**UNITED STATES DISTRICT COURT**
**NORTHERN DISTRICT OF ILLINOIS**
**EASTERN DIVISION**

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| **CUMBERLAND PHARMACEUTICALS, INC.,** | ) | |
| | ) | |
| **Plaintiff,** | ) | |
| | ) | |
| **v.** | ) | **No. 12 C 3846** |
| | ) | |
| **MYLAN INSTITUTIONAL LLC, and MYLAN INC.,** | ) | **Judge Rebecca R. Pallmeyer** |
| | ) | |
| **Defendant.** | ) | |

## MEMORANDUM OPINION AND ORDER

Plaintiff Cumberland Pharmaceuticals, Inc. ("Cumberland") develops, manufactures and sells pharmaceutical products, including Acetadote, an intravenous treatment for suspected acetaminophen overdoses. Cumberland brought this patent infringement suit against Defendants Mylan Institutional, LLC and Mylan, Inc. (collectively "Mylan") for infringement of two patents related to Acetadote: United States Patents No. 8,148,356 and No. 8,399,445. Specifically, Cumberland charges Mylan with infringing these patents in violation of 35 U.S.C. § 271(e)(2) by attempting to obtain FDA approval for a generic formulation of Acetadote. The parties have presented competing interpretations for three terms in the claims of the patents at issue. The court's construction of these terms follows.

## BACKGROUND

### I. The Patent

Acetaminophen overdose sends as many as 78,000 Americans to the emergency room each year. Jeff Gerth & T. Christian Miller, *Use Only as Directed*, ProPublica, Sept. 20, 2013, http://www.propublica.org/article/tylenol-mcneil-fda-use-only-as-directed (last visited Feb. 25, 2014). Overdoses are so common, in part, because the over-the-counter pain reliever (best known under the brand name Tylenol) is also found in varying doses in several hundred common cold remedies and combination pain relievers. Acetaminophen poisoning can cause acute hepatic (i.e., liver) failure, severe brain damage, or even death. *Id.* Plaintiff Cumberland

Pharmaceuticals, Inc. manufactures and sells Acetadote, an intravenous formulation of N-acetylcysteine[1] ("NAC"), used to treat suspected acetaminophen overdoses in order to prevent or diminish hepatic injury. (Pl.'s Resp. Br. on Claim Construction [165], hereinafter "Pl.'s Resp. Br." at 2.) At issue in this case are two patents Cumberland holds related to Acetadote: No. 8,148,356 ("the '356 patent") and No. 8,399,445 ("the '445 patent"). The '356 patent, which issued on April 3, 2012, "relates to novel acetylcysteine compositions in solution, comprising acetylcysteine and which are substantially free of metal chelating agents, such as EDTA[2]." U.S. Patent No. 8,148,356, hereinafter "'356 patent," abstract (filed Aug. 24, 2005) (issued April 3, 2012). The '445 patent claims the methods of administering the compositions covered by the '356 patent. As the '445 patent is divisional of the '356 patent, the two share a common specification.

Prior to the patents-in-suit, acetylcysteine was marketed worldwide generically as well as under several trade names as an inhalable mucolytic[3] and as both an injectable and an oral agent to treat acetaminophen overdose. '356 patent, col. 1 ll. 26-36. In fact, Plaintiff's own previous version of Acetadote is one of the prior art products that contained acetylcysteine as

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[1] Cysteine is a sulfur-containing nonessential amino acid produced by the enzymatic or acid hydrolysis of proteins. The N-acetyl derivative of l-cysteine is used as a mucolytic agent for adjunct therapy in bronchopulmonary disorders to reduce the viscosity of mucus and facilitate its removal, administered by instillation or nebulization; and as an antidote for acetaminophen poisoning, administered orally or intravenously. *Dorland's Medical Dictionary* 14, 469 (31st ed. 2007).

[2] Edetic (ethylenediaminetetraacetic) acid. Salts of EDTA are used as chelating agents for direct treatment of metal poisoning because they bind the toxic metal ions more strongly than do the vulnerable components of the living organism. *Encyclopaedia Britannica Online Academic Edition*, http://www.britannica.com/EBchecked/topic/108427/chelate?anchor=ref49109 (last visited Jan. 6, 2014).

[3] An agent "capable of reducing the viscosity of mucus." *Dorland's Medical Dictionary* 1204 (31st ed. 2007).

an active ingredient. (*Id.*) The earlier Acetadote formula was the same as the asserted claims here except that the earlier formula, like other acetaminophen overdose antidotes, contained chelating agents.[4] (Def.'s Opening Claim Construction Br. [147], hereinafter "Defs.' Opening Br.," at 3.) It is the absence of chelating agents that is the key advancement of the invention, as chelators have "undesirable effects" including fatality and "reproductive developmental toxicity." '356 patent, col. 2 ll. 12–20.

## II. The Disputed Claims

The '356 and '445 patents, titled "Acetylcysteine Composition and Uses Thereof," set forth fourteen and sixteen claims, respectively. The parties dispute three terms that appear throughout the patents' claims: (1) "acetylcysteine", (2) "free from a chelating agent"/"free of a chelating agent" (hereinafter "free of/from a chelating agent"), and (3) "stable aqueous pharmaceutical composition." The usage of these terms in the first claim of the '356 patent is exemplary (disputed terms emphasized below):

> 1. A **stable aqueous pharmaceutical composition** comprising between 200 and 250 mg/mL **acetylcysteine**, wherein the composition is **free from a chelating agent**, or pharmaceutically acceptable salts thereof, wherein said composition is in a suitable form for intravenous injection, wherein the pH of the composition is from 6 to 7, and wherein said composition is sealed in an airtight container comprising a fill volume of said composition and a headspace volume occupied by a pharmaceutically inert gas.

