UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF NEW JERSEY

AMAG PHARMACEUTICALS, INC., Plaintiff/Counterclaim-Defendant, v. SANDOZ, INC., Defendant/Counterclaim-Plaintiff.	)	Civil Action No: 16-cv-1508 (PGS)(LHG) **MEMORANDUM AND ORDER**

SHERIDAN, U.S.D.J.

This matter comes before the Court on Joint Claim Construction submitted by Amag Pharmaceuticals, Inc. ("AMAG" or "Plaintiffs") and Sandoz, Inc. ("Sandoz" or "Defendant") pursuant to L. Pat. R. 4.3 (see D.I. 38).

In order to market and sell pharmaceutical drug Feraheme®, AMAG has listed the following U.S. Patents—6,599,498 (the "'498 patent); 7,553,479 (the "'479 patent); 7,871,597 (the "'597 patent"); 8,591,864 (the "'864 patent"); and 8,926,947 (the "'947 patent") (collectively "Patents-in-Suit")—in Food and Drug Association's ("FDA") Approved Drug Products with Therapeutic Equivalence Applications, commonly known as the Orange Book. See 21 U.S.C. § 355(B)(1). Feraheme® is used to treat iron deficiencies in people with chronic kidney disease.

Thereafter, Sandoz filed an Abbreviated New Drug Application ("ANDA") with the FDA in order to seek approval to market a generic version of Feraheme®. See 21 U.S.C. § 355(j)(1). Accordingly, pursuant to 21 U.S.C. § 355(j)(5)(B)(iii), AMAG initiated this suit against Sandoz because Sandoz's request to market the generic version of Feraheme® was done prior to the expiration of the Patents-in-Suit.

On April 26-27, 2017, pursuant to L. Pat. R. 4.6, a Markman hearing was conducted before the Court for multiple claim terms recited in the Patents-in-Suit. These terms are construed below.

BACKGROUND

Feraheme® (ferumoxytol) is an FDA approved pharmaceutical drug approved for the use of treating iron deficiencies in people with chronic kidney disease ("CKD"). Feraheme® is administered either as a bolus or as an intravenous solution. (See the '498 patent, col. 3, ll. 17-19 and 29).

I. THE PATENT FAMILY

Amongst the Patents-in-Suit, the '498 patent is the parent patent as it issued from the first-filed patent application. The '479 and '597 patents claim priority to the '498 patent as their respective patent applications are continuation-in-part patent applications of the '498 patent.[1] As such, the disclosure of the '479 and '597 patents include additional subject matter that is not disclosed in the '498 matter.

Further, the patent application of the '864 patent is a continuation application[2] of the U.S. Patent 8,501,158, whose patent application is a divisional application[3] of the '597 patent. As such, the disclosure of the '864 patent is the same as the disclosure of the '597 patent because no new

[1] See Manual of Patent Examining Procedure ("MPEP") 201.08 ("A continuation-in-part application is an application filed during the lifetime of an earlier nonprovisional application, repeating some substantial portion or all of the earlier nonprovisional application and adding matter not disclosed in the earlier nonprovisional application.").

[2] See MPEP 201.07 ("A continuation application is an application for the invention(s) disclosed in a prior-filed co-pending non-provisional application […]. The disclosure presented in the continuation must not include any subject matter which would constitute new matter if submitted as an amendment to the parent application.").

[3] See MPEP 201.07. ("A later application for an independent or distinct invention, carved out of a nonprovisional application […] is known as a divisional application.").

matter is added to the ’864 patent. Likewise, the ’947 patent shares the same disclosure as the ’864 and ’597 patent because it is a continuation application of the ’864 patent.

In short, the three patents with three distinct, non-overlapping, disclosures are—the ’498 patent, the ’479 patent, and the ’597 patent. The disclosures of the ’864 and ’947 patents are the same as the ’597 patent.

II. THE ’498 PATENT

A. Disclosure of the ’498 Patent

The ’498 patent is directed towards pharmaceutical compositions that are used for providing enhanced magnetic resonance imaging (“MRI”) of a patient’s internal organs, such as liver, spleen, or lymph nodes, during an MRI scan. The compositions are imaging agents that comprise carboxyalklayed reduced polysaccharides coated ultra-small superparamagnetic iron oxides. (See Abstract of the ’498 patent).

The ’498 patent identifies that the conventional contrast agents are distributed into two classes of imaging agents—namely, low molecular weight gadolinium complexes such as Magnevist® and colloidal iron oxides. The conventional contrast agents face the following problems—expense, inefficiency, loss of coating of sterilized agent by autoclaving, narrow range of organ uptake for purposes of imaging. (Id. at col. 1, ll. 25-35). During the autoclaving process, for example, the polymer coating becomes dissociated from the iron oxide cores due to exposure to heat. The polymer dissociation results in functional consequences, such as, physical changes in the material (i.e., clumping), bio-distribution changes (i.e., changes in plasma half-life), and changes in toxicity profile (i.e., potential increases in adverse events). (Id. at col. 7, ll. 60-65).

In order to mitigate dissociation of the coating from the iron oxide when the material is subject to heat stress, the ’498 patent discloses a method for the synthesis of a colloid of an iron

oxide that is associated with a water soluble polysaccharide coating. (Id. at col. 10, ll. 30-35). The term "heat stress" being defined as "heating the colloid to approximately 121°C or higher for about 30 minutes at neutral pH […] that are well known in the art to autoclave (or terminally sterilize) an injectable drug." (Id. at col. 10, ll. 35-40).

In an example embodiment, the '498 patent discloses that a coated colloid may be prepared by adding a polysaccharide to an iron oxide sol (a colloidal dispersion in a liquid). Wherein the term "colloid" includes "any macromolecule or particle having a size less than about 250 nm [(nanometer)]". The iron oxide polysaccharide colloids of the invention have improved physical characteristics and manufacturability such as ability to withstand heat stress and show less evidence of polysaccharide dissociation under stress. (Id. at col. 11, ll. 5-20).

The colloids of the '498 patent can be used as contrast agents for MRI scanning or in other applications such as magnetic fraction of cells, immunoassays, magnetically targeted drug delivery, and as therapeutic injectable iron supplements. (Id. at col. 11, ll. 40-45). In particular, the colloids are suited for parenteral administration because the final sterilization is autoclaving. Autoclaving being a preferred method because it eliminates viability of all cellular life forms including bacterial spores and viruses. (Id. at col. 11, ll. 45-50).

Accordingly, the improvements provided in these colloids that can be used as contrast agents over the prior art include—(i) heat sterilization by autoclaving that optimizes long-term storage at ambient temperatures; (ii) being non-toxic to mammals, including humans, at higher doses; and (iii) ability to obtain additional images during a single clinical visit and use of the imaging apparatus due to successive doses being administered after a brief interval after administration of a first dosage. (Id. at col. 11, ll. 60-67—col. 12, ll. 1-5).

According to the various example embodiments, the ’498 patent discloses that a reduced polysaccharide iron oxide complex or a derivatized reduced polysaccharide iron oxide complex, which is a reduced polymer of glucose, is produced by sterilizing the same by autoclaving. An example of a reduced polymer of glucose is a reduced dextran. (Id. at col. 2, ll. 1-15). In another example embodiment, the ’498 patent discloses that a complex such as a reduced derivatized polysaccharide iron oxide complex may be stable at a temperature of at least approximately 100°C or 121°C. (Id. at col. 5-20).

The ’498 patent includes a total of 26 claims, wherein claims 1, 13, 23 and 25 are independent claims. Claims 1 and 23 being method claims and claims 13 and 25 being product claims.

B. Prosecution History of the ’498 Patent

i. Applicant’s Arguments/Remarks filed October 9, 2001.

In its response to the July 5, 2001 non-final Office action, the Applicant responded by arguing that none of the cited references disclosed a “reduced polysaccharides” or “carboxyalkylated polysaccharides” such as reduced carboxymethylated dextran as required in then pending claims 1-13, 18-29-35-36, 39-52 and 57-66. (See Image File Wrapper[4] of the ’498 Patent; Applicant’s Arguments/Remarks at 6-7, filed October 9, 2001). Additionally, with respect to a particular reference cited against the claimed invention, Applicant argued that there was no disclosure of autoclavability of the MRI contrast agents. (Id. at 8). With respect to then claims 18-20 and 29, the Applicant argued that the methods and compositions are “stable after autoclaving, with respect to certain physical and chemical properties (e.g., stability at particular elevated

[4] See Manual of Patent Examining Procedure (“MPEP”), Section 719 (“The electronic file record in which the U.S. Patent and Trademark Office maintains the application papers is referred to as an image file wrapper. The electronic file record is the official record of the [patent] application.”); available at https://portal.uspto.gov/pair/PublicPair.

temperatures, or stability of colloidal suspensions without aggregation)," which were not disclosed by any of the prior art references. (Id. at 9).

Further, in the same response, in order to distinguish the claimed invention over the cited art, the Applicant equates the term "complex" to "polysaccharide," by arguing that "Golman et al. neither teaches nor suggests autoclaving, either of a polysaccharide or of a complex." (Id. at 11).

ii. Applicant's Arguments/Remarks filed April 25, 2002.

Next, in response statements made on April 25, 2002, the Applicant noted that preamble "for administration to a mammalian subjection," would be understood by one of ordinary skill in the art to mean that "the iron oxide complex must have an acceptable profile with respect to stability and risk of adverse reaction, and if the mammal is a human, must typically be approved by a regulatory authority such as the Food and Drug administration." (See Applicant's Arguments/Remarks at 4, filed April 25, 2002). Further, in order to distinguish over the cited art, the Applicant primarily relies on an affidavit of one of the co-inventors of the '498 patent.

Pursuant to 37 C.F.R. § 1.132, in support of its response, the Applicant submitted an affidavit of Dr. Jerome Lewis. Dr. Lewis is a co-inventor of polysaccharide superparamagnetic iron oxide complexes and related materials and methods. (Id. at Declaration of Jerome Lewis ("Decl. of Lewis") at ¶ 1). Dr. Lewis noted that from a regulatory and commercial perspective, to have a "polysaccharide superparamagnetic iron oxide complex as a pharmaceutical that when terminally sterilized (autoclaved) does not form particulates and that has minimal edematous response." (Id. at ¶ 3). Terminal sterilization (autoclaving) being favored over filter sterilization because—(i) terminal sterilization provides a much higher level of sterility assurance; and (ii) their opaque nature prevents ordinary visual inspection by the physician during administering the drug, thereby making terminal sterilization more desirable. (Id. at ¶¶ 4-5 (internal citations omitted)).

