuit, the patent teaches that hot-dipped aluminum steel is produced "by passing heated steel strips through molten aluminum; however, it is challenging to get the aluminum to adhere or "wet" well on to the steel." *Id*. The inventors solved the problem by maintaining the steel strip in a hydrogen atmosphere prior to entry into the aluminum coating bath and using aluminum that is substantially pure. *Id*. The inventors also determined that the invention did not work unless the aluminum was substantially pure. *Id*.

The claim at issue in *AK Steel* included both a "comprising" and "consisting essentially of" transitional phrase, as does the claim at issue here. The Federal Circuit, in construing "consisting essentially of," noted the ambiguous nature of the term, but stated "it has long been understood to permit inclusion of components not listed in the claim, provided that they do not 'materially affect the basic and novel properties of the invention.'" *Id.* at 1239 (citing *PPG Indus. V. Guardian Indus. Corp*., 156 F.3d 1351, 1354 (Fed. Cir. 1998). The Federal Circuit framed the issue of construing "consisting essentially of" as follows: "[T]he claim construction issue presented by the '135 patent in this case is whether an amount of silicon in excess of 0.5% in the aluminum coating materially affects the basic and novel properties of the invention." *Id.* The Federal Circuit went on to identify the basic and novel properties of the invention as "good wetting,"[9] citing the patent specification which stated: "It is a principal object of this invention to form hot dip aluminum coated ferritic chromium alloy steels having enhanced wetting by the coating metal." *Id.* at 1240.

---

said coating layer being tightly adherent to said strip and resistant to crazing or flaking during bending. (Emphasis added.)

[9] Wetting problems can result in crazing or flaking of the aluminum coating during subsequent bending of the strip. *See AK Steel*, 156 F.3d at 1236.

The Federal Circuit noted the specification's recitation that "silicon exceeding 0.5% by weight decreases the reactivity of the aluminum coating metal needed to react with a ferritic chromium alloy steel substrate. Accordingly, silicon contents in the coating metal should not exceed about 0.5% by weight," and found that an excess of 0.5% aluminum in the coating metal, as stated in the specification, "materially affects the basic and novel properties of the invention." *Id.* In *AK Steel*, the Federal Circuit considered the material effects of additional ingredients in the claim element modified by the transitional phrase—the aluminum coating—with regard to the basic and novel properties of the invention as a whole—the enhanced wetting provided by the aluminum coating in its reaction with the steel—and not to the basic and novel properties of the aluminum coating alone or in isolation.

Defendant cites a number of cases to bolster its position that a transitional phrase such as "consisting essentially of" modifies the specific claim limitation containing the phrase. (*See* Dkt. No. 53 at 18-19.) A review of these cases, however, indicates that the transitional phrase at issue in many of these cases was "consisting of," a closed-ended transitional phrase that excludes unlisted ingredients. In *Digene Corp. v. Third Wave Techs., Inc.*, 323 Fed. Appx. 902, 909 (Fed. Cir. Apr. 1, 2009), the Federal Circuit noted that a claim with the overall transitional phrase "comprising" and containing a limitation with the transitional phrase "consisting of" allowed for the addition of other elements to the overall claim, but it does limit the clause for which "consisting of" acts as a transition to only those elements found in that particular clause. That is not the case, however, with the term "consisting essentially of," wherein non-listed ingredients can be included within the element provided such non-listed ingredients do not materially alter the basic and novel properties of the invention. Accordingly, the Court does not find the reasoning in limiting the

transitional phrase "consisting of" to the specific element modified to be necessarily applicable to the transitional phrase "consisting essentially of."