'356 Patent.

## III. Prosecution History

Cumberland first sought Food and Drug Administration ("FDA") approval of Acetadote in June 2002, when it filed New Drug Application ("NDA") No. 21-539. (*Id.*) On January 23, 2004,

[4] "Chelating agents, or chelators, are organic agents that bond with and thereby sequester free metal ions from solution. A widely used chelator is edetic acid or ethylenediaminetetraacetic acid, commonly referred to as EDTA[.]" '356 patent, col. 1 ll. 44-49.

the FDA approved Acetadote as an "orphan drug."[5] (Defs.' Opp'n to Mot. to Dismiss [45] at 2.) Because of this status, Cumberland enjoyed a seven-year period of exclusivity during which it faced no competition in the market. 21 U.S.C. § 360cc. On August 24, 2005, Cumberland filed patent application no. 11/209,804 (the "'804 patent application").[6] The prosecution of that application, which resulted in issuance of the '356 patent, spanned nearly seven years. During that period, the Patent Office issued three separate final rejections to which Cumberland responded with several claim amendments and three applications for continued examination. (Defs.' Opening Br., Ex. C, at 304 (03/11/2008 Claim Amendments); 328 (05/28/2008 Final Rejection), 340 (08/12/2008 Request for Continued Examination with Claim Amendments), 436 (12/03/2008 Claim Amendments), 451 (03/06/2009 Final Rejection), 460 (04/24/2009 Claim Amendments), 481 (05/27/2009 Request for Continued Examination with Claim Amendments), 536 (11/25/2009 Claim Amendments), 563 (07/09/2010 Final Rejection), 616 (10/08/2010 Claim Amendments), 656 (10/21/2010 Request for continued Examination with Claim Amendments), 664 (11/16/2010 Claim Amendments), 760 (07/22/2011 Claim Amendments), 875 (02/08/2012 Examiner Claim Amendments.) By the time the '356 patent issued, several of the claims in the issued patent had been amended substantially from the initial application.

Relevant to this suit, the phrase "free of/from a chelating agent" was the result of several iterations during the course of the '356 patent's prosecution. Claim 1 of the initial application read, "An aqueous pharmaceutical composition comprising acetylcysteine, wherein the composition is substantially free of EDTA or pharmaceutically acceptable salts thereof." (*Id.* at

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[5] Orphan drugs are products used to treat diseases or afflictions that are rare (i.e., affecting less than 200,000 people in the United States annually). *See* 21 U.S.C. §§ 360bb(a)(1), 360cc(a).

[6] Leo Pavliv ("Pavliv"), a senior executive at Cumberland, is the named inventor on the '804 patent application. For the purposes of this opinion, however, the court will refer to "Cumberland" for purposes of discussing both Plaintiff's and Mr. Pavliv's actions during prosecution.

70-74.) However, the phrase "substantially free of EDTA" was rejected as "indefinite" under 35 U.S.C. § 112. (*Id.* at 292.) Cumberland responded to this rejection by deleting the offending phrase, leaving the application as decribing a composition containing "less than 0.04% w/v EDTA," "less than 0.03% w/v EDTA," "less than 0.01% w/v EDTA," "less than 0.0025% w/v EDTA," or "no EDTA." (*Id.* at 341–55.) Later, Plaintiff again amended the claims by replacing "EDTA" in the above phrases with "a chelating agent." (*Id.* at 665.) At the same time, dependent claims were also added to reflect a limit on EDTA specifically. (*E.g., id.* at 665 (Claim 3: "The aqueous pharmaceutical composition of Claim 2, wherein the chelating agent is EDTA, and the composition contains less than 0.02% w/v EDTA"); (Claim 71: "The composition of Claim 64, wherein the chelating agent is EDTA."[7]) Finally, in February 2012, Examiner Christopher Stone ("Examiner")—with Plaintiff's consent—replaced these weight-per-volume limitations with the phrase "is free from a chelating agent" and "is free of a chelating agent." (*Id.* at 875–76.) The claims of the '356 patent—issued on April 3, 2012—contain these phrases, while the phrase "substantially free of chelating agents" remains in the specification. Cumberland filed the application for the '445 patent on February 27, 2012. This patent, which was issued on March 19, 2013, claims methods for administering the compositions covered by the '356 patent. The '445 patent uses the phrase "free of chelating agents" and does not refer to EDTA or any other chelator in separate dependent claims. U.S. Patent No. 8,399,445, hereinafter "'445 patent," col. 9 ll. 21–22.