In his declaration, Dr. Lewis provides a background on the development of these types of pharmaceutical drugs. In particular, he notes that the drug disclosed in the present application is a third generation drug. The two previous generation drugs had issues. The first generation drug was Feridex® disclosed in U.S. Patent 4,827,945. The material used in Feridex® had issues such as particulate formulation and adverse reactions such as edematous response (i.e., accumulation of an excessive amount of watery fluid in cells, tissues, or body cavities). (Id. at ¶ 7). The second generation drug being Combidex®, a complex of ultra-small particles. This drug is filtered by a process of filtration, instead of terminal sterilization, at the time it is administered to the patient. The risks with this drug being—edematous response, administration of the material only after dilution, and slow administration.

Unlike the first and second generation drugs, this third generation drug, which is a complex of ultra-small particles and has a favorable bio-distribution, has sufficiently small risk of particulate formulation such that no filtration is required during administration. (Id. at ¶¶ 7-9). And, because of low risk of adverse reaction, the drug disclosed in the ’498 patent can be administered more rapidly and without dilution. (Id. at ¶ 10). In short, Dr. Lewis notes that the new material disclosed in the ’498 patent is sterilized using the autoclaving method. And, unlike the conventional drugs, Combidex® and Feridex®, the new material does not require filtration during administration, no dilution, no slow administration, and no edematous response. Accordingly, noting that such properties are commercially and medically desirable in an iron based colloidal MRI contrast agent. (Id. at ¶ 11).

In distinguishing the third generation agent disclosed in the ’498 patent from the conventional drugs, Dr. Lewis states that “autoclaving normally requires temperatures of at least 121 degrees [C] (see, for example, Exhibit C), and in any event at least 115 degrees C.” (Id. at ¶

15). Dr. Lewis notes that the material disclosed in the prior art references, noted in the Office action dated November 2, 2001, namely, Lewis and Groman references, are autoclaved in the presence of citrate. Doing so has a risk of particulate formulation requiring administration through a filter, and an adverse reaction risk requiring dilution and slow administration. (Id. at ¶ 15). In other words, the cited references fail to teach anything about creating a material without degradation or decreased risk of adverse reactions. (Id.)

Under the section titled "Consideration of Certain Terms in the Patent Application," Dr. Lewis notes, "[i]n the present invention, the reduced polysaccharide is a poly alcohol compound; thus, it contains multiple OH groups. All the OH groups are functional groups and thus potential reactive sites to form derivatives of the original compound." (Id. at ¶ 16). With respect to "ultrasmall" term, Dr. Lewis relied on a publication to define this term as a new class of contrast agents "small enough to migrate across the capillary wall, a prerequisite in the design of targetable particulate pharmaceuticals." (Id. at ¶ 19 (internal citations omitted)).

In support of Dr. Lewis' declaration, Applicant submits multiple exhibits to the Patent Office. One of these exhibits, Exhibit D, is entitled "European Pharmacopoeia, 3rd Edition, 1997." Exhibit D states, "[s]terility is the absence of viable micro-organisms […] [which] is assured by the application of a suitably validated production process." As such, failure to follow a meticulously validated process involves the risk of a non-sterile product or of a deteriorated product. Wherever possible, "a process in which the product is sterilized in its final container (terminal sterilization) is chosen." For terminal sterilization, it is essential to take into account the non-uniformity of the physical and chemical conditions within the sterilizing chamber. By establishing a terminal sterilization process, knowledge of its performance in routine use is gained

wherever possible, by monitoring and suitably recording the physical and chemical conditions achieved within the load in the chamber throughout each sterilizing cycle.

Additionally, attached Exhibits H and I, note that ultrasmall superparamagnetic iron oxide (USPIO) are small enough to migrate across the capillary wall, a prerequisite in the design of targetable particulate pharmaceuticals. As such, the applications of USPIO being—(i) used as an intravenous contrast agent for the lymphatic system, (ii) a bone marrow contrast agent, (iii) a long-half-life perfusion agent for brain and heart, and (iv) the magnetic moiety in organ-targeted superparamagnetic contrast agents for magnetic resonance imaging. (Id. at Exhibit I, "Radiology").

iii. Applicant's Arguments/Remarks filed June 4 2002, October 8, 2002 and November 13, 2002.

With respect to the remarks filed June 4, 2002, no significant comments were made by the Applicant.

However, with respect to the remarks filed October 8, 2002, the Applicant noted "[t]he change in claims such as 53 and 54 from 'colloid' to 'complex' is intended to be a broadening amendment; similar language already appeared in numerous claims." (See Applicant's Arguments/Remarks at 6, filed October 8, 2002). Additionally, Dr. Lewis' attached declaration notes that the material in the patent application of the '498 patent employs a synthetic method that "does not require a reflux step or centrifugation. And the resulting material falls apart upon autoclaving – i.e., heating at 121°C for 30 min. does not result in an increase in particulate formulation." (Decl. of Lewis at ¶ 11, dated September 25, 2002). In addition, Dr. Lewis notes that his experimental data indicates that such "autoclaved materials are stable (as measured by no increase in particulate level per mL of material) for up to 3 years." (Id. at ¶ 12).

Whereas, in the remarks filed November 13, 2002, Applicant again noted that the changing of claim terms from "colloid" to "complex" is intended to be a broadening amendment.

iv. Notice of Allowance mailed on January 22, 2003.

Under the reasons for allowance, the Examiner noted that the claimed subject matter was novel and nonobvious because the prior art references did not disclose—(i) a reduced carboxyalkylated polysaccharide iron oxide complex wherein the complex is stable at a temperature of about 121°C; and (ii) a method of providing an iron oxide complex for administration to a mammalian subject consisting of producing a carboxyalkylated reduced polysaccharide iron oxide complex and sterilizing the complex by autoclaving. The Examiner further noted that the declaration filed by Dr. Lewis on October 8, 2002, was sufficient and persuasive to overcome the prior art references because the material disclosed in the prior art was "not stable upon autoclaving (heating at 121 C for 30 minutes)," unlike the material of the patent application of the '498 patent.

III. THE '479 PATENT

A. Disclosure of the '479 Patent

The Court notes that the patent application for the '479 patent is a continuation-in-part patent application for the patent application for the '498 patent. As such, a substantial portion of the disclosure in the '479 patent is recited in the '498 patent. (See supra fn. 1).

Based on a review of the disclosure of the '479 patent, additional disclosure regarding the colloid particles is made in the '479 patent. The '479 patent explains that unlike the conventional drugs, Combidex® and Feridex®, the colloid particles disclosed in this patent application show less evidence of polysaccharide dissociation under stress, and exhibiting no appreciable change in size. The '479 patent identifies the shortcomings with the conventional drugs such as loss of dextran

coating when subjected to heat stress, increase in particle diameter size, and clumping of material. (See the ’479 patent, col. 11, ll. 5-20).

The ’479 patent discloses an improved method of administration, which comprises injection of an autoclaved reduced polysaccharide iron oxide complex in a volume of 15 mL or less. In another aspect of the embodiment the injected volume is injected as a bolus. (See the ’479 patent, col. 3, ll. 20-25).

The ’479 patent includes two (2) claims wherein claim 1 is in independent form, and is directed to a pharmaceutical composition in a vial. Claim 1 of the ’479 patent, unlike the claims of the ’498 patent, recites carboxymethylated dextran iron oxide complex, which comprises at least 750 micromole and less than 1500 micromole of carboxyl groups per gram of dextran. (See the ’479 patent, col. 38, ll. 25-30).

B. Prosecution History of the ’479 Patent

i. Applicant’s Arguments/Remarks filed December 14, 2006.

In responding to the rejections set forth in the outstanding Office action issued by the patent examiner, the Applicant argued, “[w]hether a composition, or in this case a complex, is terminally sterilizable – i.e. autoclavable – depends on the chemical composition of the disclosed complex, it does not describe a purpose or intended use.” (See Applicant’s Arguments/Remarks at 9, filed December 14, 2006). The Applicant further states that “[a]utoclavability is a physical property that reflects a chemical property and thus chemical composition.” (Id. at 10).

The Applicant further notes that the term “terminally sterilizable” also “adds patentable weight to the claimed iron oxide composition, because not all reduced carboxyalkylated polysaccharide iron oxide complexes are terminally sterilizable and stable at temperatures of at least 100°C.” As such, the term “terminally sterilizable” imparts essential chemical structure via

this physical property because a composition that is "terminally sterilizable" is chemically different from one that is not. (Id. at 10). The Applicant argued that they have developed "unexpectedly and surprisingly" developed a process that prepares reduced carboxyalkylated polysaccharide iron oxide complexes that can be autoclaved without precipitating or degrading.

In support of its arguments, the Applicant submitted a declaration by one of the inventors', Dr. Jerome Lewis. Generally, the declaration of Dr. Lewis submitted with the Applicant's remarks was substantially similar to the declaration by Dr. Lewis in the '498 patent.

ii. Applicant's Arguments/Remarks filed February 23, 2007.

In its remarks, the Applicant addressed indefiniteness rejections under 35 U.S.C. § 112, first paragraph by making certain amendments. Next, the Applicant addressed obviousness rejection by asserting that the cited art failed to disclose "an injectable complex in a vial that is stable at a temperature of about 100°C, or an injectable complex in a vial that is terminally sterilizable (autoclavable) within the vial." (See Applicant's Arguments/Remarks at 4, filed February 23, 2007).

iii. Applicant's Arguments/Remarks filed May 4, 2007.

In its remarks, relying on the declaration by Dr. Lewis and Dr. Timothy Frigo, the Applicant argued that unlike the conventional drugs, PCU-USPIO iron oxide complex, showed an insignificant change in size upon autoclaving. (See Applicant's Arguments/Remarks at 5, filed May 4, 2007). Dr. Timothy Frigo is an assignee of the '479 patent and one of the senior scientists who prepared and analyzed the substances disclosed in this patent. Dr. Frigo's declaration indicates that the size of PCU-USPIO after autoclaving did not change drastically, as it did for the conventional drugs. (See Declaration of Dr. Frigo ("Decl. of Frigo) at ¶¶ 10-11, filed May 4, 2007).

iv. Notice of Allowance mailed on April 10, 2009.