Defendant also cites *Lonza Inc. v. Nalco Co.*, 2011 U.S. Dist. LEXIS 86642, *17-19 (D.N.J. Aug. 4, 2011) (*Lonza I*), wherein the district court considered whether the transitional phrase "consisting essentially of," which modified only a single element in the claim,[10] modified and applied to the specific element or the entirety of the claim. The district court reasoned that because "consisting essentially of" was used at the end of the body of the claim to modify only one element, and not at the beginning of the claim to modify the entirety of the claim, its construction must be limited to that single element. *Id*. at *19. The district court construed the term "consisting essentially of" to mean "a mixture that includes an N-hydrogen compound and that excludes any unspecified materials that materially affect the basic and novel characteristics of the mixture." *Id*. Subsequently, in denying a motion for reconsideration on the issue, the district court further reasoned that "consisting essentially of" "only modifies and applies to the mixture element of the process claim in which it appears." *Lonza Inc. v. Nalco Co.*, 2011 U.S. Dist. LEXIS 112548 *8-11 (D.N.J. Sept. 29, 2011) (*Lonza II*). In distinguishing *AK Steel*, the district court found that the Federal Court did not address the issue of whether "consisting essentially of" modified the claim in its entirety or an element of the claim thereof. *Id*. at *8-9.

[10] The claim at issue in Lonza, Inc. provided:
14. In a process for making paper from pulp fiber wherein from 0.2 to 3 weight percent of organic matter comprising from 95 to 99 weight percent pulp fiber is maintained in a circulating water slurry in the presence of sizing, the improvement of performing said process in the presence of a slimicidally effective amount of an N-hydrogen compound and a slimicide in a molar ratio of from 0.1:1 to 10:1 in said circulating water slurry; wherein said N-hydrogen compound is [] and the amount of the N-hydrogen compound present in said circulating water slurry is sufficient to enhance the biocidal efficacy of the slimicide and reduce absorbable organic halogen (AOX) by-product formation, wherein the N-hydrogen compound is directly added to the slurry before or after the addition of the slimicide or with the slimicide in a mixture consisting essentially of the slimicide and the N-hydrogen compound. (Emphasis added.)

This Court, however, is not bound by the decision in *Lonza I* or *Lonza II*. Instead, the Court finds the Federal Circuit's decision in *AK Steel*, which addressed a claim of similar structure to claim 1 of the '282 patent having both "comprising" and "consisting essentially of" transitional phrases, to be controlling. It is this Court's opinion that *AK Steel* compels a construction that focuses on the basic and novel properties of the claimed invention as a whole, that is the adhesive patch for transdermal delivery of granisetron, and not the basic and novel properties of the acrylic adhesive in isolation.

As discussed *supra*, Plaintiff has identified three basic and novel properties of the adhesive patch: 1) increased transdermal delivery of granisetron, 2) granisetron stability in the patch, and 3) the complete release of granisetron from the patch. (Dkt. No. 50 at 20.). The intrinsic record of the '282 patent supports Plaintiffs' position. The specification of the '282 patent explicitly states that the use of "adhesives comprising hydroxyl groups are significantly better than non-nucleophilic, electroneutral adhesives, and that such adhesives substantially enhance flux[11] of granisetron, for example." ('282 patent at 3:39-42.) In addition, the specification states: "However, in the patches of the present invention, the presence of the polar residues has a surprising effect on the transdermal flux, increasing permeation to a level where substantially the whole load can be dispensed in a 24-hour period." (*Id*. at 4:39-43.) "In the accompanying Examples, we demonstrate that the presence of hydroxyl groups in the adhesive actually substantially facilitates release []." (*Id*. at 4:45-48.) With regard to stability, the specification states that the inclusion of hydroxyl groups in the polymer chains "increases formulation options as it allows cross-linking of the adhesives to be achieved if required, thereby improving cohesion

[11] Flux is the amount of drug delivered through the skin as a function of time. (*See* Dkt. No.52 at 20.)

of the adhesive matrix in terms of three-dimensional stability." (*Id*. at 6:58-62.) Furthermore, the Examples of the specification focus on the improved delivery of granisetron using adhesives with non-acidic hydroxyl functional groups. Example 1 compares the permeation, average flux, and absolute flux of granisetron from patches of the present invention with adhesives that did not contain non-acidic hydroxyl functional groups, and reports that the flux from the improved patches was "sufficiently high to deplete the device of granisetron after only 24 hours." (*Id.* at 9:1-57.) Example 2 provides stability data, stating: "There was no observed decrease in granisetron content of the patches indicating that, even under accelerated conditions at 40° C., the drug is stable in these devices." (*Id.* at 9:59-65.) In addition, claims 1 and 28 of the '282 patent contain limitations related to stability. (*Id*. at 12:63 & 14:31.)