**IV. This Lawsuit**

In December 2011 (shortly before the '356 patent issued in April 2012), Mylan filed Abbreviated New Drug Application ("ANDA") No. 20-3624 seeking FDA approval of a generic version of Acetadote. (Defs.' Opp'n at 2.) Mylan subsequently provided the FDA with a

[7] Claim 71, which became Claim 14 in the final version of the patent, is dependent on Claim 64, which became Claim 9.

certification under 21 U.S.C. § 355(j)(2)(A)(vii) ("Paragraph IV certification") that its ANDA product does not infringe upon any valid claim of the '356 patent. (Defs.' Opp'n at 2.) Mylan also sent notice of the Paragraph IV certification to Cumberland. (Id.) Cumberland filed the instant suit for infringement on May 17, 2012, pursuant to the Hatch Waxman Act, 21 U.S.C. § 355(j)(5)(B)(iii), alleging that Mylan's filing of its ANDA with a Paragraph IV certification constituted an act of infringement of the '356 patent under 35 U.S.C. § 271(e)(2)(A). (Pl's Compl. [1].) The next day, Cumberland filed a Citizen Petition with the FDA, requesting that the FDA not approve any ANDA for Acetadote. (Citizen Petition, Ex. 2 to Defs.' Opp'n at 2.)

In the months following the filing of this suit, Mylan filed a motion to dismiss [42] and a motion for summary judgment [52]. Subsequently, Plaintiff amended its complaint in May 2013, clarifying its allegations and adding, among other things, a second count of infringement related to the '445 patent. (Pl.'s Am. Compl. [126].) As a result of the amended complaint, Mylan's motion to dismiss was stricken and its motion for summary judgment withdrawn without prejudice to later renewal of Mylan's request for fee shifting. (Minute Order of May 30, 2013 [136].)

The parties now dispute three terms in the '356 and '445 patents. They have submitted a series of claim construction briefs, and the court conducted a claim construction hearing in August 2013 [174]. The court addresses the disputed language below.

## DISCUSSION

### I. Legal Standards Governing Claim Construction

Because an invention is defined by the claims of the patent, claim construction—the process of giving meaning to the claim language—defines the scope of the invention. *Phillips v. AWH Corp.*, 415 F.3d 1303, 1311–12 (Fed. Cir. 2005) (en banc) (citing 35 U.S.C. § 112). Claim construction is a matter of law for the court to determine. *Markman v. Westview Instruments, Inc.*, 517 U.S. 370, 391 (1996). As the Federal Circuit clarified in *Phillips*, the court begins its

claim construction analysis with the words of the claims themselves, giving those words their ordinary and customary meaning, that is, the "meaning that the term would have to a person of ordinary skill in the art in question at the time of the invention." *Phillips*, 415 F.3d at 1312–13. And that person is assumed to read the claim terms "in the context of the entire patent, including the specification." *Id.* In certain circumstances, however, "the specification may reveal an intentional disclaimer, or disavowal, of claim scope by the inventor." *Id.* at 1316. In such cases, courts "interpret[] the claim more narrowly than [they] otherwise would to give effect to the inventor's intent to disavow a broader claim scope." *Ventana Med. Sys. v. Biogenex Labs., Inc.*, 473 F.3d 1173, 1181 (Fed. Cir. 2006) (citing *Phillips*, 415 F.3d at 1316).

In addition to reading the claim terms in the context of the specification, the court may also consider the record of the patent's prosecution, as the record is evidence of how both the inventor and the Patent and Trademark Office understood the patent. *Phillips*, 415 F.3d at 1317. The court must, however, be mindful that the prosecution history represents an "ongoing negotiation," so it "often lacks the clarity of the specification and thus is less useful for claim construction purposes." *Id.* The specification, on the other hand, "is always highly relevant to the claim construction analysis . . . [;] it is the single best guide to the meaning of a disputed term." *Id.* at 1315. Finally, in some cases, the court must go beyond the claim, the specification, and the prosecution history—the so-called intrinsic evidence—to consider extrinsic evidence such as technical dictionaries, treatises, and expert testimony. *Id.* at 1317-18. That extrinsic evidence is deemed less reliable than the intrinsic evidence for several reasons outlined by the Federal Circuit in *Phillips*. *Id.* at 1318–19.

With these legal standards in mind, the court turns to construction of the disputed terms in the patents-in-suit.

## II. Free From a Chelating Agent/Free of a Chelating Agent

| Claim Term | Plaintiff's Proposed Construction | Defendants' Proposed Construction |
|---|---|---|
| "Free From A Chelating Agent" & "Free Of A Chelating Agent" | Lacking one or more added chelating agents. | Lacking any chelating agents |

The term "free of/from a chelating agent" appears in claims 1, 7, 8, and 9 of the '356 patent. Claim 1 of the '445 patent also includes the similar phrase "free of chelating agents." Although the parties agree that "free of chelating agents" means "lacking any chelating agents" (Joint Claim Construction Chart [172] at 4), they differ as to the meaning of the similar expressions "free of a chelating agent" and "free from a chelating agent." The parties do agree, however, that "free of a chelating agent" and "free from a chelating agent" share a meaning. As such, the parties both use—and the court adopts—the shorthand "free of/from a chelating agent" when discussing these disputed phrases. Mylan argues that this contested term is identical in meaning to "free of chelating agents" (i.e., "lacking any chelating agents"). (*Id*.) Cumberland disagrees, and takes the position that the phrase should be read as "lacking *one or more added* chelating agents." (*Id.* (emphasis in original).) Thus, the parties' respective constructions of "free of/from a chelating agent" actually differ in two key respects: (1) whether "a" means "any" or "one or more"; and (2) whether the phrase limits all chelating agents (including those present as impurities) or only those that are "added" to the composition.

