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

ALLERGAN, INC. *Plaintiff*, v. TEVA PHARMACEUTICALS USA, INC., et al., *Defendants*.	§ § § § § § § § § §	Case No. 2:15-CV-1455-WCB

CLAIM CONSTRUCTION MEMORANDUM OPINION AND ORDER

On August 26, 2016, the Court held a hearing to address the proper construction of the disputed terms of the six patents at issue in this case, U.S. Patent Nos. 8,629,111 ("the '111 patent"); 8,633,162 ("the '162 patent"); 8,642,556 ("the '556 patent"); 8,648,048 ("the '048 patent"); 8,685,930 ("the '930 patent"); and 9,248,191 ("the '191 patent"). After considering the arguments made by the parties at the hearing (Dkt. No. 182), in their claim construction briefing (Dkt. Nos. 155, 165, and 171), and in their supplemental claim construction briefs (Dkt. Nos. 190, 211, and 213), the Court issues this order setting forth the Court's construction of the claim terms identified by the parties as being in dispute.

The patents in suit are directed to an emulsion containing cyclosporin, a compound that is useful for treating an ophthalmic condition known variously as "dry eye," "dry eye disease," or "dry eye syndrome," and a related condition known as keratoconjunctivitis sicca.[1] The

[1] Cyclosporin is often spelled cyclosporine, including in many research papers. The patents generally spell the term cyclosporin (with a few inconsistencies). The Court will spell the term as the asserted patents (generally) do. The difference in spelling does not reflect any difference in the designated compound or group of compounds.

patents are mainly directed to the composition of the emulsion containing the cyclosporin component.

All six patents are entitled "Methods of Providing Therapeutic Effects Using Cyclosporin Components." The patents share a common specification, except for a 14-line passage found in the '111 patent, the '048 patent, and the '930 patent that is not found in the other three.[2] The emulsion that is the subject of many of the claims of the patents contains cyclosporin A, water, and castor oil (a hydrophobic component), as well as certain other named constituents. The claims recite that cyclosporin A is present in an amount of about 0.05% by weight of the composition and castor oil is present in an amount of about 1.25% by weight of the composition.

It was known as early as the 1980s that cyclosporin was effective in treating dry eye. See U.S. Patent No. 4,839,342 to Kaswan. By the mid-1990s, it was known that an emulsion consisting of between about 0.05% and about 0.40% by weight of cyclosporin A and between about 0.625% and 5.0% by weight of castor oil, along with certain other components, could be used in direct administration to the eye. See U.S. Pat. No. 5,474,979 to Ding. The claimed improvement described in the group of asserted patents at issue in this case is that at the particular percentages of cyclosporin A and castor oil recited in the claims, the emulsion surprisingly has therapeutic efficacy roughly equal to that of an emulsion having twice the relative concentration of cyclosporin. The low concentration of cyclosporin in the claimed emulsion had the advantage of not resulting in substantial concentrations of cyclosporin in the patient's bloodstream. The claimed emulsion thus avoided triggering the side effects that often accompany treatments employing higher concentrations of cyclosporin.

[2] That passage is found at column 2, line 65, through column 3, line 11, of the '111 patent; column 2, line 65, through column 3, line 11, of the '048 patent; and column 2, line 64, through column 3, line 10, of the '930 patent.

The claim construction issues that are in dispute fall into eight categories. One claim term that was initially in dispute has been agreed upon by the parties: The parties have agreed that the phrase "substantially no detectable concentration of cyclosporin A" should be construed to mean "a blood concentration under one-tenth nanogram per milliliter." The Court accepts that construction of the term. The remaining terms in dispute are addressed below.

1. dry eye, dry eye disease, dry eye syndrome, and keratoconjunctivitis sicca

The patents use the terms "dry eye," "dry eye disease," and "dry eye syndrome" at different times. The term "dry eye" is used in claims 20, 23, and 25 of the '111 patent and claims 13 and 23 of the '930 patent. The term "dry eye disease" is used in claims 1, 22, and 23 of the '162 patent; claims 1, 11, and 13 of the '556 patent; and claims 1 and 17 of the '191 patent. The term "dry eye syndrome" is used in claims 18 and 21 of the '162 patent. All three terms are used in the common specification of the six patents. See '111 patent, col. 12, line 4 ("dry eye"); id., col. 2, ll. 40, 66, and col. 14, ll. 34, 39, 44, 67 ("dry eye disease"); id., col. 2, ll. 60-61, 64, and col. 5, ll. 14-15, 19, 29-30, and col. 14, line 55 ("dry eye syndrome"). Allergan argues that all three terms refer to the same condition and that the difference in terminology is not significant. Allergan proposes the following definition for "dry eye" and "dry eye disease": "a group of disorders of the tear film, including those caused by reduced tear production or tear evaporation or an imbalance of tear film components associated with clinical signs, ocular discomfort and/or visual symptoms."

The term keratoconjunctivitis sicca ("KCS") is used in claims 21 and 26 of the '111 patent; claims 18, 21, and 22 of the '048 patent; claims 1, 11, 25, and 35 of the '930 patent; and in the portion of the common specification that is found only in the '111, '048, and '930 patents, see '111 patent, col. 2, line 66, and col. 3, ll. 4-5; '048 patent, col. 2, line 66, and col. 3, ll. 4-5;

'930 patent, col. 2, line 65, and col. 3, ll. 3-4. Allergan argues that KCS is a subset of the condition known as dry eye, and that in patients suffering from KCS the symptoms of dry eye are associated with inflammation of the conjunctiva, the tissue that lines the inside of the eyelids. It proposes the following definition for KCS: "a subset of dry eye disease, characterized by inflammation of the conjunctiva and of the cornea, associated with decreased tears."

The defendants offer no competing definitions of these terms. Instead, they argue that the term "KCS" and all three variants of the term "dry eye"—"dry eye," "dry eye disease," and "dry eye syndrome"—are indefinite. The defendants point out that none of those terms are explicitly defined in the common specification, and they argue that the terms have been used in varying ways in the field over time. Accordingly, they contend that none of the terms would convey a well-understood meaning to a person of ordinary skill in the art.