In its reasons for allowance, the Examiner indicated that the claimed subject matter is patentable over the cited art because the compositions disclosed in the references are not stable when subjected to autoclaving. As such, the compositions in the claimed subject matter do "not form into a gel or form substantial particulates and remains clear and can be micro-filtered." (See Notice of Allowance at 3, mailed on April 10, 2009).

IV. THE '597 PATENT

A. Disclosure of the '597 Patent

The '597 patent is directed towards administrating an effective amount of a pharmacological composition that uses an iron oxide complex with a polyol or polyether. The complex is formulated in a biocompatible liquid that provides minimal detectable free iron in a subject and minimal incidence of anaphylaxis (i.e., allergic reaction). (See the '479 patent, col. 2, ll. 5-10). The '479 patent notes that unlike the existing iron oxide complexes, polyol or polyether iron oxide complexes disclosed herein, when administered parenterally to a patient for use as a pharmacological agent, provides minimal detectable free iron and anaphylaxis in a patient. (Id. at col. 11, ll. 15-20).

Accordingly, the improvement comprising that of parenteral administration to a mammalian subject of an effective dose of the complex formulated in a biocompatible liquid delivered at a rate substantially greater than 1 mL/min. (Id. at col. 3, ll. 40-45). The method of administration comprising—injection of an autoclaved reduced polysaccharide iron oxide complex in a volume of 15 mL or less. (Id. at col. 6, ll. 60-67).

Further, this patent notes that four of the conventional types of iron oxide compounds used as MRI contrast agents and/or hematinic agents (i.e., agents for increasing the amount of

hemoglobin in the blood) have serious drawbacks. (Id. at col. 15, ll. 45-65 and col. 16, ll. 1-25). Accordingly, the embodiments of the ’597 patent are directed to polyol or polyether iron oxide complex, when administered to a patient, provides both minimal detectable free iron in a subject and minimal anaphylaxis in a patient. For example, as discussed in examples 6 and 7 and examples 8 and 9 of the ’597 patent. (Id. at col. 19, ll. 45-50). The polyol or polyether iron oxide complex of the ’597 patent are administered parenterally by bolus injection at a dosage of from about 1 mg to about 4 mg of iron/kg of body weight. (Id. at col. 26, ll. 30-35).

The ’597 patent identifies autoclave or terminally sterilize as synonyms. (Id. at col. 10, ll. 65-67). “Terminal sterilization (autoclaving) is a preferred method of sterilizing drugs for injection.” (Id. at col. 13, ll. 4-5). “These colloids are particularly suited to parenteral administration, because the final sterilization typically is autoclaving, a preferred method since it eliminates viability of all cellular life forms including bacterial spores, and viruses.” (Id. at col. 18, 35-40).

In example 62, the ’597 patent discloses that following autoclaving for 30 minutes at 121˚C, USPIO coated with reduced dextran maintained its small size. Whereas, USPIO coated with native dextran increased in size 28-fold following autoclaving. (Id. at col. 45, ll. 35-45). Additionally, a second type of increased stability was achieved by use of reduced dextran to coat USPIO is the property of pH of the bulk solvent. (Id. at col. 45, ll. 50-55). The data in both Tables 12 and 13 show that the particles coated with reduced dextran had significantly improved pH stability upon autoclaving, compared to those coated with native dextran. As such, the effect of autoclaving on pH, size, and bound polysaccharide of colloids coated with native and reduced dextran was observed. (Id. at col. 45, ll. 55—col. 46, ll. 1-30).

An example embodiment disclosed in the ’597 patent is that of a method that comprises mixing the polyol, reduced polysaccharide, or polyether with iron salts in an acidic solution selected from the group comprising ferric salts, ferrous salts, or a mixture of ferrous and ferric salts, cooling the solution, neutralizing the solution with a base, and recovering the coated iron oxide colloid. (Id. at col. 17, ll. 30-35). Cooling the solution to 5°C as noted in example 5 or cooled to a room temperature as noted in example 36. (Id. at col. 25, ll. 40-45; col. 37, ll. 25-35).

B. Prosecution History of the ’597 Patent

i. Applicant’s Arguments/Remarks filed July 3, 2006.

In responding to the rejections set forth in the outstanding Office action, the Applicant argued that the claimed subject matter is directed to ‘pharmacological compositions,’ which requires a composition that will be acceptable for use in humans. That is, the aforementioned term informs a person of ordinary skill in the art that the iron oxide complex must have an acceptable profile with respect to stability and risk of adverse reaction in humans. (See Applicant’s Arguments/Remarks at 7, filed July 3, 2006). Applicant further goes onto indicate that those skilled in the art recognize that in the art of contrast agents, use of terminal sterilization (autoclaving) over filter sterilization is preferred because terminal sterilization provides a much higher level of sterility assurance. (Id. at 7). As such, being desirable to have polyol/polyether superparamagnetic iron oxide complex as pharmacological composition that is capable of being autoclaved and that can be administered after autoclaving to provide minimal detectable free iron and minimal incidence of anaphylaxis. (Id. at 8).

The Applicant further identifies that the drug disclosed in the patent application is better than the conventional drugs, Combidex® and Feridex®, because it has a sufficiently small risk of particulate formulation after autoclaving that no filtration is required during administration of the

drug. Thereby, providing minimal free iron to the subject upon administration. And, the risk of adverse reaction is lower compared to the conventional drugs, which results in more rapid administration of this new drug without dilution. (Id. at 9).

Next, the Applicant argues that the prior art cited did not disclose a pharmacological composition that is "capable of being parenterally administered (composition), or actually administered (method), at a rate substantially greater than 1mL/min." (Id. at 11). Further, the Applicant argues that the reduced carboxyalkylated polysaccharide iron oxide complexes claimed in the instant application can be autoclaved, and the claims require that they be autoclaved or autoclavable. (Id. at 14).

ii. Applicant's Arguments/Remarks filed January 29, 2007.

In support of its remarks, Applicant submitted a declaration of Dr. Lewis, one of the inventors of this patent. In order to distinguish over the cited art, the Applicant amended the claims to include claim term "autoclavable" in the body of the claim in order to give patentable weight to this claim term. The Applicant asserted that "[a]utoclavability is a physical property that reflects a chemical property and thus limits the chemical composition." (See Applicant's Arguments/Remarks at 8, filed January 29, 2007). And, because not all reduced carboxyalkylated polysaccharide iron oxide complexes are autoclaved and thus stable, the term "autoclavable" adds patentable weight. (Id. at 9). Dr. Lewis points out that that the "distinguishing property of the complexes of the present application compared to the previous generation complexes Feridex and Combidex, and the [reference] Maruno EP compound, is autoclavability." (Id. at 10).

iii. Applicant's Arguments/Remarks filed May 18, 2007.

In support of its remarks, Applicant submitted a declaration of Dr. Timothy Frigo, an assignee and one of the senior scientists who prepares and analyzes the substances disclosed in the

this patent. Dr. Frigo noted that PSC-USPIO proprietary iron oxide complex showed an insignificant change in size upon autoclaving. (See Applicant's Arguments/Remarks at 7-8, filed May 18, 2007).

iv. Applicant's Arguments/Remarks filed December 4, 2007.

In support of its remarks, the Applicant submitted a declaration of Dr. Frigo. In differentiating the claimed invention over the cited art, the Applicant asserted that the disclosure of "free flowing" with regard to complexes A and B in prior art reference Maruno, is not proof of autoclaving. The Applicant cites to paragraph 13 of Dr. Frigo's declaration and argues that the use of filter sterilization in Maruno confirms that complexes in the cited art cannot be autoclaved. (See Applicant's Arguments/Remarks at 7-8, filed December 4, 2007).

In short, the Applicant, relying upon the declaration of Dr. Frigo, essentially argued that the complexes disclosed in the prior art references do not anticipate the claimed invention because the complexes disclosed deteriorate before autoclaving. As such, one of ordinary skill in the art would not rely on the complexes disclosed in the cited art to be autoclavable. (Id. at 9-10).

v. Applicant's Arguments/Remarks filed September 26, 2008.

In its remarks, the Applicant, in differentiating over the cited art, argued, "[o]f particular interest, the claim for that patent covered a composition very similar to Applicants' own compositions – namely, a complex of dextran with an iron compound. […] A composition comprising a substantially nonionic complex of ferric hydroxide with a dextran having an average intrinsic viscosity […]." (See Applicant's Arguments/Remarks at 8, filed September 26, 2008).

vi. Applicant's Arguments/Remarks filed August 14, 2009.

In responding to the outstanding Office action, the Applicant argued that the cited art of Maruno EP "gives no information about how to make a complex that is autoclavable […]. The

declaration of Dr. Timothy Frigo, filed herein on December 4, 2007, reports specifically on his synthesis of the foregoing complexes 3, 5, and 7, and reports that none of them are stable [for] autoclaving." (See Applicant's Arguments/Remarks at 7-8, filed August 14, 2009; citing Decl. of Frigo at ¶ 4). In paragraph 4 of Dr. Frigo's declaration, he notes that "[o]f these six complexes, the only ones disclosed as stable at 80°C by Maruno are the three shown in Maruno EP, Table 7 (complexes 3, 5 and 7) […]." And, the Maruno EP reference, EP 0450092, discloses, in-part, as follows—

> "Processes for preparing complexes of the invention from the foregoing polysaccharide carboxyalkyl ethers and magnetic metal oxides can roughly be classified into the following two processes. Namely, the first process is a process which comprises first preparing an aqueous sol or suspension containing magnetic metal oxide particles which will be the core of the complex, and subjecting it to reaction with a carboxyalkyl ether of a polysaccharide. The second process is a process which comprises mixing a divalent metal salt, a trivalent metal salt and a base with stirring in an aqueous system in the presence of a polysaccharide carboxyalkyl ether to progress reaction."

(See Maruno EP at p. 4, ll. 41-46). Accordingly, the Applicant asserted that the cited art does not disclose complexes that are autoclavable or are stable to autoclaving.

vii. Notice of Allowance mailed on September 10, 2010.

Under its reasons for allowance, the Examiner noted that Maruno EP is the closest prior art reference to the claimed invention. Further, the Examiner explained that the claimed invention is patentable over the cited art because "Applicants have shown that their compositions as claimed are stable to autoclaving, meaning that it does not form into a gel or form substantial particulates and remains clear and can be micro-filtered. On the other hand, the complexes of Maruno [EP] showed degredation, an increase in the number and size of particulates and could not be micro-filtered after autoclaving thus proving that Applicants complexes are different from Maruno's [EP] complexes." (See Notice of Allowance at 3, mailed on September 10, 2010).