### A. Meaning of "A"

At first blush, the phrases "lacking any" and "lacking one or more" seem to be synonymous. There is an important distinction, however, between the proposed constructions. Mylan's interpretation (i.e., "lacking any chelating agents") describes a composition completely devoid of any chelating agents, while Cumberland's version (i.e., "lacking one or more added chelating agents") requires only that at least one otherwise-added chelating agent be absent. That is, a composition that falls within Cumberland's construction may contain numerous chelating agents, so long as it does not include *every* chelating agent (and also adheres to the

claim's other limitations). The court concludes that Cumberland's reading of "a," though quite broad in scope, is the proper construction due to the nature of dependent claims and the related doctrine of claim differentiation.

Patent claims may be either independent or dependent. Dependent claims, as their name suggests, are claims that refer to and depend on the limitations laid out in a previous claim in the patent. A dependent claim is "construed to incorporate . . . all of the limitations of the claim to which it refers," and "then specif[ies] a further limitation[.]" 35 U.S.C. § 122. As a result, each dependent claim serves to narrow the scope of the invention in relation to the claims that precede it. Based on this relationship between dependent and independent claims, the concept of claim differentiation provides that the existence of a limitation in a dependent claim implies that the independent claim on which it depends is not subject to that limitation. *See Free Motion Fitness, Inc. v. Cybex Int'l, Inc.*, 423 F.3d 1343, 1351 (Fed. Cir. 2005). In other words, claim differentiation demands a construction under which each claim has a different scope and no claim is superfluous. *Id.*

Claim differentiation is relevant to a number of asserted claims in the patents-in-suit. For instance, Claim 14 of the '356 patent depends on Claim 9. They read as follows:

> 9. A container comprising: an aqueous pharmaceutical composition comprising between 200 and 500 mg/mL acetylcysteine, wherein the composition is **free of a chelating agent** and has a pH of about 6 to less than 7, or pharmaceutically acceptable salts thereof, and wherein said composition is in a suitable form for intravenous injection; and a headspace consisting essentially of a pharmaceutically inert gas. . . .
>
> 14. The composition of claim 9, **wherein the chelating agent is EDTA**.

'356 patent (emphasis added). As Plaintiff points out, Defendants' construction of "a" would render Claim 14 superfluous. (Pl.'s Resp. Br. at 12) That is, if "a" means "any," then Claim 9 would describe a composition without any chelating agents whatsoever, and Claim 14's limitation would add nothing to the patent. Defendant responds by pointing out that claim differentiation is "not absolute in its application," rather "it is just one of many tools used by

courts in the analysis of claim terms." (Defs.' Reply Br. [170] at 8 (quoting *ERBE Elektromedizin GmbH v. Canady Techn. LLC*, 629 F.3d 1278, 1286 (Fed. Cir. 2010)).) Further, Mylan argues, adhering to the claim differentiation doctrine in this instance would run afoul of Federal Circuit guidance that "[a] claim construction that renders asserted claims facially nonsensical cannot be correct." *Becton, Dickinson & Co. v. Tyco Healthcare Grp., LP*, 616 F.3d 1249, 1255 (Fed. Cir. 2010). Mylan suggests that Plaintiff's construction would be "nonsensical," because "the only composition that falls outside of [Cumberland's construction] is that which contains every single chelating agent in the world."[8] (Defs.' Reply Br. at 8.) While Cumberland's interpretation does render the scope of the disputed term especially broad, an especially broad term does not necessarily render the claim "facially nonsensical." The case Defendants cite for this proposition is illustrative of the distinction. In *Becton*, the Federal Circuit rejected a proposed construction as "nonsensical" because it would have rendered the invention a "physical impossibility."[9] *Becton*, 616 F.3d at 1255. The *Becton* court, in turn, relied on *Schoenhaus*, a case that rejected a proposed construction that would have resulted in a claim that read: "[a] footwear product having as an element thereof [a shoe built to have the shape of the interior of

[8] Mylan's assertion ignores the remaining limitations within the claims in question. Claim 1 of the '356 patent not only describes a composition that is "free of a chelating agent," but also one that is "stable," contains "between 200 and 250 mg/mL acetylcysteine," "is in a suitable form for intravenous injection," has a pH "from 6 to 7," and "is sealed in an airtight container." '356 patent, col. 9 ll. 17–21.

[9] In *Becton*, the plaintiff was the assignee of a patented design for a safety needle intended to prevent accidental needle stick injuries. The invention consisted of four distinct elements: (1) a needle, (2) a guard that rides on the needle, (3) a hinged arm attached to the guard, and (4) a spring means connected to the hinged arm. When not in use, the needle guard covered the needle's tip. The plaintiff argued that the "spring means" and the "hinged arm" were the same thing. The Federal Circuit found this construction "nonsensical," because the patent described the spring means as being "connected to" the hinged arm and also "extending between" the hinged arm and a mount. Thus, the plaintiff's construction would require the hinged arm to be "connected to" itself and also "extend between" itself and the mount, which the Federal Circuit deemed "a physical impossibility." *Becton*, 616 F.3d at 1254–55.

the insert]." *Schoenhaus v. Genesco, Inc.*, 440 F.3d 1354, 1357 (Fed. Cir. 2006). Both of these cases rejected proposed constructions that can be described as illogical, internally inconsistent, or physically impossible. By contrast, Cumberland's construction of "a" is neither illogical nor physically impossible; it is simply broad. Further, as discussed above, this is the only interpretation of the '356 patent's independent claims that does not render its dependent claims redundant.