As the defendants point out, medical literature acknowledges that there is "considerable confusion regarding the definition of dry eye." Stephen C. Pflugfelder et al., The Diagnosis and Management of Dry Eye: A Twenty-five-Year Review, 19 Cornea 644 (2000). The defendants' expert, Dr. Andrew F. Calman, said the same thing in his declaration. He stated that "[a] number of different terms have been used by various authors to describe various subgroups of patients with 'dry eye' symptomatology: dry eye, dry eye syndrome, dry eye disease, keratoconjunctivitis sicca (KCS), keratitis sicca, sicca syndrome, sicca complex, Sjogren syndrome, aqueous deficient dry eye, evaporative dry eye, dry eye associated with Meibomian gland dysfunction, and others." Declaration of Andrew F. Calman, Dkt. No. 165-24, at 7. He explained that different authors have used those terms in different ways, and that the terminology in the field "has been murky and inconsistent at best, and self-contradictory at worst." Id. His declaration

cites several authorities that have noted the heterogeneity of dry eye and the variety of tear film abnormalities that are included within the general category of "dry eye." Id. at 8-11.

Allergan responds that despite differences in usage, persons of ordinary skill in the art know the meaning of KCS and "dry eye," including the terms "dry eye disease" and "dry eye syndrome." Allergan's expert, Dr. Robert J. Noecker, stated that "[d]ry eye encompasses a broad group of tear film disorders generally caused by reduced tear production, tear evaporation, or an imbalance in tear film components (leading to decreased tear quality)." Declaration of Robert J. Noecker, M.D. in Support of Plaintiff Allergan's Claim Constructions, Dkt. No. 155-35, ¶ 19, at 7. Dr. Noecker defined KCS as "a disease falling within the broader category of 'dry eye' disease," which is characterized by inflammation of the conjunctiva and cornea "associated with decreased tears and decreased tear quality." Id. ¶ 22, at 9; id. ¶¶ 30-31, at 12-13. He added that although KCS is sometimes colloquially referred to as "dry eye," a person of ordinary skill in the art "would understand that dry eye is a broader category of disorders of the tear film, and that KCS is a subset of dry eye disease or dry eye syndrome." Id. ¶ 30, at 12.

In support of those assertions, Dr. Noecker referred to various resources, including a 2011 publication of the American Academy of Ophthalmology, which defined "dry eye syndrome" as referring to "a group of disorders of the tear film that are due to reduced tear production or excessive tear evaporation that is associated with ocular discomfort and/or visual symptoms and may cause disease of the ocular surface. This group of disorders is usually referred to as dry eye." American Academy of Ophthalmology Cornea/External Disease Panel, Dry Eye Syndrome—Limited Revision 3 (2011). Dr. Noecker also relied on the definition set forth in a 1999 patent, which stated: "Dry eye generally refers to any tear film abnormality, usually with epithelial abnormalities. A specific deficiency of the aqueous component of the tear

film is known as keratoconjunctivitis sicca (KCS) . . . . Literally, the term denotes inflammation of the cornea and conjunctiva secondary to drying." U.S. Patent No. 5,981,607, col. 1, ll. 18-24.

With respect to Dr. Calman's views on the indefiniteness issue, Allergan notes that during his deposition Dr. Calman provided a general definition of the term "dry eye," which he said he used colloquially to refer to a complex of related conditions. While he stated that there is "a lot of different terminology in this field . . . . a lot of confusion and contradictions, many different definitions," he explained that he used the term "dry eye" as a non-specific term to encompass "a group of disorders that have in common some feature of symptoms and/or signs and/or objective findings related to problems with the tear film, whether it's problems of quantity or quality or other conditions that may manifest with similar symptomatology and/or signs or objective findings. So it's a catch-all term." Videotaped Deposition of Andrew Calman, M.D., Dkt. No. 165-2, at 15:4 to 15:10. The upshot of Dr. Calman's testimony is that, while there is disagreement about the precise definition of "dry eye" and its related terms, "dry eye" is generally used to refer to tear film disorders that result in a reduction in the quantity or quality of tears.

Allergan also points to articles and other patents in the field that use the term "dry eye" or its variants in a way that indicates a consensus as to the general meaning of the term, while recognizing that there has for some time been a lack of precision in the definitions used by experts in the field. An article by Dr. Kenneth Sall and others that was cited and "incorporated in its entirety . . . herein by reference" in the patents in suit, see, e.g., '111 patent, col. 1, ll. 52-53,[3] referred to "dry eye disease" as a condition that is characterized by "discomfort, burning,

[3] The parties dispute whether the definitional discussion in the Sall article was properly incorporated by reference in the patents in suit. For present purposes, however, it is not important to resolve that question. At minimum, the article represents the views of persons of

irritation, photophobia, and . . . blurred vision, gradual contact lens intoleration, and the inability to produce emotional tears." Kenneth Sall et al., Two Multicenter, Randomized Studies of the Efficacy and Safety of Cyclosporine Ophthalmic Emulsion in Moderate to Severe Dry Eye Disease, 107 Ophthalmology 631 (2000). Other articles in the field had much the same thing to say about what was variously termed "dry eye" and "dry eye disease." As the disorder has become better understood over time, the definition has become more precise.

A 1995 report summarized the results of the meetings of the National Eye Institute/Industry Workshop on Clinical Trials in Dry Eyes, held at the National Institutes of Health in 1993 and 1994. The meetings were held to identify areas of consensus and disagreement in the design and interpretation of clinical trials regarding dry eye. Michael A. Lemp, Report of the National Eye Institute/Industry Workshop on Clinical Trials in Dry Eyes, 21 CLAO Journal 221 (1995). The report noted that there were varying definitions of the terms "dry eye" and "KCS" among practitioners in the field. The report recommended the following definition: "Dry eye is a disorder of the tear film due to tear deficiency or excessive tear evaporation which causes damage to the interpalpebral ocular surface and is associated with symptoms of ocular discomfort." Id. at 222; see also Stephen C. Pflugfelder, The Diagnosis and Management of Dry Eye, 19 Cornea 644, 645-46 (2000).

Other contemporaneous authorities offered similar definitions. A text published in 1998 referred to the "colloquial, nonspecific" term "dry eye" as referring to "any tear film abnormality, usually with corneal epithelial abnormalities." The text equated "dry eye" with tear film dysfunction, which it defined as "any tear film abnormality and specifically includes

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skill in the art at a time near the September 15, 2003, priority date of the patents. For that reason, regardless of whether the article was properly incorporated by reference in the common specification, it is relevant to the indefiniteness issue.

disorders of the aqueous, mucin and lipid components of the tear film." R. Doyle Stulting et al., Diagnosis and Management of Tear Film Dysfunction in Corneal Disorders: Clinical Diagnosis and Management 482-83 (2d ed. 1998). The text defined KCS as denoting "inflammation of the cornea and conjunctiva caused by drying," and it characterized "dry eye" as resulting from decreased aqueous tear production or from increased evaporative loss. Id. at 483. A subsequent publication of the American Academy of Ophthalmology characterized dry eye disorders generally as a "common disorder of the tear film [that] results from either decreased tear production or excessive tear evaporation." American Academy of Ophthalmology, Basic and Clinical Science Course: External Disease and Cornea—Section 8 75 (2002).