The prosecution history is consistent with the specification in maintaining that these aspects were the basic and novel properties of the invention, repeatedly indicating that "the combination of adhesive having non-acidic hydroxyl moieties and granisetron provides numerous advantages, e.g.,

- the combination has been found to be remarkably stable;
- the combination has been found to have surprisingly good drug release properties; and
- the combination has been found to have surprisingly good skin flux properties."

(Dkt. No. 50-5 at 15; see also Dkt. 50-6 at 10; Dkt. 50-7 at 2-3.) The Court fails to note anything in the specification or in the prosecution history to suggest that some other basic and novel properties were contemplated or suggested, for example adhesion, shear, and/or tack, and the specification is largely absent of any discussion, other than a passing reference, relating to the importance of these characteristics in the adhesive patch, conveying to a person of skill that the inventors did not consider them to be the basic and novel properties of the invention. This is even

more evident in the exemplified embodiments, which are wholly absent of any comparative studies related to adhesion, shear, or tack, and focus instead on release, delivery, and stability of granisetron within the patch over time.

Finally, Defendant argues that the term "consisting essentially of" should be interpreted as a narrow closed-ended transitional phrase limiting the analysis of the novel and basic features to the adhesive layer alone based on the Examiner's Stated Reasons for Allowance and the Plaintiffs' subsequent Comments on Statement of Reasons for Allowance ("Comments"). (*See, e.g.*, Dkt. 61 at 30:15-33:21.) In the Reasons for Allowance, the examiner stated that the prior art does not:

> [T]each the claimed transdermal patch that consisting of [sic] an acrylic adhesive layer that consisting of granisetron, and two monomers, the non-acidic hydroxyl moieties monomer, and the 2-ethylhexyl acrylate or butyl acrylate. The use of the transitional phrase "consisting of" to preclude all other monomers and/or polymers in the acrylic adhesive layer taught in the cited prior arts. The present specification shows that the acrylic adhesive layer exhibits an unchanged granisetron content, as well as no crystallization of the granisetron when stored at 25°C for six weeks.

(*See* Dkt. No. 50-7: Comments on Statement of Reasons for Allowance.) According to Defendant, the use of the term "consisting of" by the examiner, instead of "consisting essentially of," is indicative of the examiner interpreting the transitional phrase as closed-ended and limiting the novel and basic feature analysis to the adhesive alone. (See Dkt. No. 61 at 30:15-20.) Furthermore, Defendant argues Plaintiffs' subsequent Comments limit the novel and basic features to those of the adhesive alone. (Dkt. No. 53 at 23-24.) In those Comments, Plaintiffs proposed revised Reasons for Allowance to apparently correct the examiner's use of the transitional phrase "consisting of." In doing so, the Plaintiffs stated that "[t]he use of the transitional phrase 'consisting essentially of' precludes all other monomers and/or polymers in the acrylic adhesive layer . . . to the extent any such monomer or polymer would materially effect [sic] the basic and novel properties of the claimed adhesive layer." (Dkt. No. 50-7 at 3.)

As an initial matter, the actual claim provides for "consisting essentially of" and not "consisting of." Thus, it appears that the examiner's statement was simply a mistake—as it is indisputable that the claims use the transitional phrase "consisting essentially of." In any event, the examiner's statement is not the Plaintiffs' statement and should not, in light of the rest of the intrinsic record, be seen to limit the scope of the claim as advanced by Defendant. *See Salazar v. Procter & Gamble Co.*, 414 F.3d 1342, 1345 (Fed. Cir. 2005) (remarks in the examiner's statement of reasons for allowance insufficient to limit claim scope); *LifeScan Scot., Ltd. v. Shasta Techs., LLC*, 734 F.3d 1361, 1379 (Fed. Cir. 2013) ("[t]his court has recognized that an Examiner's Statement of Reasons for Allowance will not necessarily limit a claim." (internal citations omitted)); *Alfred E. Mann Found. for Sci. Research v. Cochlear Corp.*, 841 F.3d 1334, 1341 (Fed. Cir. 2016)) ("an examiner's unilateral statement does not give rise to a clear disavowal of claim scope by the applicant.").