LEGAL STANDARD

"It is a 'bedrock principle' of patent law that 'the claims of a patent define the invention to which the patentee is entitled the right to exclude.'" Phillips v. AWH Corp., 415 F.3d 1303, 1312 (Fed. Cir. 2005) (en banc) (quoting Innova/Pure Water Inc. v. Safari Water Filtration Sys., Inc., 381 F.3d 1111, 1115 (Fed. Cir. 2004)). Claim construction determines the correct claim scope, and is a determination exclusively for the court as a matter of law. Markman v. Westview Instruments, Inc., 52 F.3d 967, 978-79 (Fed. Cir. 1995) (en banc), *aff'd*, 517 U.S. 370 (1996). The focus in construing disputed terms in claim language "is on the objective test of what one of ordinary skill in the art at the time of the invention would have understood the term[s] to mean." Id. at 986.

To determine the meaning of the claims, courts start by considering the intrinsic evidence. Phillips, 415 F.3d at 1313; C.R. Bard, Inc. v. U.S. Surgical Corp., 388 F.3d 858, 861 (Fed. Cir. 2004); Bell Atl. Network Servs., Inc. v. Covad Comms. Group, Inc., 262 F.3d 1258, 1267 (Fed. Cir. 2001). The intrinsic evidence includes the claims themselves, the specification, and the prosecution history. Phillips, 415 F.3d at 1314; C.R. Bard, Inc., 388 F.3d at 861.

The claims themselves provide substantial guidance in determining the meaning of particular claim terms. Phillips, 415 F.3d at 1314. First, the context in which a term is used in the asserted claim can be very instructive. Id. Other asserted or non-asserted claims can aid in determining the claim's meaning because claim terms are normally used consistently throughout a patent. Id. Differences among claims can also assist in understanding a term's meaning. Id. For example, when a dependent claim adds a limitation, there is a presumption that the independent claim does not include that limitation. Id. at 1314-15.

"[C]laims 'must be read in view of the specification of which they are a part.'" Id. at 1315 (quoting Markman, 52 F.3d at 979). "[T]he 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.'" Id. (quoting Vitronics Corp. v. Conceptronic, Inc., 90 F.3d 1576, 1582 (Fed. Cir. 1996)). This is true because a patentee may define his own terms, give a claim term a different meaning than the term would otherwise possess, or disclaim or disavow the claim scope. Id. at 1316. In these circumstances, the inventor's lexicography governs. Id. The specification may also resolve the meaning of ambiguous claim terms "where the ordinary and accustomed meaning of the words used in the claims lack sufficient clarity to permit the scope of the claim to be ascertained from the words alone." Teleflex, Inc. v. Ficosa N. Am. Corp., 299 F.3d 1313, 1325 (Fed. Cir. 2002). But, "[a]lthough the specification may aid the court in interpreting the meaning of disputed claim language, particular embodiments and examples appearing in the specification will not generally be read into the claims." *Comark Commc'ns, Inc. v. Harris Corp.*, 156 F.3d 1182, 1187 (Fed. Cir. 1998) (quoting Constant v. Advanced Micro-Devices, Inc., 848 F.2d 1560, 1571 (Fed. Cir. 1988)); also see Phillips, 415 F.3d at 1323 ("although the specification often describes very specific embodiments of the invention, we have repeatedly warned against confining the claims to those embodiments.").

The prosecution history is another tool to supply the proper context for claim construction. It "can often inform the meaning of the claim language by demonstrating how the inventor understood the invention and whether the inventor limited the invention in the course of prosecution, making the claim scope narrower that it would otherwise be." Phillips, 415 F.3d at 1317.

"Extrinsic evidence consists of all evidence external to the patent and prosecution history, including expert and inventor testimony, dictionaries, and learned treatises." Markman, 52 F.3d at 980. Although extrinsic evidence can be useful, it is "less significant than the intrinsic record in determining 'the legally operative meaning of claim language.'" Phillips, 415 F.3d at 1317 (quoting C.R. Bard, Inc., 388 F.3d at 862).

Dictionaries and treatises may aid a court in understanding the underlying technology and the manner in which one skilled in the art might use claim terms, but dictionaries and treatises may provide definitions that are too broad or may not be indicative of how the term is used in the patent. Id. at 1318. Similarly, expert testimony may aid a court in understanding the underlying technology and determining the particular meaning of a term in the pertinent field, but an expert's conclusory, unsupported assertions as to a term's definition are entirely unhelpful to a court. Id.

Generally, extrinsic evidence is "less reliable than the patent and its prosecution history in determining how to read claim terms." Id. The Supreme Court recently explained the role of extrinsic evidence in claim construction:

> In some cases, however, the district court will need to look beyond the patent's intrinsic evidence and to consult extrinsic evidence in order to understand, for example, the background science or the meaning of a term in the relevant art during the relevant time period. . . . In cases where those subsidiary facts are in dispute, courts will need to make subsidiary factual findings about that extrinsic evidence. These are the "evidentiary underpinnings" of claim construction that we discussed in Markman, and this subsidiary fact finding must be reviewed for clear error on appeal.

Teva Pharm. USA, Inc. v. Sandoz, Inc., 135 S.Ct. 831, 841 (2015).

Overall, in construing the claims, "[t]he judge's task is not to decide which of the adversaries is correct. Instead, the judge must independently assess the claims, the specification, and if necessary the prosecution history […], and declare the meaning of the claims." Exxon Chem. Patents, Inc. v. Lubrizol Corp., 64 F.3d 1553, 1556 (Fed. Cir. 1995).

ANALYSIS

Now, the Court will construe the claim terms listed in the Patents-in-Suit.

A. "COMPLEX"

AMAG's Proposed Construction	Sandoz's Proposed Construction
Plain and ordinary meaning: "substance formed by the association of two or more substances."	"a macromolecule or particle having indeterminable chemical structure made through specific synthetic parameters and having particular physiochemical properties, which include: (i) it is autoclavable without the addition of excipients such as citrate and low-molecular weight sugars (e.g., mannitol), (ii) the desired particle size is achieved at outset during synthesis, without any filtration, centrifugation, or other reduction step, (iii) it may be safely administered as a bolus or IV push, and (iv) it provides an acceptable profile with respect to risk of adverse reaction upon administration, including minimal incidence of anaphylaxis and minimal incidence of free iron"

Representative claim 1 of the '498 patent recites,

1. A method of providing an iron oxide **complex** for administration to a mammalian subject, the method consisting of:
   producing a carboxyalkylated reduced polysaccharide iron oxide complex; and
   sterilizing the complex by autoclaving.

AMAG asserts that "complex" should be construed to mean a "substance formed by the association of multiple substances," because such definition is supported by intrinsic evidence and it is a common chemistry term with a well-understood meaning. (See Pl.'s Br. at 9; D.I. 48). AMAG cites to col. 4, ll.35-43 of the '498 patent to assert that when "viewed in context of the whole specification, a person of ordinary skill would understand the term 'complex' refers to a substance (the disclosed iron oxide complex) formed by association of multiple substances (iron

oxide and a polysaccharide)." (Id. at 10); also see Markman Hearing Transcript, April 26, 2017 ("Trans.") at 30:6-11).

Further, AMAG asserts that Sandoz's proposed construction should be rejected because it imports numerous limitations about the specific synthetic parameters that are used to make the iron oxide complex identified in the specification and the prosecution history. Thereby improperly importing specific preferred embodiments into the claims. (Id. at 10-11; citing Kara Tech. Inc. v. Stamps.com Inc., 582 F.3d 1341, 1347-48 (Fed. Cir. 2009) ("The claims, not specification embodiments define the scope of patent protection.")). In addition, AMAG argues that Sandoz's disavowal argument, discussed below, should be not considered because the statements made by Dr. Lewis during the prosecution of the Patents-in-Suit describe the unexpected results of the claimed iron oxide "complex," and not define the full scope of the term "complex." (Id. at 14). Because the Applicants never argued that the term "complex" be limited to something with those particular properties or results, the term "complex" should not be limited with those particular properties or results, as proposed by Sandoz. (Id.).

During the Markman hearing, AMAG's counsel pointed out that Sandoz's proposed construction should not be adopted because the features recited in their proposed construction are already recited in claim 1 of the '597 patent. (See Trans. at 31:7-14 ("And our position simply is if all of these are separately called out in the claim, why would you read them into the word complex.").

In contrast, Sandoz sets forth a detailed argument as to why each of its proposed limitations should be incorporated into the definition of "complex." With respect to the limitation—"a macromolecule or particle having indeterminable chemical structure made through specific synthetic parameters and having particular physiochemical properties"—Sandoz relies on the

Applicant's statements made during the prosecution of the Patents-in-Suit in order to differentiate over the cited art, Maruno reference (EP 0450092). Sandoz indicates that the Applicants, on behalf of AMAG, repeatedly made statements differentiating their claimed complex from the complex disclosed in Maruno based on—(i) different and specific synthetic parameters, (ii) different resulting properties, and (iii) different chemical structures resulting in different chemical compositions. (See Def.'s Br. at 6-8; D.I. 46). As such, Sandoz holds the position that the aforementioned limitation should be incorporated in defining the term "complex."

Next, with respect to the limitation—"autoclavable without the addition of excipients such as citrate and low-molecular weight sugars (e.g., mannitol)"—Sandoz again relies on the statements made by the Applicants during the prosecution history, in which the Applicants argued that the "presence of excipients during autoclaving frequently leads to changes in the nature of the complex, which increases the risk of adverse reaction." (Id. at 9 (internal citations omitted)). In addition, the Applicants described the claimed complex being able to heat sterilized without using excipients like mannitol and citrate as part of autoclaving or subsequent storage processes. (Id.). As such, based on the intrinsic evidence, Sandoz holds the position that the aforementioned limitation directed to the autoclaving should be incorporated in defining the term "complex."

Next, with respect to the limitation—"the desired particle size is achieved at outset during synthesis, without any filtration, centrifugation, or other reduction step"—Sandoz again relies on the statements made by the Applicants during the prosecution history of the '498 patent. During prosecution of the '498 patent, the Applicants indicated the following—

> "In contrast [to Maruno], **the presently claimed material** (see in particular Example 31, p. 36 of the Application) can be prepared without any filtration or centrifugation step at all. Our disclosed synthetic method produces a very narrow size range of ultrasmall particles **having the desired particle size from the outset without any filtration or need to limit the particle size below a specific diameter. Our synthetic method does not require a reflux step or centrifugation.**"

(Id. at 10 (internal citations omitted)). Sandoz asserts that the aforementioned argument made by the Applicants is evidence that the specific example embodiments (example 31), relied upon to differentiate the claimed invention over the cited art, are to be incorporated when defining "complex." As such, based on the intrinsic evidence, Sandoz argues that the aforementioned limitation directed to the process steps should be incorporated in defining the term "complex."