The American Academy of Ophthalmology has continued to use that definition. Moreover, as noted above, the Academy uses the terms "dry eye syndrome" and "dry eye" synonymously, defining "dry eye syndrome" as "a group of disorders of the tear film," usually referred to as "dry eye," that are "due to reduced tear production or excessive tear evaporation." American Academy of Ophthalmology Cornea/External Disease Panel, Dry Eye Syndrome—Limited Revision 3 (2011).[4]

A 2007 report of the Dry Eye Workshop, an international panel of experts in dry eye disease, reviewed the definition of dry eye disease adopted in the 1995 report of the National Eye Institute/Industry Dry Eye Workshop. The Definition and Classification of Dry Eye Disease, 5 The Ocular Surface No. 2 (2007). The 2007 report contained a glossary that defined "dry eye syndrome" as "that collection of clinical conditions that produce abnormalities of the tears and ocular surface, usually by decreased tear production or increased tear evaporation"; it defined

[4] A 2006 study recommended the use of the term "dysfunctional tear syndrome" in place of "dry eye" as a more appropriate term for the disease. Ashley Behrens et al., Dysfunctional Tear Syndrome—A Delphi Approach to Treatment Recommendations 25 Cornea 900, 902-03 (2006).

KCS as "the condition of dry eye and inflammation of the ocular described by Henrik Sjogren, MD. Now commonly used interchangeably with dry eye syndrome." Id. at 73. The text of the 2007 report suggested that the definition set forth in the 1995 workshop report could be improved in light of "new knowledge about the roles of tear hyperosmolarity and ocular surface inflammation in dry eye and the effects of dry eye on visual function." Id. at 75. Accordingly, the 2007 report defined "dry eye" as "a multifactorial disease of the tears and ocular surface that results in symptoms of discomfort, visual disturbance, and tear film instability with potential damage to the ocular surface. It is accompanied by increased osmolarity of the tear film and inflammation of the ocular surface." Id.

In addition to citing these publications by experts in the field, Allergan relies on statements by defendant Mylan during the inter partes review proceedings relating to the patents in suit, in which Mylan adopted the definition of KCS as "an 'inflammation of the conjunctiva and of the cornea' that is 'associated with decreased tears' and is a species of, and is often used interchangeably with, or as a partial synonym of, dry eye disease." Petition for Inter Partes Review of U.S. Patent No. 8,629,111, Case No. IPR2016-01128 (June 3, 2016), Dkt. No. 155-27, at 14. Allergan also relies on a statement by one of the defendants' experts, Dr. Erning Xia, who stated in a declaration submitted in the inter parties review proceeding that, as of the priority date of the patents, "it was known that dry eye disease was an ophthalmic condition that resulted in many troublesome symptoms, such as burning, irritation, discomfort, photophobia, blurred vision, lack of natural tear production, contact lens intolerance, and an increased risk of ocular surface damage and infection." Declaration of Erning Xia, Ph.D. (May 21, 2015), Dkt. No. 155-26, at 21. A person of ordinary skill in the art, according to Dr. Xia, "would have known that dry eye was characterized by an elevated inflammatory state of certain eye tissues."

In light of all the evidence presented by the parties, the Court is persuaded that as of the patent's September 15, 2003, priority date the terms "dry eye," "dry eye disease," and "dry eye syndrome" were used interchangeably in the art to describe the same disorder. That disorder was subject to somewhat varying definitions, but the core meaning was clear. In light of the 1995 report on the National Eye Institute/Industry Workshop, it is clear to the Court that at least as of that time, the terms dry eye, dry eye disease, and dry eye syndrome were generally used synonymously in the art and that the meaning of those terms was reasonably certain. The Court concludes that the meaning of that group of terms to a person of ordinary skill as of the patents' priority date is best captured by the American Academy of Ophthalmology's 2002 definition: "a tear film dysfunction, or a disorder of the tear film that is due to reduced tear production or excessive tear evaporation."

As for the term "KCS," the Court's analysis is affected by the fact that the three patents that contain claims referring to KCS (the '111 patent, the '048 patent, and the '930 patent) contain a specification passage that provides enlightenment as to the patentees' understanding of that term.[5] In that passage, the specification of those three patents equates KCS to "dry eye disease" and refers to KCS as "an absolute or partial deficiency in aqueous tear production." See '111 patent, col. 2, line 65, and col. 3, ll. 3-5. In effect, then, the '111 patent, the '048 patent, and the '930 patent offer a definition of KCS. Although that definition is arguably somewhat broader than the definition used by practitioners in the art at the time, the Court regards that definition as controlling for purposes of those three patents. And because the term KCS has

[5] The portion of the common specification that contains those references to KCS is found in the patents that contain claims referring to KCS, but not in the other three patents. See '111 patent, col. 2, line 65, through col. 3, line 11; '048 patent, col. 2, line 65, through col. 3, line 11; '930 patent, col. 2, line 64, through col. 3, line 10.

what amounts to an explicit definition in those three patents, the Court concludes that the term as used in the claims of those patents is not indefinite.

With respect to the remaining challenged terms, the defendants point out that the patents use the terms "dry eye," "dry eye disease," and "dry eye syndrome" in different claims without clearly distinguishing among them. For example, the '111 and '930 patents use the term "dry eye" or KCS in each of the claims in which any form of dry eye disorder is referenced. The '556 and '191 patents exclusively use the term "dry eye disease." The '048 patent exclusively uses the term "KCS." The '162 patent uses the term "dry eye disease" in most of the claims that refer to the disorder, but it uses the term "dry eye syndrome" in one independent claim and in the claims that depend form that claim (claims 18 through 22).