Likewise, the Court does not find the Plaintiffs' statement in the Comments to be anything more than an attempt to correct the examiner's incorrect usage of the transitional phrase "consisting of." Plaintiffs' statement that "to the extent any such monomer or polymer would materially effect [sic] the basic and novel properties of the claimed adhesive layer," when viewed in the context of the entirety of the comment, cannot be seen as an intention to limit the novel and basic properties of the invention to the adhesive layer alone. *See, e.g., Biogen Idec, Inc. v. GlaxoSmithKline LLC*, 713 F.3d 1090, 1100 (Fed. Cir. 2013) ("We have long followed the rule that even a poorly-phrased prosecution argument does not a disclaimer make."). Importantly, the examiner, in his Reasons for Allowance, explicitly identifies stability of granisetron in the acrylic adhesive as an important feature of the overall transdermal patch: "The present specification shows that the acrylic adhesive layer exhibits an unchanged granisetron content, as well as no

crystallization of the granisetron when stored at 25°C for six weeks." (See Dkt. No. 50-7.) Plaintiffs' Comments did not disturb or dispute this point. When read in context, nothing in the Reasons for Allowance or the Plaintiffs' Comments support restricting the term "consisting essentially of" as argued by Defendant.

In light of the above, the Court finds that 1) increased transdermal delivery of granisetron, 2) granisetron stability in the patch, and 3) the complete release of granisetron from the patch are the basic and novel properties of the invention.[12]

Defendant further contends that, regardless of what specific basic and novel properties the Court may find, the '282 patent fails to provide any data or information regarding the necessary respective values of the properties which would allow a quantitative assessment of the effect on the basic and novel properties of the invention if components of the adhesive were changed. (Dkt. No. 53 at 29.) In addition, Defendant argues that the intrinsic record does not provide any guidelines to allow a person of skill to assess what additional, unclaimed ingredients would affect the properties and whether such affect would be material. (*Id*.)

As part of construing claims, the Court can assess whether a claim term is indefinite, and reach "a legal conclusion that is drawn from the court's performance of its duty as the construer of patent claims." *In re Aoyama*, 656 F.3d 1293, 1299 (Fed. Cir. 2011); *Ethicon Endo-surgery, Inc. v. Covidien, Inc.*, 796 F.3d 1312, 1317 (Fed. Cir. 2015) ("Indefiniteness is a question of law for the court."). The Federal Circuit has found that the definiteness requirement of 35 U.S.C. § 112, ¶ 2 applies to a "consisting essentially of" claim. *See PPG Indus.*, 156 F.3d at 1354-55;

[12] Because the Court finds the intrinsic record determinative in identifying the basic and novel properties of the invention, it need not consider Defendant's proffered extrinsic evidence. (*See L'Oréal S.A.*, 2014 U.S. Dist. LEXIS 190268, *4 ("As with claim construction, the court determines the basic and novel properties of an invention as a matter of law, while resorting to the same sources of evidence used for claim construction.").

Horizon Pharma Ir., Ltd., 2016 U.S. LEXIS 109068, *16. A claim is indefinite if the claim, read in light of the specification delineating the patent, and the prosecution history, fail to inform, with reasonable certainty, those skilled in the art about the scope of the invention. *Nautilus Inc. v. Biosig Instruments, Inc.*, 134 S. Ct. 2120, 2129 (2014); s*ee also Horizon Pharma Ir., Ltd.*, 2016 U.S. LEXIS 109068 *23 ("Because the basic and novel properties of an invention are part of the construction of a claim containing the phrase "consisting essentially of," the *Nautilus* standard applies to the assessment of an invention's basic and novel properties.").