Mylan also objects to Plaintiff's construction as (1) inconsistent with the plain and ordinary meaning of the phrase; (2) an attempt to "re-write claim language" to reclaim ground surrendered in prosecution; and (3) inconsistent with a distinction drawn against prior art during prosecution. (Defs.' Opening Br. at 14–16.) These objections misconstrue the disagreement between the parties and the relevant prosecution history.

First, Mylan argues that the terms "free of" and "free from" forbid the presence of any chelating agent based on the "widely accepted" definition of their meaning as "lacking" or "not having or using." (Defs.' Opening Br. at 12.) But this argument misses the actual point of disagreement here. The parties, in fact, agree that "free of" and "free from" should be construed as "lacking." (Joint Construction Chart at 4.) The real argument is about what exactly the composition is lacking. On this score, as Plaintiff points out, the ordinary meaning of "a," according to the Federal Circuit, is "one or more."[10] (Pl.'s Resp. Br. at 11–12 (citing *Baldwin Graphics Sys., Inc. v. Siebert, Inc.*, 512 F.3d 1338, 1342–43 (Fed. Cir. 2008)).)

[10] Mylan argues that the ordinary meaning of "a" should not apply here because, unlike in the cases cited by Cumberland, in this instance the word is used as part of "negative claim limitations" (i.e., "Cumberland defined its invention by what it is not."); and, when used in a negative sense, "a" means "any." (Defs.' Reply Br. at 4.) Mylan's position inaccurately represents the way "a" is used in the English language, however. In reality, the meaning of "a" as plural or singular depends significantly on context. In some instances, even when one defines things by what they lack, "a" does mean "any" ("I don't have a chance"); but in other instances it may still mean "one" ("My shirt is missing a button").

Second, Mylan points to amendments during prosecution that modified the claim limitations on chelating agents to argue that Cumberland's proposed construction here seeks to reclaim ground it was forced to cede in prosecution. As discussed above, the initial application used the term "substantially free of EDTA," which was deemed ambiguous. That term was subsequently changed to "less than [a certain percentage] w/v EDTA" on August 12, 2008. Additional amendments on November 16, 2010 altered this language to "less than [a certain percentage] w/v of a chelating agent." In the end, the specific w/v limits on chelating agents were replaced with "free of/from a chelating agent." The effect of this series of amendments, according to Mylan, was to repeatedly narrow the scope of the claims. Based on this theory, Defendants argue that the November 2010 amendments served to "exclude [a certain percentage of] all chelating agents" rather than just EDTA; and the ultimate change to "free of/from a chelating agent" was intended to exclude any amount of any chelating agent. Mylan's interpretation of the prosecution history fails, however, because it ignores the fact that claim limitations on "chelating agents" never existed without dependent claims that specifically limited EDTA. Thus, Cumberland's insistence on adhering to the principle of claim differentiation now is not a last-ditch effort to reclaim ceded territory; rather, it is consistent with each iteration of the claims throughout prosecution.

Finally, Defendant argues that Plaintiff's construction is inconsistent with the position it took concerning prior art during prosecution. On March 2, 2011, the Examiner rejected Cumberland's application for the '356 patent as anticipated by European Patent 0639375 ("EP '375"). (Defs.' Opening Br., Ex. C, at 748–49.) On July 22, 2011, Cumberland amended[11] its application and responded to the Examiner's rejection based on EP '375. Mylan characterizes

[11] This amendment did not modify the amount or type of chelating agents in the composition; rather it added a clause specifying that the composition is "sealed in an airtight container" with "headspace . . . occupied by a pharmaceutically inert gas." (Defs.' Opening Br., Ex. C, at 761.)

Plaintiff's response as "argu[ing] that EP '375 disclosed an acetylcysteine composition that contained sodium bicarbonate, which is 'a compound that has chelating properties,' and, therefore, did not read on [Plaintiff's] claims which exclude all chelating agents." (Defs.' Opening Br. at 8-9.) This mischaracterizes the prosecution history. In reality, Plaintiff did not distinguish its invention from EP '375 based on an argument that Cumberland's claims excluded *all* chelating agents. Rather, the sentence following the passage quoted by Mylan above states that, "EP '375 fails to disclose or suggest an acetylcysteine composition compris[ing] less than 0.05% w/v of a chelating agent."[12] (Defs.' Opening Br., Ex. C, at 773.) The chelating content of EP '375 was also only one of several grounds on which Plaintiff sought to distinguish its invention, including that the prior art "fails to disclose or suggest at least . . . a composition sealed in an air-tight container, and . . . a composition with a headspace volume occupied by an inert gas." (*Id.*)

**B. "Added" Chelating Agents**

The second source of disagreement between the parties regarding the term "free of/from a chelating agent" is whether the phrase refers to all chelators or only those added to the composition (i.e., not those included merely as impurities). The plain meaning of the term, as Defendants correctly observe, would reach any chelating agent, not just those added to the composition. (Defs.' Opening Br. at 13.)