That pattern of inconsistent usage is not explained, and it makes construing the patents more difficult, but in the end it is not fatal. The common specification of the patents in suit uses the terms "dry eye syndrome" and "dry eye disease" interchangeably, with no apparent intent to assign those terms different meanings. See, e.g., '111 patent, col. 2, ll. 64, 66; and col. 14, ll. 34, 39, 67 (all referring to "dry eye disease"); col. 2, line 64; col. 5, ll. 14-15, 18, 29-30; col. 14, line 55 (all referring to "dry eye syndrome"); and col. 12, line 4 (referring to "dry eye"). For example, in the discussion of Example 1, the specification refers to the two exemplary compositions as being employed in a study of the treatment of "dry eye disease," id., col. 14, ll. 34, 39; then, in connection with the reference to composition II from that example, the specification refers to the benefits of castor oil "to assist in treating dry eye syndrome," id., col. 14, line 55. The text then notes that the breakdown of the emulsion facilitates the therapeutic effectiveness of the composition "in treating dry eye disease." Id., col. 14, line 67. It is apparent

from that passage that the terms "dry eye disease" and "dry eye syndrome" are being used interchangeably.

The defendants argue that the terms "dry eye," "dry eye disease," dry eye syndrome," and "KCS" cannot all have the same meaning in the patents, because of the manner in which they are used in the some of the asserted claims. For example, claim 20 of the '111 patent claims the topical emulsion of claim 1, "wherein the topical ophthalmic emulsion is therapeutically effective in treating dry eye," while claim 21 claims the same topical emulsion "wherein the topical emulsion is therapeutically effective in treating keratoconjunctivitis sicca." In another context, the use of those two different terms in parallel claims might suggest that the terms were intended to have a different meaning. In this context, however, the Court interprets the claims to be structured so as to ensure that, given the sometimes varying meaning attached to those terms, the claims would cover the entire range of disorders generally grouped under the terms dry eye or KCS. The intended purpose of obtaining breadth of coverage is further revealed by claim 22, the third dependent claim in that series, which claims the same topical emulsion "wherein the topical emulsion is therapeutically effective in increasing tear production."

The same analysis applies to other sets of claims throughout the asserted patents, such as dependent claims 21 and 22 of the '162 patent. Claim 21 refers to the use of a particular emulsion "for treating dry eye syndrome," while claim 22 refers to the use of the same emulsion "in treating dry eye disease."

An example that is instructive in suggesting how the claim terms should be construed is found in claims 18 and 22 of the '162 patent. Claim 18 recites a method of "reducing the side effects in a human being treated for dry eye syndrome." Claim 22, which depends from claim 18, recites the method of claim 18, "wherein the emulsion is effective in treating dry eye

disease." While the use of different terms in the independent and dependent claims might ordinarily suggest that they be assigned different meanings, it does not have that effect here. The independent claim recites the use of a particular emulsion to reduce side effects; the dependent claim adds that, in addition to reducing side effects, that particular emulsion provides effective treatment for the underlying disorder. Read together, the two claims make sense only if the terms "dry eye disease" and "dry eye syndrome" mean the same thing. Otherwise, the dependent claim would have the odd effect of claiming an emulsion that was effective in treating one condition while reducing side effects in persons treated for a different condition. The Court therefore concludes that the terms are used to mean the same thing.

Because the Court finds that the meanings of the terms "dry eye," "dry eye disease," and "dry eye syndrome" would be reasonably clear to a person of ordinary skill in the art as of the patents' priority date, the Court concludes that the defendants have failed to show that the claims containing those terms are indefinite. As for the term KCS, the Court is satisfied that that term is adequately defined in the common specification. For purposes of the asserted patents, the Court will give that term the meaning it has in the specification.

Accordingly, the Court construes the terms "dry eye," "dry eye disease," and "dry eye syndrome," as those terms are used in the asserted patents, to mean **"a disorder of the tear film due to reduced tear production or excessive tear evaporation that is associated with ocular discomfort and/or visual symptoms and may cause disease of the ocular surface."** The Court defines keratoconjunctivitis sicca to mean **"a type of dry eye disease involving an absolute or partial deficiency in aqueous tear production."** The Court concludes that none of those terms is indefinite.

2. "effective in treating dry eye/dry eye disease/keratoconjunctivitis sicca; therapeutically effective in treating dry eye/dry eye disease/keratoconjunctivitis sicca; therapeutic effectiveness; therapeutic efficacy"

Allergan argues that these related phrases should be given their plain and ordinary meaning, which is "effective in treating the underlying disease." The defendants offer no competing definitions, but argue that all of the "efficacy" phrases in the patents are indefinite.

The defendants' principal argument with respect to these limitations is that the claimed invention cannot be effective in treating the underlying disease because, in light of "the imprecise and haphazard use of the dry eye terms and KCS within the claims and specification," the patents "fail to state the precise disease being treated." Because the Court has rejected the defendants' argument that the identity of the diseases being treated is indefinite, the Court likewise rejects the argument that it is necessarily indiscernible whether the invention is effective in treating the underlying disease.

The defendants also argue that it is impossible to determine whether a particular treatment is effective against a particular disease without knowing "which of the underlying causes of dry eye, dry eye disease, dry eye syndrome, or KCS are to be treated using the alleged invention." Defendants' Responsive Claim Construction Brief, Dkt. No. 165, at 11. Because "there are multiple causes of dry eye and KCS," the defendants argue that a person of ordinary skill in the art "would not be able to pinpoint the underlying disease to be treated, and would not understand with a reasonable certainty the metes and bounds of the asserted claims." Id.

In fact, however, it is not uncommon that an effective remedy for particular maladies is discovered even though those who have devised the remedy do not understand the causes of the maladies or the mechanism by which the remedy works. In this case, the test of efficacy is

simply whether the invention successfully treats the condition. It is not necessary that the process by which the emulsion works to address the condition be fully understood.

The defendants suggest that because dry eye symptoms can be produced by a variety of causes, such as, for example, environmental pollution, the claims cannot be therapeutically effective against dry eye because there are some forms of dry eye that will not respond to the treatments set forth in the claims. Nothing in the claims, however, requires that the claimed emulsions be effective against all forms of dry eye, no matter what the cause of the condition. The "therapeutic efficacy" claims simply recite an emulsion that is generally effective against dry eye disorders, or at least against some subset of all dry eye disorders. An emulsion that is not effective against at least some types of dry eye disorders will not infringe. Thus, it is incumbent upon the plaintiff in an infringement action to prove that the accused product is therapeutically effective against the recited condition in at least some instances. The plaintiff's inability to show that a particular emulsion is effective against the pertinent dry eye disorder in at least some category of cases will result in a judgment for the defendant.

The defendants argue that the patents fail to describe methods for determining whether a particular emulsion is effective, but a protocol for measuring efficacy is not required as a prerequisite for patenting the emulsion. An emulsion that is shown to have therapeutic benefits by relieving the underlying disease condition, either wholly or to some discernible extent and in some category of cases, will fall within the scope of the pertinent claims. There is no need for a separate construction of the "efficacy" terms.