Next, with respect to the limitation—"may be safely administered as a bolus or IV push"—Sandoz relies on the disclosure of the Patents-in-Suit and the prosecution history to assert that the aforementioned limitation should be incorporated into the term "complex." In particular, Sandoz cites to the following statement made by the Applicants, on behalf of AMAG—

> "[T]he claims require that **the pharmacological composition must be capable of being parenterally administered** (composition), **or actually administered** (method), **at a rate substantially greater than 1 mL/min** (with dependent claims requiring a rate of about 1 mL/sec)."

(Id. at 10 (internal citations omitted)). Sandoz asserts that based on the intrinsic evidence, a skilled artisan would understand that a complex that could not be safely administered as a rapid bolus is chemically different from AMAG's complex, and as such was disclaimed by AMAG. (Id. at 11).

Lastly, with respect to the limitation—"provides an acceptable profile with respect to risk of adverse reaction upon administration, including minimal incidence of anaphylaxis and minimal incidence of free iron"—Sandoz relies on the intrinsic evidence to assert that the aforementioned limitation should be incorporated in defining the term "complex." Sandoz relies on the following statement made during prosecution of the Patents-in-Suit—

> "In contrast [to the complexes of Maruno], **the presently claimed pharmacological compositions are a brilliant and nonobvious improvement** over Maruno **because** they are autoclavable, **can be safely administered to provide minimal detectable free iron and minimal incidence of anaphylaxis**, at a fast rate of substantially greater than 1 mL/min, and as fast as even 1 mL/sec."

(Id. at 12 (internal citations omitted)). Sandoz asserts that recitation of "minimal incidence of anaphylaxis" and "free iron" are structural properties of the claimed complex; and as such should be incorporated into the claim term "complex."

During the Markman hearing, Sandoz's counsel essentially argued with respect to the claim term "complex" that the statements made by AMAG during the prosecution history are AMAG's own representations, which AMAG should be held accountable for. (See Trans. at 56 at 19-23 ("And all we're asking the Court again is to hold them to their own representation.")).

The Court notes that the prosecution history is relevant intrinsic evidence, but the Court's 2005 en banc Phillips opinion reduced the importance to be given to the file history, as it represents an "ongoing negotiation" between the Applicant and the Patent & Trademark Office ("PTO") rather than a final product. Phillips, 415 F.3d at 1317. The Federal Circuit cases broadly state that an Applicant's statements to the PTO characterizing its invention may give rise to a prosecution disclaimer. Hockerson-*Halberstadt, Inc. v. Avia Group Int'l, Inc.*, 222 F.3d 951, 957 (Fed. Cir. 2000). For a prosecution disclaimer inquiry, "we examine the entire prosecution history." *Seachange Int'l, Inc. v. C*-COR Inc., 413 F.3d 1361, 1372 (Fed. Cir. 2005).

"Regardless of the examiner's motives, arguments made during prosecution shed light on what the applicant meant by its various terms." E.I. du Pont de Nemours & Co. v. Phillips Petroleum Co., 849 F.2d 1430, 1438 (Fed. Cir. 1988). In Uship Intellectual Properties, LLC, the Court noted that the "applicant's argument persuaded the examiner, who noted in the ensuing Office Action that the restriction requirement was overcome. From this exchange, a competitor would reasonably conclude that the applicant clearly and unmistakably limited all of the method claim steps to performance by an automated shipping machine […]." Uship Intellectual Properties, LLC v. U.S., 714 F.3d 1311, 1316.

The definition of a claim term can be affected through "repeated and definitive remarks." Computer Docking Station Corp. v. Dell, Inc., 519 F.3d 1366, 1374 (Fed. Cir. 2008). For example, in InTouch Technologies, Inc., the Court ruled that repeatedly explaining a "call back mechanism" during the prosecution made it clear as to what was meant by this term. InTouch Technologies, Inc. v. VGO Communications, Inc., 751 F.3d 1327, 1341-42 ("The prosecution history of the '357 patent removes any remaining doubt that the call back mechanism requires a message to a specific user that requested and was denied access."). Similarly in Saffran, the Court found the claimed invention to be limited in scope based on the statements made by the patentee to distinguish the claimed invention over a prior art reference. Saffran v. Johnson & Johnson, 712 F.3d 549, 559 (Fed. Cir. 2013).

Based on the case law, and the intrinsic evidence brought before the Court, the Court does not find AMAG's proposed construction to suffice the true meaning of "complex." In light of the statements made by the Applicants, on behalf of AMAG, one skilled in the art, such as a competitor, would not define the term "complex" to mean a "substance formed by the association of two or more substances." As such, the Court rejects AMAG's proposed construction.

Now, the Court considers Sandoz's proposed construction for this term. As correctly pointed out by AMAG, Sandoz's proposed construction does have issues, and as such should not be adopted in its entirety. For example, the term "indeterminable chemical structure," as recited in Sandoz's proposed construction is ambiguous and vague. By defining "complex" to mean an "indeterminable" structure would not only be unclear to one skilled in the art, but would also run counter to the intrinsic evidence as the intrinsic evidence appears to indicate the particle size and the chemical structure of the iron oxide complex.

Further, the Court takes issue of certain process steps introduced into Sandoz's proposed claim construction, such as—"specific synthetic parameters," "autoclavable," and "without any filtration, centrifugation, or other reduction step."

The Court recognizes that during the prosecution of the Patents-in-Suit, the Applicant repeatedly made assertions that the "complex" recited in the claimed invention was different from the complex recited in the Maruno reference because the claimed "complex" was—(i) autoclavable, (ii) had different and specific synthetic parameters, (iii) had different resulting properties, and (iv) had different chemical structures and compositions. (See Def.'s Br. at 9-10; D.I. 46). The Court agrees with AMAG's assertion that introduction of these features in defining "complex" introduces process steps in defining a product. (See Pl.'s Br. at 12; D.I. 47). "Even though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. In addition, statements made regarding specific example embodiments from the specification (example 31) during prosecution are generally not introduced into the claim language itself. Augme Technologies, Inc. v. Yahoo! Inc., 755 F.3d 1326, 1340 (Fed. Cir. 2014) ("Yahoo!'s discussion of an embodiment did not amount to lexicography or disavowal").

In addition, Sandoz's proposed construction with respect to "safely administered as a bolus or IV push," is directed to an intended use, which are generally not given patentable weight. (See MPEP 2111; In re Sinex, 309 F.2d 488, 492 (CCPA 1962) (statement of intended use in an apparatus claim did not distinguish over the prior art apparatus)).

Lastly, with respect to the recitation of "provides an acceptable profile with respect to risk of adverse reaction upon administration," is directed to a resultant effect, and does not define the structure of the "complex" itself.

The Court does note that the prosecution of the Patents-in-Suit contain repeated and definitive remarks regarding "complex," and as such affect the scope of this claim term. Based on the intrinsic evidence presented, the Court determines that one skilled in the art would define the term "complex" to mean—"a macromolecule or particle configured to be autoclavable without the addition of excipients such as citrate." The Court finds support for this construction in the prosecution history of the '498 patent, where Dr. Lewis argued that autoclaving in the presence of citrate, as done in the prior art references Lewis and Groman, resulted in a risk of particulate formulation. (See the '498 patent, Applicant's Arguments/Remarks filed April 25, 2002).

Accordingly, the claim term "complex" is defined—"a macromolecule or particle configured to be autoclavable without the addition of excipients such as citrate."

B. "COLLOID"

AMAG's Proposed Construction	Sandoz's Proposed Construction
"Any macromolecule or particle having a size less than about 250 nm."	"a mixture comprising any macromolecule or particle of the complex of the present invention having a size less than about 250 nanometers dispersed through a second substance"

Representative claim 4 of the '864 patent recites,

> 4. A pharmacological composition comprising:
> an autoclaved **colloid** comprising particles of a superparamagnetic iron oxide coated with a carboxymethylated reduced dextran, the reduced dextran having an average molecular weight of about 10 kDa; and
> a biocompatible liquid, wherein the particles in the autoclaved **colloid** having a diameter between about 10 nm and about 50 nm.

The Court notes that the ’864 patent is a continuation of the ’597 patent, and as such the ’864 patent shares the same disclosure as the ’597 patent. And, wherein the ’597 patent is a continuation-in-part of the ’498 patent. (See supra fn. 2, 3).

AMAG asserts that its proposed definition should be adopted because it is consistent with the definition provided in the specification of the ’864 patent. As its own lexicographer, the inventor defined “colloid” to mean “any macromolecule or particle having a size less than about 250 nm [nanometer].” (See Pl.’s Br. at 16, fn. 22; D.I. 47, (citing the ’864 patent at 11:15-17 (‘“Colloid’ […] shall include any macromolecule or particle having a size less than about 250 nm [nanometer].”)).

AMAG asserts that Sandoz’s proposed construction should not be adopted because the specification never describes “colloid” as a mixture comprising of a macromolecule and a particle, and that it is contrary to the definition recited in the specification. (See Pl.’s Br. at 17).

In contrast, Sandoz asserts that in reading the specification of the ’864 patent, one skilled in the art would understand that “macromolecule or particle having a size less than about 250 nm” is a reference to the complex of the alleged invention, which is dispersed through a second substance or phase. (See Def.’s Br. at 23; D.I. 46). During the Markman hearing, Sandoz’s counsel added that when interpreting the term “colloid” in claim 4, we look at the claim itself, which recites “an autoclaved colloid comprising two things […] and a biocompatible liquid.” Sandoz’s counsel further noted that because claim 4 is directed to a mixture of particle of the complex, which is dispersed through a second substance. (See Trans. 84: 6-13).

Here, the Court finds Sandoz’s position persuasive in-part. Sandoz is correct in noting that in interpreting “colloid,” we look at the claim itself. Here, claim 4 is directed to a pharmacological composition, which comprises of two things—(i) an autoclaved colloid, and (ii) a biocompatible

liquid. The structure of the autoclaved colloid is further limited or defined by "particles of a superparamagnetic iron oxide coated with a carboxymethylated reduced dextran."