Surprisingly, Plaintiff does not address this aspect of its proposed construction head-on: neither its *Markman* presentation, its response brief, nor its supplemental reply brief explicitly argues why the word "added" should be read into the term "free of/from a chelating agent." Based on this notable omission, it appears that Cumberland may have included the word

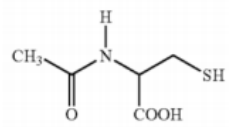
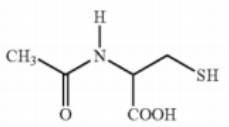
[12] The EP '375 composition is 9.52% sodium bicarbonate, which has chelating properties. (Defs.' Opening Br., Ex. C, at 773.) Thus, EP '375 contains considerably more than the 0.05% w/v of a chelating agent that was recited in Plaintiff's claims at that time.

"added" in its proposed construction to reinforce its interpretation of "acetylcysteine" as including its associated impurities (discussed below). As such, Plaintiff may have considered its arguments in favor of including impurities in the definition of acetylcysteine as relevant to this issue, as well. Two such arguments are particularly relevant: first, Cumberland points to numerous passages of the specification which allow for the presence of chelating agents as impurities. (Pl.'s Resp. Br. at 6–8.) Indeed, the very innovation of Plaintiff's invention was the discovery that an acetylcysteine composition could remain stable "without the addition of a chelating agent." '356 patent, col. 2 l. 48. Second, Cumberland argues that Mylan's construction of "acetylcysteine" without its impurities would exclude certain embodiments in the specification in violation of Federal Circuit precedent. (Pl.'s Resp. Br. at 5–6 ("[a] claim construction that excludes the preferred embodiments . . . in the patent specification 'is rarely, if ever, correct and would require highly persuasive evidentiary support' to be sustained.") (quoting *Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1583 (Fed. Cir. 1996)).) This argument is relevant to the inclusion of "added" in the construction of "free of/from a chelating agent," because one embodiment in the '356 patent describes a composition in which "chelating agents are not added . . . but may be present otherwise. For instance, the chelating agent may be present as an impurity or undesired contaminant." '356 patent, col 3 l. 67–col. 4 l. 3.

Defendants respond by pointing out that the specification is actually inconsistent as to whether it excludes the presence of chelating agents or simply their addition. For instance, at one point, the specification describes the invention as a composition of acetylcysteine capable of maintaining stability "without the need of a chelating agent." (Def.'s Reply Br. at 7 (quoting '356 patent, col. 4 ll. 6–11.) They further argue that the including the word "added" in the construction of free of/from a chelating agent "wrongly imports a process limitation into composition claims." (Defs.' Reply Br. at 8.)

Without reaching the merits of either of these arguments, however, the court is satisfied that the intrinsic evidence here provides no basis for disregarding the ordinary meaning of the disputed term at issue. The court's interpretation of "a" as "one or more" (discussed above) moots both of Plaintiff's potential arguments in favor of reading "added" into this disputed term. Even without reading the word "added" into the construction of "free of/from a chelating agent" (as construed above), the term would not exclude the embodiment Plaintiff cites (i.e., one that contains chelating agents as impurities). In fact, so long as a composition does not contain *all* chelating agents—whether as impurities or added ingredients—the term "free of/from a chelating agent" would not exclude it. Accordingly, the court adopts the following construction for "free of/from a chelating agent": "lacking one or more chelating agents."

**III. Acetylcysteine**

| Claim Term | Plaintiff's Proposed Construction | Defendants' Proposed Construction |
|---|---|---|
| "Acetylcysteine" | An antioxidant having a molecular weight of 163.2 and the following chemical structure:<br>  <br><br>Acetylcysteine is the nonproprietary name for the N-acetyl derivative of the naturally occurring amino acid, L-cysteine (also known as N-acetyl-L-cysteine and NAC) **and impurities associated therewith**. | An antioxidant having a molecular weight of 163.2 and the following chemical structure:<br>  <br><br>Acetylcysteine is the nonproprietary name for the N-acetyl derivative of the naturally occurring amino acid, L-cysteine (also known as N-acetyl-L-cysteine and NAC). |

The term "acetylcysteine" appears in every asserted claim of both patents-in-suit. Cumberland proposes reading "acetylcysteine" as "[t]he nonproprietary name for the N-acetyl derivative of L-cysteine (also known as N-acetyl-L-cysteine and NAC) *and impurities associated*

*therewith*." (Joint Claim Construction Chart at 4 (emphasis added).) Defendants, on the other hand, would construe the term to reach only acetylcysteine and not its impurities.[13] (*Id*.)

Cumberland bases its construction of acetylcysteine on both the specification and the "ordinary meaning" of the term. (Pl.'s Resp. Br. at 6–9.) Notably, the specification seems to expressly anticipate impurities in its definition of "acetylcysteine": "Acetylcysteine includes derivatives of acetylcysteine, and pharmaceutically acceptable salts thereof." '356 patent, col. 4 ll. 41–42. The specification also includes a table—"Table 1"—that tracks the stability of acetylcysteine compositions over time. *Id.*, col. 8 55–70. The table identifies each of the components added to create the composition, as well as "various impurities, including L-cysteine,[14] impurity C (disulfide), impurity D, and other impurities or degradation products." '356 patent, col. 8 ll. 32–34. The "ordinary meaning" of acetylcysteine also supports Cumberland's construction, as "impurities normally associated with the component of a claimed invention are implicitly adopted by the ordinary meaning of the components themselves." *Conoco Inc. v. Energy & Envtl. Int'l, L.C.*, 460 F.3d 1349, 1360–61 (Fed. Cir. 2006).