Accordingly, **the disputed phrases will be given their ordinary meaning, which is "effective in treating the underlying condition."** The Court concludes that none of those phrases is indefinite.

3. "effective amount in treating dry eye/dry eye disease/keratoconjunctivitis sicca"

Four claims among the asserted claims of the six patents in suit contain limitations relating to an "effective amount" of the claimed emulsion. All four claims follow the same pattern. Each recites an emulsion which, when administered in "an effective amount" in treating either KCS, dry eye, or dry eye disease, results in the blood of the patient having substantially no detectable concentration of cyclosporin A. See '048 patent, claim 21; '556 patent, claim 11; '930 patent, claims 11 and 23.

Allergan argues that these related phrases should be given their plain and ordinary meaning, which is "an amount effective to treat the underlying disease." The defendants offer no competing definitions; instead, they argue that all of the "effective amount" phrases in the patents are indefinite.

The analysis applied to the "efficacy" limitations applies to this limitation as well. The claims do not set forth a quantitative measure of the amount of the emulsion necessary to be effective, nor do they set forth the degree of efficacy that must be attained. What they require is that when a sufficient amount of the emulsion is delivered to the patient to be therapeutically effective, at least to some measurable degree in some category of cases, substantially no detectable cyclosporin A will be found in the patient's bloodstream. Those claims are consistent with one of the underlying objectives of the invention, which is to avoid the potential side effects that result when cyclosporin treatments result in some of the administered cyclosporin finding its way into the patient's bloodstream.

The "effective amount" limitation requires the patentee to prove that (1) an accused product is delivered in an amount that is therapeutically effective, i.e., it has discernible effects in ameliorating the underlying condition, and (2) when a therapeutically effective amount is

delivered, it does not result in a substantial amount of cyclosporin entering the patient's bloodstream. The first element is not indefinite, since it can be established by proof of therapeutic efficacy which, as noted above, is not an indefinite limitation. The second element is likewise not indefinite, as the parties have agreed on the amount of cyclosporin that constitutes a "substantially detectable" amount. That element can be established simply by testing.

Accordingly, the Court concludes that **the term "effective amount" in the phrases that use that term will be given its ordinary meaning, which is "an amount effective to treat the underlying condition."** The Court holds that the term "effective amount" is not indefinite.

4. "as substantially therapeutically effective as a second emulsion/achieves at least as much therapeutic effectiveness/efficacy as a second emulsion; second topical ophthalmic emulsion"

Thirteen claims among the various asserted patents contain limitations comparing the effectiveness of the claimed emulsion with the effectiveness of a second emulsion having twice the concentration by weight of cyclosporin as the first emulsion, but the same concentration by weight of castor oil. In each claim, the first composition contains 0.05% cyclosporin by weight and 1.25% castor oil by weight, while the second composition contains 0.1% cyclosporin by weight and 1.25% castor oil by weight. See '162 patent, claim 14; '556 patent claims 1, 13-15; '048 patent, claims 13-16; '191 patent, claims 1, 13, 17, 21.

The defendants offer no competing definitions, but argue that the phrases at issue are indefinite. Allergan argues that these phrases should be construed to mean that the first emulsion is "substantially as effective in treating the underlying disease as a second emulsion" and that the first emulsion "achieves as much effectiveness/efficacy in treating the underlying disease" as the second emulsion.

The defendants point out that while the claims list all the constituents of the first emulsion, they list only the cyclosporin and castor oil components of the second. Because the other components are not specified, the defendants argue that those other components could include anything at all, and thus those claim limitations are essentially meaningless.

This hypertechnical approach to the construction of these claims is wholly unpersuasive. The specification contains an example that sets forth a comparison of two emulsions, the first with 0.05% cyclosporin and 1.25% castor oil, and the second with 0.1% cyclosporin and 1.25% castor oil. The example lists the other constituents of both emulsions, which are exactly the same. See '111 patent, col. 14, ll. 11-49. Although the claims do not explicitly say so, the context makes it clear that the "second emulsion" referred to in each claim is exactly the same as the first except with regard to the concentration of cyclosporin. That is the entire point of the comparison and, indeed, one of the principal points of the invention: that the relative concentration of cyclosporin can be reduced, in an otherwise identical emulsion, without substantial loss of therapeutic effectiveness. Given that the claims are plainly drawn to track the example given in the specification, the Court finds that the language of the claims is not indefinite and that the unspecified constituents of the "second emulsion" are understood to be the same as the non-cyclosporin constituents of the first emulsion.

Accordingly, the Court construes these limitations to mean that **"the first emulsion is "substantially as effective in treating the underlying disease as a second emulsion" and "achieves as much effectiveness/efficacy in treating the underlying disease."** In light of that construction, the Court holds that those limitations are not indefinite.

5. "enhancing [lacrimal gland] tearing" and "restoring [lacrimal gland] tearing"

The phrase "enhancing tearing" or "enhancing lacrimal gland tearing" appears in four of the asserted claims: independent claim 13 and dependent claims 14, 15, and 16 of the '191 patent. Claim 13 recites in pertinent part "[a] method of enhancing tearing in a human eye . . . ." Dependent claims 14 and 15 add specific features to the composition of the claimed emulsion. Dependent claim 16 recites the method of claim 13, "wherein the method is effective in enhancing lacrimal gland tearing."

The phrase "restoring tearing" or "restoring lacrimal gland tearing" appears in seven of the asserted claims: independent claim 21 and dependent claims 22 through 27 of the '191 patent. Claim 21 recites in pertinent part "[a] method of restoring tearing . . . ." Dependent claims 22 through 25 and 27 add specific features to the method. Dependent claim 26 claims the method of claim 21, "wherein the method is effective in restoring lacrimal gland tearing."

Allergan argues that these phrases should be given their plain and ordinary meaning. In the context of the patents in suit, according to Allergan, the terms "enhance" and "restore" refer not just to an increase in the amount of tearing, but also to an increase in "the quality of a patient's tears." Once again, the defendants offer no competing definition for the phrases at issue, but argue that the phrases are indefinite.

The ordinary meaning of the term "enhance" is to "advance, augment, elevate, heighten, [or] increase." Webster's Third New Int'l Dictionary 753 (2002 ed.). The ordinary meaning of the term "restore" is "to bring back or put back into a former or original state, to renew, rebuild, reconstruct"; to "bring back to a healthy state"; or "to bring back from a state of injury or decay or from a changed condition"; "to bring (as a person) back to some former state." Id. at 1936. That is, the term "enhance" simply means to increase or make better. The term "restore" in the

context of medical treatment, means to return a person to a prior, healthy state. Nothing in the claims or the specification indicates that the patents in suit have assigned the terms "enhance" or "restore" a special meaning for these patents that differs from their ordinary meaning in the context of medical treatment.