The Court first turns to the specification to determine whether it provides sufficient data or information regarding the necessary respective values of the properties which would allow a quantitative assessment of the effect on the novel and basic properties of the invention if components of the adhesives were changed. Example 1 in the specification describes the results of permeation and flux experiments using four different adhesives, one containing polymers with no functional groups, two containing polymers with acidic functional groups, and one containing polymers with non-acidic hydroxyl groups. ('252 patent at 8:38-9:57.) The contours of the testing are explicitly laid out, for example, for mouse skin testing each of the adhesives were formulated with 3% granisetron, a coating weight of 85 g/m^2, and a drug loading of approximately 260 $\mu g/cm^2$. (*Id*. at 8:56-61.) These different formulations were then tested in mice to determine permeation and flux, wherein the adhesive having the non-acidic hydroxyl moieties showed levels of flux 30X higher than the next closest formulation. (*Id*. at 8:62-67.) According to the specification, the flux observed in the non-acidic hydroxyl containing adhesive was sufficiently high to deplete the patch of granisetron after 24 hours, as shown in Figure 2. (*Id*. at 9:44-57.). Human skin permeation and flux were also tested, and the conditions of the testing are explicitly defined. (*Id*. at 10:12-32.) Likewise, the stability of granisetron in the non-acidic hydroxyl containing adhesive, and the basis

of said determination, is described in Example 2. (*Id.* at 9:61-67.) It is the Court's opinion that the specification provides sufficient data and information to a person of skill on how that data was achieved to guide them on how to determine whether an unlisted ingredient materially affects the basic and novel properties of the invention with reasonable certainty, and thus, the term meets the definiteness requirement of 35 U.S.C. § 112, ¶ 2.

Finally, Defendant further alleges that the '282 patent is indefinite because it fails to disclose which unlisted ingredients[13] and the amount thereof would materially affect the basic and novel properties of the invention. (Dkt. No. 53 at 24.) The Court, however, has failed to find any authority which requires a patent using the term "consisting essentially of" to explicitly lay out the metes and bounds of which unlisted ingredients would materially affect the basic and novel features of the invention, provided the basic and novel features of the invention are disclosed with reasonable certainty. Authority does exist to exclude a particular unlisted ingredient from the scope of a claim in situations where the intrinsic record indicates that the unlisted ingredient would materially affect the basic and novel properties of the invention. *See AK Steel*, 344 F.3d at 1238-40 (construing "the coating metal consisting essentially of aluminum" to exclude aluminum with a silicon content of greater than 0.5% due to the specifications explicit statement that "silicon contents in the coating metal should not exceed about 0.5% by weight."). In this case, neither party asserts that the '282 patent has done this. Nevertheless, as described above, the Court finds that the '282 patent provides sufficient guidance on the basic and novel properties of the invention. Whether an unlisted ingredient present in a given amount materially affects the basic and novel properties of the invention can be determined by a person of skill following the guidance provided

[13] In particular, Defendant identifies modifying monomers such as vinyl acetate or a crosslinking monomer such as glycidylmethacrylate as potentially materially affecting the basic and novel properties of the invention. (Dkt. No. 53 at 24.)

in the Examples in the specification. Changes in the delivery, release, and stability of granisetron within any adhesive formulation are readily discernable. Whether such changes are material, however, is an issue of fact, and in this particular instance are not properly determined during claim construction. *PPG Indus.*, 156 F.3d at1357 (holding that the determination of whether a particular unlisted ingredient has a material effect on the basic and novel properties of the glass is a fact issue for the jury.).

2. "physiologically effective amount of granisetron"

Plaintiffs' Proposed Construction	**Defendant's Proposed Construction**
Prostrakan disagrees with Actavis's proposal that this term is indefinite, and submits that a person of ordinary skill in the art would understand the scope of this claim term in view of the words of the claims themselves, as well as the intrinsic record, and background knowledge possessed by a person of ordinary skill in the art. Thus, Prostrakan submits that this term should have its plain and ordinary meaning as understood by a person of ordinary skill in the art. If the Court believes this term requires construction, the Court should construe this term to mean "an amount of granisetron capable of doing that which granisetron is known to do, e.g., prevent and/or treat nausea and vomiting in a subject in need thereof."	The term is indefinite because it does not inform a person of ordinary skill with reasonable certainty of what is claimed. Alternatively, to the extent this term can be construed, it should be construed as: "the effective amount of granisetron that produces a physiological effect." The claim is nevertheless indefinite because the '282 patent fails to provide reasonable certainty to one of ordinary skill in the art as to the amount of granisetron that produces a physiological effect.