Mylan agrees that the ordinary meaning of acetylcysteine would include its impurities, but nevertheless argues that the specification here provided an "express definition [that] supersedes Cumberland's argument for interpretation based on plain and ordinary meaning." (Defs.' Reply Br. at 11 (quoting *Phillips*, 415 F.3d at 1316) ("[T]he specification may reveal a

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[13] Mylan initially argued that acetylcysteine itself is a "chelating agent." Thus, based on Mylan's proposed construction of "free of/from a chelating agent" (discussed above), the claims at issue would paradoxically include acetylcysteine and be "free of/from" it at the same time. In their reply brief, however, Defendants withdrew this interpretation and acknowledged that "'chelating agent' need not be construed to include 'acetylcysteine.'" (Defs.' Reply Br. at 10.)

[14] The parties disagree about L-cysteine in two respects, neither of which the court must determine at this time: (1) whether L-cysteine is a chelating agent (Mylan says yes, Cumberland says no) (Defs.' Opening Br. at 17 n.4); and (2) whether it is possible to have a composition of acetylcysteine without L-cysteine being present (Mylan again says yes; Cumberland says no) (Defs.' Supp. Br. [179] at 1; Pl.'s Supp. Reply Br. [181] at 3–4).

special definition given to a claim term by the patentee that differs from the meaning it would otherwise possess. In such cases, the inventor's lexicography governs.") (internal citations omitted)).) But this argument relies on Mylan's construction of "free of/from a chelating agent," which the court rejected above. As Defendants see it, Cumberland disavowed the ordinary meaning of acetylcysteine by excluding all chelating agents in the claims that contain the phrase "free of/from a chelating agent." (Defs.' Reply Br. at 11.) Based on that theory, acetylcysteine cannot be construed to include impurities insofar as those impurities may be chelating agents. But, as the court discussed at length above, Mylan's construction of "free of/from a chelating agent" is incorrect; and, as a result, there is no reason to understand that term as a disavowal of the ordinary meaning of acetylcysteine. Accordingly, the court adopts Plaintiff's proposed construction of "acetylcysteine" as "the nonproprietary name for the N-acetyl derivative of the naturally occurring amino acid, L-cysteine (also known as N-acetyl-L-cysteine and NAC) and impurities associated therewith."

**IV. Stable Aqueous Pharmaceutical Composition**

| Claim Term | Plaintiff's Proposed Construction | Defendants' Proposed Construction |
|---|---|---|
| "Stable Aqueous Pharmaceutical Composition" | A composition that exhibits minimal change **for at least 3 months** relative to when it was manufactured. | A composition that exhibits minimal change **over time** relative to when it is manufactured. |

The final disputed term is "stable aqueous pharmaceutical composition." Under Plaintiff's construction, a composition is stable if it "exhibits minimal change for at least 3 months" from manufacture. (Joint Construction Chart at 4.) Defendants, meanwhile, argue for an interpretation that requires stability "over time" rather than "for at least three months." (*Id.*)

The specification defines a composition as "stable" if it "exhibits minimal change over time relative to when it is manufactured." '356 patent, col. 3 ll. 43–44. Mylan argues that "the unambiguous language of the specification" supports Defendants' construction. (Defs.' Reply Br. at 12.) The specification goes on, however, to clarify that "[s]tability is measured at various

time points . . . as described in Example 3." *Id.* at 44–51. Example 3, in turn, identifies the process by which Plaintiff tested the stability of its invention: various acetylcysteine formulations were kept at 25 or 40 degrees Celsius. Sample vials of each iteration were removed after three months, six months, and twelve months, and their contents were compared to the initial compositions. *Id.* at c. 8 ll. 13–53. Example 3 refers to Table 1, which catalogues the results of these tests:

| Time point | Disodium EDTA | Temp | NAC Content | L-Cysteine | Impurity C (Disulfide) | Impurity D | Highest Unknown | Total Unknowns |
|---|---|---|---|---|---|---|---|---|
| Initial | 0.00% | N/A | 202.4 | 0.150 | 0.550 | 0.180 | 0.010 | 0.020 |
| Initial | 0.02% | N/A | 203.9 | 0.190 | 0.440 | 0.230 | 0.030 | 0.050 |
| Initial | 0.05% | N/A | 204.7 | 0.200 | 0.500 | 0.300 | 0.040 | 0.100 |
| 3 Mos. | 0.00% | 25˚ C | 204.2 | 0.181 | 0.482 | 0.137 | 0.053 | 0.080 |
| 3 Mos. | 0.00% | 40˚ C | 201.8 | 0.370 | 0.540 | 0.900 | 0.070 | 0.132 |
| 3 Mos. | 0.02% | 25˚ C | 204.9 | 0.259 | 0.436 | 0.191 | 0.074 | 0.141 |
| 3 Mos. | 0.02% | 40˚ C | 204.5 | 0.463 | 0.467 | 0.142 | 0.065 | 0.183 |
| 3 Mos. | 0.05% | 25˚ C | 206.1 | 0.299 | 0.444 | 0.214 | 0.044 | 0.119 |
| 3 Mos. | 0.05% | 40˚ C | 205.4 | 0.532 | 0.507 | 0.165 | 0.045 | 0.154 |
| 6 Mos. | 0.00% | 25˚ C | 202.4 | 0.262 | 0.523 | 0.106 | 0.013 | 0.013 |
| 6 Mos. | 0.00% | 40˚ C | 201.7 | 0.707 | 0.509 | 0.053 | 0.133 | 0.133 |
| 6 Mos. | 0.02% | 25˚ C | 205.9 | 0.338 | 0.391 | 0.167 | 0.013 | 0.013 |
| 6 Mos. | 0.02% | 25˚ C | 207.1 | 0.369 | 0.483 | 0.186 | 0.013 | 0.013 |
| 6 Mos. | 0.05% | 40˚ C | 204.6 | 0.932 | 0.509 | 0.104 | 0.135 | 0.135 |
| 6 Mos. | 0.05% | 40˚ C | 204.3 | 0.856 | 0.525 | 0.093 | 0.135 | 0.135 |
| 12 Mos. | 0.00% | 25˚ C | 204.5 | 0.364 | 0.597 | 0.079 | 0.034 | 0.071 |
| 12 Mos. | 0.02% | 25˚ C | 206 | 0.435 | 0.475 | 0.134 | 0.042 | 0.130 |
| 12 Mos. | 0.05% | 25˚ C | 207.1 | 0.514 | 0.435 | 0.160 | 0.055 | 0.122 |