The specification contains two pertinent uses of the terms "enhance" (or "enhancement") and "restore" (or "restoring"). The first appears in the passage of the specification that is found only in the '111, '048, and '930 patents. There, the specification states: "Cyclosporin has been found as effective in treating immune mediated keratoconjunctivitis (KCS or dry eye disease) in a patient suffering therefrom. The activity of cyclosporine [sic] is as an immunosuppressant and in the enhancement or restoring of lacrimal gland tearing." '111 patent, col. 2, line 65, through col. 3, line 2. The second reference in the common specification appears in a further discussion of the role of the cyclosporin component as an immunosuppressant. The pertinent sentence reads: "Without wishing to be limited to any particular theory of operation, it is believed that, in certain embodiments of the present invention, the cyclosporin component acts to enhance or restore lacrimal gland tearing in providing the desired therapeutic effect." '111 patent, col. 9, ll. 8-12. In both of those references, it is evident that no special meaning of the terms "enhance" or "restore" is intended; the passages simply state that the cyclosporin component has the desired therapeutic effect of enhancing or restoring lacrimal gland tearing, i.e., increasing tearing or returning the patient's tearing function to its prior healthy state. The Court finds nothing indefinite about those terms.

a. In support of their contention that the term "enhanced" is indefinite, the defendants rely on the district court decision in Andrulis Pharmaceuticals Corp. v. Celgene Corp., Civil Action No. 13-1644 (RGA), 2015 WL 3978578 (D. Del. June 26, 2015), which was summarily

affirmed without opinion by the Federal Circuit, Andrulis Pharms. Corp. v. Celgene Corp., No. 2015-1962 (Fed. Cir. July 14, 2016). That case, however, is of no help to the defendants, as it involved an entirely different issue regarding the use of the term "enhanced."

The principal claim at issue in Andrulis was to a method of treatment of neoplastic diseases comprising "administering to [the afflicted patient] enhanced therapeutically-effective amounts of thalidomide in combination with effective amounts of other alkylating agent . . . wherein said neoplastic diseases are sensitive to said enhanced combination." The problem identified by the court was that it was entirely unclear whether the term "enhanced" referred to efficacy from the combination of components that was less than additive, additive, or greater than additive. Thus, the problem was not with the term "enhanced," which the court defined, according to its common usage, to mean improve, increase, or intensify. The problem had to do with the degree of enhancement, which the court found was left unspecified in a setting in which the degree of enhancement was critical.

In this case, there is no issue regarding the requisite degree of enhancement of tearing. The claims that recite "a method of enhancing tearing" or a method "effective in enhancing lacrimal gland tearing" simply requires some degree of enhancement, i.e., some augmentation or increase. That interpretation of the term is consistent with the specification and the ordinary meaning of the word "enhance."

Although Allergan argues that "enhancing," as that term is used in the claims, entails an increase in both the quantity and the quality of tears, the Court is not persuaded that "enhancing" includes such a requirement. In support of its argument, Allergan points to the study by Kenneth Sall et al. cited in the common specification, which states that the composition that is the subject of the asserted patents results in increases in the quantity and quality of tears. While that may be

true, it does not justify interpreting the term "enhancing" to require increases in both quantity and quality. Enhancement, according to its ordinary meaning, would be satisfied by an increase in either metric.

In further support of its argument, Allergan contends that "enhancing" must mean more than just an improvement in the amount of tears, since other claims in the patents refer to "increasing tear production." See '111 patent, claims 22, 24; '930 patent, claim 25-36. That argument, too, is unconvincing. As noted, the patents contain various overlapping terms and claims, such as the claims variously referring to "dry eye," "dry eye disease," and "dry eye syndrome." As to those terms, Allergan argues that the terms overlap (or even have identical scope), and that the use of different terms does not mean that they must have different meanings. The same argument applies with at least equal force to the terms "enhancing" and "increasing tear production." Enhancement covers an increase in tear production, and it also covers an increase in tear quality. But nothing in the term "enhancement," or the way it is used in the patents, suggests that tear production is not "enhanced" unless there is an increase in both the quantity and quality of the tears.

b. The defendants argue that the term "restoring" suggests "an increase in the amount of tears from a zero or near-zero level of tear production," but that a person of ordinary skill in the art "would have no idea how much increase in tearing would occur as a result of using the alleged invention, or whether such increase would restore tear production to normal or some other level." Defendants' Responsive Claim Construction Brief, Dkt. No. 165, at 14. As noted above, the ordinary meaning of the term "restore" in the medical context is to return the patient to a previous, healthy state. While that may not entail returning the patient to a condition regarded as normal for the general population, it does contemplate that the patient's tear

production will be returned to the status the patient enjoyed prior to the onset of the condition in question, or something close to it. As such, the term would be reasonably clear to a person of skill in the art.

Accordingly, the phrases **"enhancing [lacrimal gland] tearing" and "restoring [lacrimal gland] tearing" will be given their ordinary meaning. As such, the Court construes the phrase "enhancing [lacrimal gland] tearing," to mean increasing the quantity and/or quality of tearing, and the Court construes the phrase "restoring [lacrimal gland] tearing" to mean returning the quantity and/or quality of tearing, in whole or in part, to a prior, healthy state.** The Court concludes that those phrases are not indefinite.

6. "about"

Allergan argues that the term "about," which appears in a number of the asserted claims, should be given its plain and ordinary meaning. The defendants disagree. Based on the prosecution history, the defendants argue that the term "about" must be interpreted to mean "precisely." In the alternative, the defendants argue that the term is indefinite and that the claims containing that term are invalid.

Almost every claim in the patents in suit that contains a limitation respecting the quantity of particular components uses the term "about" to modify the recited amount.[6] For example, claim 1 of the '111 patent recites, in pertinent part: "A topical ophthalmic emulsion for treating an eye of a human comprising cyclosporin A in an amount of about 0.05% by weight, polysorbate 80, acrylate/C10-30 alkyl acrylate cross polymer, water, and castor oil in an amount of about 1.25% by weight."

[6] There are a few exceptions: claims 13, 14, and 16 of the '162 patent and claims 13, 14, and 16 of the '048 patent.