In other words, "colloid" comprises of superparamagnetic iron oxide particles that are coated with a carboxymethylated reduced dextran. As such, based on a plain and ordinary reading of claim 4, it would be apparent to one of ordinary skilled in the art that "colloid" does not include a mixture as argued by Sandoz. Instead, the "colloid" simply consists of a single particle or macromolecule.

The Court recognizes that "colloid" is defined in the specification of the '864 patent to mean, "any macromolecule or particle having a size less than about 250 nm [(nanometer)]". (See the '864 patent at 11:15-17).

However, incorporating a limitation from the specification into a claim is improper. SciMed Life Sys. Inc. v. Advanced Cardiovascular Sys. Inc., 242 F.3d 1337, 1340 (Fed.Cir.2001) (reading a limitation from the specification into a claim is "one of the cardinal sins of patent law."). As such, the Court does not construe "colloid" to mean "having a size less than about 250 nm." Instead, based on a reading of the claims and intrinsic evidence, the Court defines "colloid" to mean—"a macromolecule or a particle."

C. "STABLE"

AMAG's Proposed Construction	Sandoz's Proposed Construction
"does not form into a gel or form substantial particulates and remains clear and can be micro-filtered"	Indefinite. Alternatively: "retaining the same chemical, physical, microbiological, therapeutic, and toxicological properties and characteristics"

Representative claim 12 of the '498 patent recites,

> 12. A reduced polysaccharide iron oxide complex produced according to the method of claim 1, wherein the produced complex is **stable** at a temperature of at least 100° C.

Sandoz asserts that the claim term "stable" as recited in the claims of the Patents-in-Suit is indefinite because it is not precise enough to afford a skilled artisan of what properties define stability. That is, a carbohydrate chemist may understand this term to mean physical and chemical properties of a complex's polymer coating, whereas a nephrologist may understand this term to mean therapeutic and toxicological properties of the complex upon administration. (See Def.'s Opening Br. at 21 (internal citations omitted); D.I. 46). As such, because this term is not capable of informing those skilled in the art about the scope of the invention with reasonable certainty, the term "stable" is definite. (Id.)

Generally, "a patent is invalid for indefiniteness if its claims, read in light of the specification delineating the patent, and the prosecution history, fail to inform, with reasonable certainty, those skilled in the art about the scope of the invention." Nautilus, Inc. v. Biosig Instruments, Inc., 572 U.S. 134 S.Ct. 2120, 2124 (2014).

Here, Sandoz, along with AMAG, has tabled the indefiniteness argument for a later proceeding—after the Court construes the term "stable." (See Trans. at 108:4-9 ("[T]he parties have agreed that we're going to push indefiniteness down to either the summary judgment phase of the case or at trial.").

"To determine whether [a] claim at issue is indefinite, we look at the patent record […] to ascertain if they convey to one of skill in the art with reasonable certainty the scope of the invention claimed." Teva Pharmaceuticals USA, Inc. v. Sandoz, Inc., 789 F.3d 1335, 1341 (Fed. Cir. 2015). "The purpose of claim construction is to 'determin[e] the meaning and scope of the patent claims

asserted to be infringed.'" O2 Micro Intern. Ltd. v. Beyond Innovation Technology Co., Ltd., 521 F.3d 1351, 1359 (Fed. Cir. 2008) (citing Markman, 52 F.3d at 976).

Granted, submission of a proposed construction for a claim term does not amount to a waiver of a later indefiniteness challenge. Leader Technologies, Inc. v. Facebook, Inc., 770 F.Supp.2d 686, 706 (D. Del. 2011) (internal citations omitted). However, construing the term "stable" at the present time is futile because the Court would be delving into the same inquiry at a later proceeding. Undertaking claim construction of this term is apt for a later time, after the Court has reviewed and considered the indefiniteness arguments by the parties.

Accordingly, at the present time, the Court does not construe the term "stable" recited in the Patents-in-Suit.

D. "AUTOCLAVING" AND "TERMINALLY STERILIZING"

i. "Autoclaving"; "Autoclaved" and "Autoclavable"

AMAG's Proposed Construction	Sandoz's Proposed Construction
Plain and ordinary meaning, which is "heating or sterilizing under pressure and steam for a period sufficient to eliminate the viability of all microorganisms" Plain and ordinary meaning, which is, "able to withstand autoclaving." Plain and ordinary meaning, which is "having undergone autoclaving."	"autoclaving": "employing an autoclave sterilization process, such that the postautoclaved material: (i) does not form substantial particulates (size or quantity), (ii) does not form a gel, (iii) remains clear, (iv) can be micro-filtered, and (v) maintains therapeutic efficacy and adequate safety with respect to risk of adverse reaction (including minimal incidence of anaphylaxis) for its intended purpose or administration" "autoclavable": "able to withstand autoclaving" "autoclaved": "having undergone autoclaving"

The representative claim for the patent term "autoclaving," is claim 1 of the '498 patent, which recites:

1. A method of providing an iron oxide complex for administration to a mammalian subject, the method consisting of:
producing a carboxyalkylated reduced polysaccharide iron oxide complex; and
sterilizing the complex by **autoclaving**.

ii. "TERMINALLY STERILIZING" AND "TERMINALLY STERILIZABLE"

AMAG's Proposed Construction	Sandoz's Proposed Construction
Plain and ordinary meaning, which is "sterilizing a substance in its final container" "terminally sterilizable": "able to withstand terminally sterilizing"	"terminally sterilizing": "employing an autoclave sterilization process of a material in its final, sealed container which results in a composition that is capable of administration" "terminally sterilizable": "able to withstand terminally sterilizing"

The representative claim for the patent term "terminally sterilizing," is claim 23 of the '498 patent recites, which recites:

23. A method of providing a hematinic agent for treating a subject deficient in iron, consisting of the steps of:
formulating a composition which is a carboxymethylated reduced ultrasmall iron oxide complex; and
terminally sterilizing the composition by autoclaving.

AMAG and Sandoz agree that the derivative terms "autoclaved" and "autoclavable" should be construed to mean "having undergone autoclaving" and "able to withstand [or capable of withstanding] autoclaving," respectively. (See Pl.'s Opening Br. at 20, fn. 30; D.I. 47, citing Joint Claim Construction and Prehearing Statement; D.I. 38 at 28—29; also see Trans. 90:14-18).

Similarly, the parties agree that "terminally sterilizing" and the derivative term "terminally sterilizable" should be construed as "able to withstand terminally sterilizing." (See Pl.'s Opening

Br. at 23, fn. 36; D.I. 47, citing Joint Claim Construction and Prehearing Statement; D.I. 38 at 39; also see Trans. 125:10-11 ("And the parties largely agree as to the definition of terminally sterilizable")).

The parties agree that "autoclaving" or autoclave sterilization process involves—"heating or sterilizing under pressure and steam for a period sufficient to eliminate the viability of all microorganisms." (See Pl.'s Opening Br. at 21, fn. 32 (citing Sandoz's Invalidity Contentions at 29—32); also see Def.'s Opening Br. at 15; D.I. 46); also see Trans. 90:25—91:1-4 ("There's not a dispute that what autoclaving is to heat something up in a wet high pressure temperature, and that's the way as Mr. Razoczy [Sandoz's counsel] said previously you kill the microorganisms. There's not a dispute [] that's the common meaning of autoclave."); also see Trans. 92:17-20 ("There's agreement that Sandoz agrees with AMAG that an autoclave sterilization process involves "heating or sterilizing under pressure and steam for a period sufficient to eliminate the viability of all microorganisms.'").

However, Sandoz argues that based on the intrinsic evidence, "a skilled artisan would understand the post-autoclaved material (i.e., the complex) to possess [certain] characteristics." (See Def.'s Opening Br. at 15; D.I. 46; also see Trans. 98:21-23 ("the process of autoclaving and it changes the material [complex]"); Trans. 100:12-15 ("property of autoclavability")). These characteristics of the post-autoclaved material being—(i) not forming substantial particulates (size or quantity); (ii) not forming a gel; (iii) remaining clear; (iv) able to be micro-filtered; (v) able to maintain therapeutic efficacy and adequate safety with respect to anaphylaxis. (See Def.'s Opening Br. at 15-16).

Sandoz asserts that one skilled in the art would construe the term "autoclaving" to mean these aforementioned characteristics because in the prosecution history of the Patents-in-Suit,

AMAG differentiated the post-autoclaved material from the cited art based on the material's characteristics (i.e., size, quantity, efficacy, etc.). (Id. at 16; citing prosecution history of the '498 patent, the '479 patent, and the '597 patent). As such, one skilled in the art would understand the term "autoclaved" to include the aforementioned characteristics.

In contrast, AMAG argues that Sandoz's proposed construction seeks to import structural characteristics with regards to the material—the iron oxide complex—which are unrelated to the term "autoclaving" itself. (See Pl.'s Reply Br. at 20; D.I. 53). As such, AMAG maintains that the term "autoclaving" should be given its plain and ordinary meaning, and additional limitations proposed by Sandoz should not be incorporated into this term.

The '498 patent discloses that the final sterilization process for the colloids of the '498 patent is autoclaving, which is a preferred method because it eliminates viability of all cellular life forms including bacterial spores and viruses. (See the '498 patent, col. 11, ll. 45-47). The agents that are embodiments of the present invention are heat sterilized by autoclaving, and thus optimized for long-term storage at ambient temperatures. Thereby, these agents, inter alia, maintain stability during the sterilization or storage process, and are non-toxic to mammals at higher doses. (See Id. at col. 11, ll. 60—col. 12, ll. 5). The "heat stress" being defined as heating the colloid to approximately 121°C, or higher for about 30 minutes at neutral pH, or other combinations of time, temperature, and pH that are known in the art to autoclave an injectable drug. (Id. at col. 10, ll. 35-40).

During prosecution of the '498 patent, in response to an Office action, the Applicant provided a declaration from Dr. Jerome Lewis, a co-inventor on the '498 patent. In his declaration, Dr. Lewis stated that "autoclaving normally requires temperatures of at least 121 degrees [C] (see, for example, Exhibit C), and in any event at least 115 degrees C." (See the '498 patent, Applicant's

Arguments/Remarks at 4, filed April 25, 2002). In the notice of allowance, the patent examiner noted that Dr. Lewis's Declaration was sufficient and persuasive to overcome the prior art because the material in the prior art was "not stable upon autoclaving (heating at 121°C for 30 minutes)," unlike the material in the '498 patent. (See the '498 patent, Notice of Allowance mailed on January 22, 2003).