'356 patent at col. 8 l. 54–col. 9 l. 14.

Based on Example 3 and Table 1, Cumberland argues that the specification "identifies a time period of 3 months as the minimum time point for stability" by first evaluating the formulations at that point. (Pl.'s Resp. Br. at 16.) Plaintiff further argues that "[c]laim differentiation reinforces that three months is the minimum time point," because Claims 5 and 6 demand longer periods of stability: twelve months at 25˚C and six months at 40˚C, respectively. (*Id.* at 17.) Finally, Cumberland points to two pieces of extrinsic evidence to support its construction. (1) FDA guidance that advises "[f]or products with a proposed shelf life of at least

12 months, the frequency of testing at the long-term storage condition should normally be every 3 months over the first year " (*id.* at 18 (quoting "Guidance for Industry," FDA, Ex. S to Pl.'s Resp. Br.)); and (2) Defendants' use of three months as a minimum for stability testing in its own ANDA application. (*Id.* at 18 (citing ANDA Application, Ex. T to Pl.'s Resp. Br.; Stability data, Ex. U to Pl.'s Resp. Br.)

Plaintiff's argument here relies on the fact that the specification's first tests of stability were conducted after three months. Cumberland supports its interpretation with citations to a pair of cases from the Federal Circuit in which that court read numerical limitations into claims based on the specification. (Pl.'s Resp. Br. at 19 (citing *Amazin' Raisins Int'l, Inc. v. Ocean Spray Cranberries, Inc.*, 306 F. Appx. 553 (Fed. Cir. 2008); *Sinorgchem Co., Shandong v. Int'l Trade Comm'n*, 511 F.3d 1132 (Fed. Cir. 2007)).) As Mylan points out, however, the terms in those cases are easily distinguishable from the disputed terms here, because, unlike here, the specifications in those cases took steps to explicitly define the terms in dispute using numerical limitations. In *Amazin' Raisins*, the Federal Circuit affirmed the district court's construction of "dried fruit" as "fruit from which natural moisture has been removed which has about 10 to 18% moisture remaining" based on the following text from the specification: "Any dried fruit which contains between about 10% to 18% moisture may be employed." 306 Fed. Appx. at 556-557. Similarly, in *Sinorgchem*, the patentee explicitly defined a disputed claim term ("controlled amount") in the specification by using a specific numerical limitation ("up to about 4% H20"), and the Federal Circuit found the inventor's intention dispositive. 511 F.3d at 1136. While the '356 specification does refer to a measure of stability after three months, this reference is not definitive in the same sense as the numerical values in *Amazin' Raisins* and *Sinorgchem*. In fact, the specification here provides a definition of "stable" that, like Mylan's construction, is silent as to time.

Plaintiff's remaining arguments based on claim differentiation and extrinsic evidence can

also be dismissed. Cumberland seems to suggest that claim differentiation demands that an independent claim must require stability over a shorter period of time than any limitation added by its dependent claims. But the claims here belie that very notion: Claim 6, which depends on Claim 5, only requires stability for six months at 40˚C, while Claim 5 requires stability for "at least 12 months at 25˚C." '356 patent, col. 9 ll. 33–38. Plaintiff's extrinsic evidence is also insufficient to support its construction, as Plaintiff asks the court to rely on FDA guidance that Plaintiff itself did not follow. As Cumberland itself acknowledges, the FDA suggests that testing "should normally be every 3 months over the first year," yet Plaintiff tested the stability of its compositions only at three, six, and twelve months. This guidance, and the fact that Defendants also tested stability first after three months, is not sufficient to establish an industry norm that requires Plaintiff's proposed construction of "stability."

Nothing in the intrinsic (or extrinsic) record here justifies a construction of "stable" that differs from the plain meaning of the term as explicitly defined in the specification. Accordingly, the court adopts the following construction for "stable aqueous solution": "a composition that exhibits minimal change over time relative to when it is manufactured."

**CONCLUSION**

Claim terms in the '356 and '445 patents are construed in accordance with the foregoing.

ENTER:

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Dated: February 26, 2014

REBECCA R. PALLMEYER
United States District Judge