The Federal Circuit has held that the ordinary meaning of the term "about" is "approximately." Ferring B.V. v. Watson Labs, Inc.-Fla., 764 F.3d 1382, 1389 (Fed. Cir. 2014). Absent a redefinition of the term discernible from the specification, the court has held that the term "about" should be given that meaning. Merck & Co. v. Teva Pharms. USA, Inc., 395 F.3d 1364, 1369-70 (Fed. Cir. 2005).

a. Pointing to the prosecution history of the patents in suit, the defendants say that the patentees limited the scope of their claims to the precise numerical values recited in the asserted claims, and thus that the term "about" must be construed to mean "precisely the amount claimed." This argument is entirely unconvincing. It would take a clear and explicit disclaimer or redefinition to justify construing the term "about," a word of approximation, to mean "precisely," a word that by definition admits of no approximation at all. The effect would be to use claim construction to define a term as meaning its own antonym, which would be an exceptional result. See Merck & Co., 395 F.3d at 1370 (intrinsic evidence "fails to redefine 'about' to mean 'exactly' in clear enough terms to justify such a counterintuitive definition of 'about.'"); Glycobiosciences, Inc. v. Innocutis Holdings, LLC, 146 F. Supp. 3d 221, 235 (D.D.C. 2015) ("[T]he entire point of using a word like 'about' is that it eschews precision; if the patentees intended to claim a precise weight range, they would have specified that precise weight range."). There is no such clear disclaimer or redefinition in the prosecution history record in this case, as a close examination of the prosecution history will reveal.

The prosecution history of the six patents in suit is complex. The prosecution began with provisional application No. 60/503,137, filed on September 15, 2003, and application serial number 10/927,857 ("the '857 application"), which was filed on August 27, 2004. The pertinent claims of the '857 application read as follows:

> 21. A composition for treating an eye of a human or animal comprising an emulsion comprising water, a hydrophobic component, and a cyclosporin component in a therapeutically effective amount of less than 0.1% by weight, the weight ratio of the cyclosporin component to the hydrophobic component being less than 0.08.
>
> 26. The composition of claim 21 wherein the hydrophobic component is present in an amount greater than 0.625% by weight of the composition.

As the defendants point out, the qualifier "about" was not found in any of the claims of the '857 application.

The examiner rejected the claims of the '857 application on several grounds, including obviousness over U.S. Patent No. 5,474,979 to Ding. Office Action (Jan. 17, 2007), Dkt. No. 165-14, at 12-16. The examiner found that Ding taught a composition containing a cyclosporin component in an amount less than 0.1% by weight and a hydrophobic component (castor oil) having a weight ration to the cyclosporin component of 0.08. The examiner further found that Ding taught that the weight ratio of the cyclosporin component to the hydrophobic component could vary between 0.02 and 0.12. Based on her analysis of Ding, the examiner concluded that the claims of the '857 application would have been obvious to one of ordinary skill in the art at the time of the invention. Id. at 13.

The applicants then added new claims reciting a composition containing 1.25% castor oil and 0.05% cyclosporin A. The pertinent amended claims 37-40 read as follows:

> 21. A composition for treating an eye of a human or an animal comprising an emulsion comprising water, castor oil, and cyclosporin A in a therapeutically effective amount of less than 0.1% by weight, the weight ratio of the cyclosporin A to the castor oil being less than 0.08.
>
> 26. The composition of claim 21 wherein the castor oil is present in an amount greater than 0.625% by weight of the composition.
>
> 37. The composition of claim 21 which includes 1.25% by weight of castor oil.

> 38. The composition of claim 21 which includes 0.05% by weight of cyclosporin A.
>
> 39. the composition of claim 38 which includes 1.25% by weight of castor oil.
>
> 40. A composition for treating an eye of a human or animal comprising an emulsion comprising water, 1.25% by weight of castor oil and 0.05% by weight of cyclosporin A, the weight ratio of the cyclosporin A to the castor oil being 0.04%.

Amendment (Mar. 27, 2007), Dkt. No. 165-15, at 10.

The applicants argued that the recited compositions produced unexpected benefits over other formulations, such as the compositions set forth in Example 1 in Ding having either a greater relative amount of cyclosporin or a greater absolute percentage of both cyclosporin and castor oil. Amendment A (Mar. 27, 2007), Dkt. No. 165-15, at 16-18. The examiner, however, entered a final rejection on July 2, 2007, again finding the application claims obvious over Ding. Office Action (July 2, 2007), Dkt. No. 165-16. The examiner found that Ding taught an emulsion that could consist of between about 0.05% and about 0.40% cyclosporin A, and between 0.625% and about 5.0% castor oil. Id. at 5-6. The examiner concluded that it would have been obvious to modify the composition of Ding by increasing the amount of castor oil or decreasing the cyclosporin concentration to the levels recited in the application claims; the examiner further found that the applicants had not shown that their claimed composition produced unexpected results as compared to the compositions disclosed in Ding. Id. at 13-18.

In the course of further proceedings on the ’857 application, the applicants argued that it was unpredictable from Ding that the claimed compositions would have overall efficacy against dry eye diseases substantially equivalent to the efficacy of compositions having twice the concentration of cyclosporin. Amendment B (Aug. 27, 2007), Dkt. No. 165-17, at 13-14. In addition, the applicants noted that “the present claim limitations do not use the term ‘about’ with

respect to these [numerical] limitations, and therefore there is no overlap with the exemplary compositions of Example 1 [of Ding]." Id. at 16.

Those arguments were unsuccessful. The applicants ultimately filed a new continuation application, serial number 11/897,177 ("the '177 application") and abandoned the '857 application. In the proceedings on the '177 application, the applicants initially conceded that it would have been obvious to modify the examples of the Ding reference to arrive at the claimed composition. Amendment (June 15, 2009), Dkt. No. 165-9, at 8-9. Subsequently, however, the applicants withdrew that concession, see Preliminary Amendment (Aug. 7, 2013), Dkt. No. 165-12, at 8, and sought to continue the prosecution of their claims through eight new applications filed in 2013, and subsequently a ninth filed in 2014.[7] In the claims of the new applications, the term "about" was added to modify most of the recited numerical values. Those applications ultimately became the six patents at issue in this case.[8]

After an initial rejection of four of those applications, again based on the compositions disclosed in Ding, see, e.g., Application Serial Number 13/967,163, Office Action (Oct. 17, 2013), the applicants responded by submitting declarations from a clinician and an Allergan research investigator, who stated that the claimed formulations provided surprising and unexpected results that were not predictable based on the data in the prior art Ding patent. See, e.g., Application Serial Number 13/967,163, Response to Non Final Office Action Dated Oct.