Based on the intrinsic evidence, the Court does not find Sandoz's proposed claim construction persuasive. The additional characteristics provided in Sandoz's proposed construction—i.e., size and quantity of the particulates; lack of gel formation; maintaining therapeutic efficacy and adequate safety, etc.—pertain to the material of the iron oxide complex. Not to the process of autoclaving.

These characteristics cannot pertain to "autoclaving" because autoclaving requires taking a series of actions or steps in order to achieve a particular end. Granted, during prosecution the Applicant made remarks pertaining to the physical and chemical properties of the material, and how it is stable after autoclaving. (See the '498 Patent; Applicant's Arguments/Remarks at 6-7, filed October 9, 2001). However, these characteristics do not pertain to a series of actions or steps. Instead, these characteristics pertain to the end product of the material that has been subjected to autoclaving.

As such, the Court does not find Sandoz's proposed construction persuasive as it incorporates limitations from the prosecution history that pertain to the material, the iron oxide complex, and not the process of autoclaving.

Absent incorporation of the aforementioned characteristics, the Court adopts in-part the agreed upon definition between the parties. The agreed upon definition between the parties includes characteristics of time and temperature to achieve the desired result—the elimination of

the viability of all microorganisms. This language of the proposed construction is consistent with the intrinsic evidence. (See the ’498 patent, col. 10, ll. 35-40 (“heating the colloid to approximately 121°C, or higher for about 30 minutes at neutral pH, or other combinations of time, temperature, and pH that are known in the art to autoclave an injectable drug”); also see the ’498 patent, Applicant’s Arguments/Remarks at 4, filed April 25, 2002 (“autoclaving normally requires temperatures of at least 121 degrees [C] (see, for example, Exhibit C), and in any event at least 115 degrees C.”)).

However, in addition to the proposed definition of “autoclaving,” the Court finds that the definition of “autoclaving” should also include “a material in a final container.” This language is adopted in-part from the proposed construction of the term “terminally sterilizing” or “terminally sterilizable.” (See Trans. 126:12-15 (“Also the prosecution history, in Dr. Lewis' declaration submitted on January 27th, 2007, in paragraph 7 states that terminal sterilization in the final container is preferred.”)).

The Court relies on the proposed construction of the aforementioned terms because the intrinsic evidence dictates that the terms “autoclaving” and “terminally sterilizing” are synonyms. ((See the ’498 patent, col. 10, ll. 40-41 (“autoclave (or terminally sterilize) an injectable drug”); also see the ’498 patent, Applicant’s Arguments/Remarks filed April 25, 2002 (“Terminal sterilization (autoclaving) being favored over filter sterilization.”); also see the ’597 patent, col. 13, ll. 4-5 (“Terminal sterilization (autoclaving) is a preferred method of sterilizing drugs for injection.”); also see the ’597 patent, Applicant’s Arguments/Remarks at 7, filed July 3, 2006 (“use of terminal sterilization (autoclaving) over filter sterilization is preferred because terminal sterilization provides a much higher level of sterility assurance”); also see Trans. 126:1-6 (“And the intrinsic record makes clear that sterilization takes place or terminal sterilization takes place in

the final container. For instance in the '498 patent at column 7, lines 53 through 54, the patent states: Terminal sterilization (autoclaving) is a preferred method of sterilizing drugs for injection.")).

Throughout the prosecution history and specification of the Patents-in-Suit, AMAG used the terms autoclave and terminal sterilization interchangeably. Often denoting and referring them to mean the same. By reciting these terms as "autoclave (or terminally sterilize)" or "terminal sterilization (autoclaving)," without providing further distinguishing characteristics or features between the two terms, the Court finds the terms "autoclaving" and "terminally sterilizing" to have the same scope and meaning. In other words, these terms are construed to be synonyms. (See Trans. 127:23—128:1 ("if the autoclaving or autoclavable was already in the claim[,] there is no need to include it in the construction in the term terminally sterilizing."). By reciting these terms interchangeably, it is evident that any "autoclaving" being done to the material is being done when the material is in a final container, which is capable of being injected into a subject.

The Court notes that Sandoz's claim construction recites "final, sealed container" as opposed to AMAG's construction, which simply recites "final container." The '498 patent does disclose a 5ml glass vial being sealed. (See the '498 patent, col. 25, ll. 1-3 and ll. 28-29). However, the Court does not incorporate the term "sealed" in construing the aforementioned terms for two reasons.

First, "sealed" container is only one example disclosed in examples 30 and 31. (See the '498 patent, col. 24, ll.50—col. 25, ll. 30). By incorporating the same in the claims, the Court would be excluding the other disclosed examples in the specification. See Phillips, 415 F.3d at 1323 (recognizing that the embodiments in a patent often are examples meant to teach a person of

ordinary skill in the art how to make and use the invention, but should not be construed to limit the invention only to a specific embodiment).

Second, including the term "sealed" into the claim language would require importing limitations from the specification into the claim, which is one of the cardinal sins of patent law. SciMed Life Sys. Inc. v. Advanced Cardiovascular Sys. Inc., 242 F.3d 1337, 1340 (Fed.Cir.2001) (reading a limitation from the specification into a claim is "one of the cardinal sins of patent law."). As such, the Court does not incorporate the term "sealed," as proposed by Sandoz, into the claim language.

Accordingly, the Court defines the terms "autoclaving" and "terminally sterilizing" to mean the same, which is— "heating or sterilizing a material in a final container under pressure and steam for a period sufficient to eliminate the viability of all microorganisms in the material."

E. "Injectable"; "Intended for administration by injection"

AMAG's Proposed Construction	Sandoz's Proposed Construction
Plain and ordinary meaning, which is "capable of being injected into a patient."	"injectable": "capable of injection from the vial directly into a mammalian subject without further sample preparation"; "intended for administration by injection": "injectable," as defined above

Representative claim 1 of the '479 patent,

1. A pharmaceutical composition in a vial comprising an **injectable** reduced carboxymethylated dextran iron oxide complex, wherein the carboxymethylated reduced dextran comprises at least 750 micromole and less than 1500 micromole of carboxyl groups per gram of dextran and wherein said complex is stable at a temperature of at least about 100°C.

Initially, the Court notes that that the claim term "injectable," recited in claim 1 of the '479 patent, and the claim term "intended for administration by injection," recited in claim 1 of the '947 patent, essentially mean the same. (See Trans. 152:10-14 ("There doesn't seem to be a dispute that intended for administration by injection is the same as injectable, so we're construing these claims together.")). In other words, construing the term "injectable" would in effect the construe the term "intended for administration by injection." As such, now, the Court will define the term "injectable."

AMAG argues that the claim term "injectable" should not be construed to mean additional terms such as "from the vial directly into a mammalian subject without further sample preparation," as proposed by Sandoz, because such construction is contrary to the plain and ordinary meaning. Moreover, AMAG asserts that Sandoz's reliance on Dr. Frigo's statements during prosecution of the Patents-in-Suit is improper because Dr. Frigo's statements were limited to distinguishing the complexes of the present invention from those disclosed in the prior art references. That is, Dr. Frigo's statements centered around complexes of prior art not being stable when autoclaved, unlike complexes of the present invention. (See Pl.'s Br. at 26, D.I. 47).

In contrast, Sandoz asserts that claim 1 of the '479 expressly recites, inter alia, "[a] pharmaceutical composition in a vial comprising an injectable reduced carboxmethylated dextran iron oxide complex […]." The pharmaceutical composition "in a vial" being "injectable," thereby requiring direct injection from a vial with further preparation. (See Def.'s Br. at 27; D.I. 46). In support, Sandoz asserts that during prosecution, AMAG repeatedly confirmed that direct injection from a vial without further sample preparation is a unique attribute to the invention, which allows for "superior administration profiles," compared to prior art complexes. As such, asserting that

one skilled in the art would understand "injectable" to mean "capable of injection from the vial directly into a mammalian subject without further sample preparation." (Id. at 28).

When reading claim 1 of the '479 patent, the Court determines that claim 1 is essentially directed to a pharmaceutical composition in a vial. Wherein the pharmaceutical composition comprises a reduced carboxymethylated dextran iron oxide complex. This complex being "injectable" from the vial. For example, the injected volume of the complex being injected as a bolus. (See the '479 patent, col. 3, ll. 25-26). The '479 patent notes that advantages of multiple bolus injections, within a single examination, being that any deficiencies in an imaging can be corrected. (Id. at col. 36, ll. 32-35).

The Court notes that Sandoz's proposed construction has two issues. First, the term "directly," proposed by Sandoz, is not recited in the '479 patent with reference to the injection of the complex from the vial. The only recitation of "directly" in the '479 patent is with respect to a mixture that is used "directly in the preparation of USPIO [Ultrasmall superparamagnetic iron oxide]." As such, the Court notes that Sandoz's proposed construction of "directly" in construing "injectable" is improper and is not supported by intrinsic evidence.

Second, and lastly, "without further sample preparation," recites a negative limitation that is also unsupported by the specification. Generally, for a negative limitation to be recited in a claim language, the specification should expressly recite the negative limitation. (See MPEP 2173.05(i) "Negative Limitation" (Any negative limitation or exclusionary proviso must have basis in the original disclosure.")). Here, the '479 patent does not expressly recite or have basis for such a negative claim limitation. As such, incorporating such a limitation can lead to indefinite issues under 35 U.S.C. 112, second paragraph.

The term "injectable," which modifies the complex recited in claim 1 of the '479 patent, should be given its plain and ordinary meaning. However, the Court does note that recitation of terms "patient" or "mammalian" to define "injectable" are not required because recitation of whom the pharmaceutical composition is administered is directed to intended use, which generally is not given patentable weight. (See MPEP 2111; In re Sinex, 309 F.2d 488, 492 (CCPA 1962) (statement of intended use in an apparatus claim did not distinguish over the prior art apparatus)).

Accordingly, the terms "injectable" and "intended for administration by injection," are construed to mean—"capable of being injected."