Court's Construction: *The term "physiologically effective amount of granisetron" has its plain and ordinary meaning, which is "an amount effective to prevent and/or treat nausea and vomiting in a subject."*

During the Claim Construction Hearing of June 22, 2017, the parties agreed to the Court's preliminary construction of the term "physiologically effective amount of granisetron," which the Court had construed according to its plain and ordinary meaning to be "an amount effective to

prevent and/or treat nausea and vomiting in a subject." (Dkt. 61, 5:4-25.) Having further reviewed the intrinsic record and determined that the '282 patent does not use the term inconsistently with or different than its plain and ordinary meaning, the Court hereby adopts this construction. *See, e.g., GE Lighting Solutions, LLC v. AgiLight, Inc.*, 750 F.3d 1304, 1309 (Fed. Cir. 2014) ("[T]he specification and prosecution history only compel departure from the plain meaning in two instances: lexicography and disavowal.")

Defendant contends that the '282 specification does not convey with reasonable certainty the amount of granisetron that must be provided in the claimed patch to produce a physiological effect in the patient being treated, and thus, the claim is indefinite (Dkt. No. 53 at 30). According to Defendant, the physiological effect will differ from patient to patient and can vary with a number of factors, rendering the determination of the amount of granisetron that provides a "physiological effect" inherently ambiguous. (*Id*. at 30.) Furthermore, Defendant maintains that the '282 patent fails to convey with reasonable certainty the actual amount of granisetron that must be loaded into the claimed patch to provide the "physiological effect." (*Id*. at 31.) Finally, Defendant contends that while the '282 patent describes a wide variety of possible product designs, it fails to provide the necessary guidance for identifying one that will produce a "physiological effect." (*Id*.)

The term "an effective amount" is frequently found in pharmaceutical patents, as the Federal Circuit has recognized. *See Erfindergemeinschaft Uropep GbR v. Eli Lilly & Co.*, 2016 U.S. Dist. LEXIS 172395 (E.D. Tex. Aug. 11, 2016) (citing *Geneva Pharms., Inc. v. GlaxoSmithKline PLC*, 349 F.3d 1373, 1383-84 (Fed. Cir. 2003) (the term "effective amount" is "a common and generally acceptable term for pharmaceutical claims"). Generally, the term "is not objectionable where the amount is not critical, and its use has been approved in many cases." *Id*. (citing *In re Halleck*, 422 F.2d 911, 914, 57 C.C.P.A. 954 (C.C.P.A. 1970)). A review of the

specification indicates that the amount of granisetron is not critical to the invention, as the patent in effect claims a method of treating or preventing nausea and/or vomiting through the transdermal administration of granisetron using an adhesive patch containing non-acidic hydroxyl moieties, without regard to the specific amount of granisetron that is administered. *See Id*. The use of the term "effective amount" therefore does not render the claims of the '282 patent fatally indefinite.

Defendant is correct that the effective amount of granisetron to be delivered may vary among patients and underlying causes of emesis, e.g., acute emesis v. delayed emesis. Nonetheless, the '282 patent is not without reasonably certain guidance. For example, the specification describes the administration of granisetron in 1 mg oral dosage form twice a day provides average peak plasma levels of 6 ng/ml and clearance values of 0.52 L/hr./kg. ('282 patent at 5:26-39.) The '282 patent indicates that, for a 60-kg patient, a flux of about 190 µg/h from a transdermal patch would be sufficient to maintain levels of 6 ng/ml, although such levels may exceed the amount required to effectively treat emesis. (*Id*.) The specification further teaches that intravenous infusion of granisetron of only 40 µg/hr. has been shown to alleviate delayed emesis in cancer patients, indicating drug plasma levels as low as approximately 1.5 ng/ml may be sufficient. (*Id*. at 5:40-47.) Accordingly, when reviewed in context, a person of skill would understand that an effective amount of granisetron in the patch is an amount that provides an average blood plasma level of between 1.5 ng/ml and 6 ng/ml, amounts which were previously shown to be efficacious.