F. "ADMINISTRATION" & "ADMINISTERING PARENTERALLY"

i. "Administration"

AMAG's Proposed Construction	Sandoz's Proposed Construction
Plain and ordinary meaning, which is "giving of a pharmacological agent"	Plain and ordinary meaning, "to deliver into a subject"

With respect to the claim term "Administration," the representative claim is claim 1 of the '597 patent, which recites—

> 1. A unit dosage of a pharmacological composition comprising a terminally sterilizable autoclavable reduced carboxymethylated dextran iron oxide complex composition which is stable at 121 C and is prepared,
>
> in a total volume of biocompatible liquid from about 1 mL to about 15 mL and for a total single dose from about 50 mg to about 600 mg, the pharmacological composition capable of being parenterally administered to a subject at a rate substantially greater than 1 mL/min and wherein the unit dosage provides upon **administration**:
>
> minimal detectable free iron in the subject; and
>
> minimal incidence of anaphylaxis.

ii. **"Administering Parenterally"; "Parenterally Administered"**

AMAG's Proposed Construction	Sandoz's Proposed Construction
Plain and ordinary meaning, which is "giving of a pharmaceutical agent by a means other than through the alimentary canal"	Plain and Ordinary meaning "administering parenterally": "delivering into a subject's body by a means other than through the alimentary canal" "parenterally administered": "delivered into a subject's body by a means other than through the alimentary canal"

With respect to the claim term "Administering Parenterally" and "Parenterally Administered," the representative claim is claim 1 of the '597 patent, which recites—

> 1. A unit dosage of a pharmacological composition comprising a terminally sterilizable autoclavable reduced carboxymethylated dextran iron oxide complex composition which is stable at 121 C and is prepared,
>
> in a total volume of biocompatible liquid from about 1 mL to about 15 mL and for a total single dose from about 50 mg to about 600 mg, the pharmacological composition capable of being **parenterally administered** to a subject at a rate substantially greater than 1 mL/min and wherein the unit dosage provides upon administration:
>
> minimal detectable free iron in the subject; and
>
> minimal incidence of anaphylaxis.

With respect to the aforementioned patent claim terms, the parties agree that they dispute only as to the term "administration." (See Trans. 136:18—137:1 ("the parties agree that the construction or the meaning of the term parenterally in the dispute for that related term is […] the parties have nothing additional to talk about with respect to parenterally administering other than, you know, the definition of administration."); also see Trans. 137:19-21 ("There's really only just one dispute here, it's whether the term administration requires delivery into a subject.")). As such,

based on the agreement between the parties as to the disputed issue, the Court is going to limit its claim construction to the term "administration."

AMAG argues that "administration" should be construed to mean "giving a pharmacological agent" because claims and specification of the '498 recites the aforementioned term to provide a composition containing the disclosed iron oxide complex to a mammalian subject. (See AMAG's Br. at 27-28; Dkt. No. 47; citing the '498 patent at col. 1:66—2:1, 3:23-59, 36:44—46; also see Trans. 136:9-17).

In contrast, Sandoz asserts that the aforementioned term should be interpreted to mean "to deliver into a subject" because an administration can only occur by actual delivery into a subject as there is detection of free iron in the subject and incidence of anaphylaxis, as required by the claim language. (See Trans. 138:7-10 ("the only way that administration can occur […] if it's delivered into a subject."). During the Markman hearing, Sandoz's counsel cited AstraZeneca, wherein the Court stated that "a person of ordinary skill in the art would understand the term administration to refer to the means of delivering the medication to an individual." AstraZeneca AB v. Hanmi USA, Inc., 2012 WL 6203602, at *5-6 (D.N.J. Dec. 12, 2012) (Trans. 138:14-18).

The Court finds Sandoz's argument persuasive that the aforementioned deals with administration to a subject because the claim language recites, "pharmacological composition capable of being parenterally administered to a subject," and "the unit dosage provides upon administration: minimal detectable free iron in the subject; and minimal incidence of anaphylaxis." (See claim 1 of the '597 patent). That is, before and after the term "administration" in claim 1 of the '597 patent, the subject is being provided the pharmacological composition, which results in detecting free iron in the subject and incidence of anaphylaxis. (See Trans. 138:21-24 ("You wouldn't have [administration of minimal detectable free iron in the subject] unless something is

actually delivered into the subject.")). Moreover, the specification of the parent patent '498 recites that the pharmaceutical drug is administered either as a bolus or as an intravenous solution. (See the '498 patent, col. 3, ll. 17-19 and 29).

The Court further notes that the term "administration" in claim 1 of the '597 patent likely relates back to the "paternally administered" step as recited in the claim. As such, instead of reciting "paternally administering" in the claim, the Applicant wrote the short hand version of "administration."

Accordingly, the Court construes the term "administration" to mean—"giving a pharmacological composition to a subject."

G. "Cooling the Resulting Solution"

AMAG's Proposed Construction	Sandoz's Proposed Construction
"cooling the solution containing the mixture of carboxymethylated reduced dextran, ferric and ferrous salts."	"cooling the solution formed by contacting the carboxymethylated reduced dextran with a mixture of ferric and ferrous salts"

Representative claim 1 of the '947 patent recites,

> 1. A method of making an autoclavable carboxymethylated reduced dextran iron oxide complex intended for administration by injection to a mammalian subject, the method comprising the steps of:
>
> (i) reacting a dextran with a borohydride salt, or hydrogen in the presence of a hydrogenation catalyst, to produce a reduced dextran;
>
> (ii) carboxymethylating the reduced dextran to produce a carboxymethylated reduced dextran;
>
> (iii) complexing the carboxymethylated reduced dextran with an iron salt to produce a carboxymethylated reduced dextran iron oxide complex; and
>
> (iv) sterilizing the carboxymethylated reduced dextran iron oxide complex by autoclaving;
>
> the complexing comprising contacting the carboxymethylated reduced dextran with a mixture of ferric and ferrous salts, **cooling the resulting solution** and adding ammonium hydroxide to neutralize the solution and recovering the carboxymethylated reduced dextran iron oxide complex; such complex being stable

at a temperature of at least about 121° C. for a period effective to sterilize the complex;

wherein the reduced dextran has an average molecular weight of about 10 kDa and a particle size of 10 nm to 50 nm; and

the carboxymethylated reduced dextran comprises at least about 1100 micromoles of carboxyl groups per gram and less than about 1500 micromoles of carboxyl groups per gram.

The aforementioned claim term was not argued during the Markman hearing. Instead, the parties stipulated to their papers in support of their argument. (See Trans. 157:19-24). In its opening brief, AMAG argues that this claim term appears only in the claims of the '947 patent. (See Pl.'s Br. at 29, fn. 42; D.I. 47). The Court notes that the disclosure of the '947 patent relates back to the disclosure of the parent patent '597 patent because the '947 patent is essentially a continuation of the '597 patent. (See supra fn. 2).

In support of its position, AMAG asserts that the common meaning of the claim merely requires cooling a solution that contains three components—the carboxymethylated reduced dextran, the ferric salts and the ferrous salts. In other words, it is the solution which contains all three components that is cooled. As such, the claim does not require that the solution be formed in a particular way, as proposed by Sandoz. (See Pl.'s Br. at 29-30).

In contrast, Sandoz asserts that its construction of the aforementioned term is based on the claim language itself. That is, as recited in claim 1 of the '947 patent, the complexing includes "contacting the carboxymethylated reduced dextran with a mixture of ferric and ferrous salts." And, because this is the only solution that would have antecedent basis for the term resulting, and one that is consistent with the chemical reactions involved, this interpretation should be maintained. (See Def.'s Br. at 29; D.I. 46).

Here, the Court finds Sandoz's claim construction persuasive. When reviewing claim 1 of the '947 patent, it is important to note that it is a method or a process claim. We know that claim

1 is a method claim because of its—(i) preamble ("A method of making […]"), and (ii) the body of the claim. It is important to remember that the elements, or the body, of a method claim are method steps, which should usually be verbal (gerundial) phrase, introduced by a gerund or verbal noun (the "-ing" form of a verb).[5] The body of claim 1 recites method steps that are introduced by gerund or verbal phrases, for example, "reacting;" "carboxymethylating;" "complexing;" and "sterilizing." From the body of claim 1, it appears that four (4) steps are recited. However, upon a closer review, it appears that claim 1 recites a fifth step of "cooling."

Line 12 of claim 1 starts as "the complexing comprising contacting the carboxymethylated reduced dextran with a mixture of ferric and ferrous salts, cooling the resulting solution and adding […]." It is clear that "the complexing" in this phrase is referring back to the third step of claim 1 in order to ensure proper antecedent basis under pre-AIA (America Invents Act) 35 U.S.C. § 112, second paragraph. In line 12 of claim 1, the inventor further defined the complexing step to "compris[e] [of] contacting the carboxymethylated reduced dextran with a mixture of ferric and ferrous salts." As such, a reasonable person of ordinary skill in the art would interpret the third step of claim 1 to recite, 'complexing comprising contacting the carboxymethylated reduced dextran with a mixture of ferric and ferrous salts to produce a carboxymethylated reduced dextran iron oxide complex.'

After performing the fourth step of sterilizing, the last step to follow is "cooling" of the resulting solution, wherein the 'resulting solution' is what was synthesized in the fourth step. And by reading the entire claim 1, it is apparent to one of ordinary skill in the art that the 'resulting solution,' includes the autoclaved carboxymethylated reduced dextran iron oxide

[5] See Chapter 4: Method or Process Claims. § 4:2 Elements of Method Claims, available at http://www.pli.edu/public/booksamples/16966_sample4.pdf, (last visited July 15, 2017).

complex. Wherein, the carboxymethylated reduced dextran iron oxide complex is formed by contacting the carboxymethylated reduced dextran with a mixture of ferric and ferrous salts.

Accordingly, the Court interprets the claim term "cooling the resulting solution" to mean—"cooling the solution formed by contacting the carboxymethylated reduced dextran with a mixture of ferric and ferrous salts."

ORDER

IT IS on this 19th day of July, 2017,

ORDERED that "complex" is defined as—"a macromolecule or particle configured to be autoclavable without the addition of excipients such as citrate";

ORDERED that "colloid" is defined as—"a macromolecule or a particle";

ORDERED that "autoclaving" and "terminally sterilizing" are defined as— "heating or sterilizing a material in a final container under pressure and steam for a period sufficient to eliminate the viability of all microorganisms in the material";

ORDERED that "injectable" and "intended for administration by injection" are defined as—"capable of being injected";

ORDERED that "administration," "administering parenterally," and "parenterally administered" are defined as—"giving a pharmacological composition to a subject"; and it is further

ORDERED that "cooling the resulting solution" are defined as—"cooling the solution formed by contacting the carboxymethylated reduced dextran with a mixture of ferric and ferrous salts."

s/Peter G. Sheridan
PETER G. SHERIDAN, U.S.D.J.