The specification provides further guidance on granisetron loading amounts and patch size, stating: "In general, at a loading of about 6% w/w granisetron, it has been found that a suitable size patch is between 10 and 100 cm^2, more preferably between 15 and 50 cm^2, with a patch of around 40 cm^2 generally providing the equivalent plasma level of a tablet containing 1 mg of

granisetron." (*Id*. at 6:43-47; *see also Id*. at 6:6-21.) The basis of this observation is the experimental data provided in Example 3, which discloses that granisetron mean blood plasma levels of 1.9 ng/mL over a 5-day period where achieved in healthy human volunteers using a patch of the invention containing 6% w/w granisetron and having a surface area of 15 cm^2, and that a slightly larger patch would deliver appropriate levels of granisetron for optimum efficacy. (*Id*. at 10:40-11:50.)

Overall, the specification explains appropriate loading ranges for granisetron, techniques for determining blood plasma levels, comparatives of oral and intravenous plasma levels previously known to be effective for treatment, and various patch sizes for delivery. In light of the teachings in the specification, the Court concludes that the amount of granisetron in the transdermal patch of the invention providing a physiologically effect amount can be readily determined by a person of skill in the art. *Geneva Pharms., Inc.*, 349 F.3d 1373, 1383-1384 (Fed. Cir. Nov. 21, 2003) ("'effective amount' is not ambiguous or indefinite, provided that a person of ordinary skill in the art could determine the specific amounts without undue experimentation."); *Takeda Pharm. Co. v. Mylan Inc.*, 2014 U.S. Dist. LEXIS 159527, *38 (N.D. Cal. Nov. 11, 2014) ("To the extent Mylan argues that the specification must disclose all variables for formulating a precise dosage form to avoid indefiniteness, that is not the law."). Accordingly, the term "a physiologically effective amount" in claim 1 is not indefinite.

3. "incorporating no plasticizers or permeation enhancers"

Plaintiffs' Proposed Construction	**Defendant's Proposed Construction**
Prostrakan submits that a person of ordinary skill in the art would understand the scope of this claim term in view of the words of the claims themselves, as well as the intrinsic record, and background knowledge possessed by a person of ordinary skill in the art. Thus,	"no plasticizers or permeation enhancers are added during development of the patch"

Plaintiffs submit that this term should have its plain and ordinary meaning as understood by a person of ordinary skill in the art. If the Court believes this term requires construction, the Court should construe this term to mean "lacking chemical compounds that function as a plasticizer or a permeation enhancer.	

Court's Construction: *The term "incorporating no plasticizers or permeation enhancers" has its plain and ordinary meaning, which is "[a patch] that does not contain plasticizers or permeation enhancers."*

During the Claim Construction Hearing of June 22, 2017, the parties agreed to the Court's preliminary construction. (Dkt. No. 61, at 6:4-6.) Having reviewed the intrinsic evidence, the Court does not find that the '282 patent uses the term "incorporating no plasticizers or permeation enhancers" in a manner inconsistent with its plain and ordinary meaning, and construes the term as having its plain and ordinary meaning, which, within the context of the claim, is "[a patch] that does not contain plasticizers or permeation enhancers."

III. CONCLUSION

The Court adopts the constructions above for the disputed terms of the '282 patent and holds that the Defendant has failed to prove claim 1 is invalid as indefinite. Furthermore, the parties should ensure that all testimony that relates to the terms addressed in this Order is constrained by the Court's reasoning.

SIGNED this 15th day of July, 2017.

ROY S. PAYNE
UNITED STATES MAGISTRATE JUDGE