[7] The applications filed in 2013 were application serial numbers 13/961,808; 13/961,818; 13/961,828; and 13/961,835, all of which were filed on August 7, 2013, and serial numbers 13/967,163; 13/967,168; 13/967,179; and 13/967,189, all of which were filed on August 14, 2013. The '808, '818, and '835 applications were later abandoned. The '828, '163, '168, '179, and '189 applications ultimately issued as the '930, '111, '048, '162, and '556 patents, respectively. The application filed in 2014 was application serial number 14/222,478. That application ultimately issued as the '191 patent.

[8] The '177 application ultimately issued as U.S. Pat. No. 8,618,064. That patent has not been asserted in this case.

17, 2013 (Oct. 23, 2013), at 8-12. In particular, the two declarants asserted that the specific combination of 0.05% by weight cyclosporin A with 1.25% by weight castor oil is surprisingly critical for therapeutic effectiveness in the treatment of dry eye/keratoconjunctivitis sicca. Declaration of Dr. Rhett Schiffman, Dkt. No. 165-20, at 6; Declaration of Dr. Mayssa Attar, Ph.D., Dkt. No. 165-21, at 3-5. In light of the studies and data described by Drs. Schiffman and Attar, the examiner allowed the pending claims of application serial number 13/967,163 ("the '163 application), which became the '111 patent. The examiner found that "it is clear that the specific combination of 0.05% by weight cyclosporine A with 1.25% by weight castor oil is surprisingly critical for therapeutic effectiveness in the treatment of dry eye or keratoconjunctivitis sicca." Notice of Allowability (Nov. 21, 2013), Dkt. No. 165-23, at 5. The '111 patent issued on January 1, 2014. In parallel proceedings, the examiner allowed the applications that became the '162, '556, '048, and '930 patents, which issued shortly thereafter. The '191 patent was separately prosecuted and issued in February 2016.

The defendants argue that by emphasizing the critical nature of the specific combination of 0.05% cyclosporin and 1.25% castor oil in the claimed emulsion, the applicants limited themselves to the precise recited percentages of those components.[9] The Court is not persuaded that the prosecution history compels such a construction. While it is true that the applicants argued to the examiner that the difference between the recited values for cyclosporin and castor

[9] In their initial claim construction brief and at the Markman hearing, the defendants seemed to take the position that "about" means "precisely," which in turn admits of no variation at all from the recited values. See Defendants' Responsive Claim Construction Brief, Dkt. No. 165, at 18-24; Claim Construction Hearing Transcript, Dkt. No. 182, at 49-54. In their supplemental claim construction brief, the defendants took the position that "precisely" allows for rounding variations, so that, for example, the claimed 0.05% cyclosporin concentration would encompass a concentration range from 0.045% to 0.054%, and the claimed 1.25% castor oil concentration would encompass a concentration range from 1.245% to 1.254%. Defendants' Responsive Supplemental Claim Construction Brief, Dkt. No. 190, at 3-5.

oil in the claimed compositions and the values set forth in Ding were critical to the unexpected results flowing from the invention, the criticality of the recited values does not answer the question as to the range of criticality, i.e., the range of values within which the unexpected results are likely to be found.

In addition, the Court attaches little significance to the applicants' statement to the examiner during the prosecution of the '857 application that the claim limitations did not use the term "about" (and thus did not overlap with the values set forth in Ding). That statement cannot reasonably be understood to mean that even after the applicants added the term "about" to the claims, the claims should be read as if they did not contain that term. If anything, the addition of the term "about" to the claims that were ultimately allowed, when previous applications had not contained that term, is an indication that the applicants adverted to the difference and wanted to ensure that their patents covered some range of values beyond the precise values set forth in the claims.

The Court therefore rejects the defendants' argument that the term "about" must be construed to mean "precisely."

b. The defendants argue that if the term "about" does not mean "precisely," it is indefinite. Because the patents do not contain a definition of the term "about" or any other clear indication of the scope to be given to that term in this context, the defendants contend that it is impossible for a person of skill in the art to know how far the claims reach beyond the specific recited parameters for the cyclosporin component (0.05% by weight) and the castor oil component (1.25% by weight) in the claimed emulsion.

Words of degree, such as "about," "approximately," or "substantially," pose special problems in applying the principles of indefiniteness. On the one hand, those terms are

extremely common in issued patents, and there is clearly no general rule that the use of such terms renders indefinite the claims in which they are found. See Deere & Co. v. Bush Hog, LLC, 703 F.3d 1349, 1359 (Fed. Cir. 2012) ("This court has repeatedly confirmed that relative terms such as 'substantially' do not render patent claims so unclear as to prevent a person of skill in the art from ascertaining the scope of the patent."); Ecolab, Inc. v. Envirochem, Inc., 264 F.3d 1358, 1367 (Fed. Cir. 2001) ("[L]ike the term 'about,' the term 'substantially' is a descriptive term commonly used in patent claims"); Andrew Corp. v. Gabriel Elecs., Inc., 847 F.2d 819, 821 (Fed. Cir. 1988) (Terms such as "close to," "substantially equal" and "closely approximate" are "ubiquitous in patent claims").

Such usages, when serving reasonably to describe the claimed subject matter to those of skill in the field of the invention, and to distinguish the claimed subject matter from the prior art, have been accepted in patent examination and upheld by the courts." Andrew Corp., 847 F.2d at 821. In fact, the Federal Circuit has held that the use of such terms "does not automatically render a claim invalid," Seattle Box Co. v. Indus. Crating & Packing, Inc., 731 F.2d 818, 826 (Fed. Cir. 1984), and that it is often permissible to include such terms even if they cannot be defined with specificity, see BJ Servs. Co. v. Halliburton Energy Servs., Inc., 338 F.3d 1368, 1372 (Fed. Cir. 2003).

In some instances, words of degree are as precise as the subject matter permits; in such instances, the use of such terms is permissible and does not render the claims indefinite. See, e.g., Andrew Corp., 847 F.2d at 821. As the Federal Circuit has explained, "a sound claim construction need not always purge every shred of ambiguity. The resolution of some line-drawing problems—especially easy ones like this one—is properly left to the trier of fact." Accumed LLC v. Stryker Corp., 483 F.3d 800, 806 (Fed. Cir. 2007).

A term such as "about" has a legitimate role to play in patent drafting when the patentee seeks to avoid "a strict numerical boundary to the specified parameter." Ecolab, Inc., 264 F.3d at 1367. "Expressions such as 'substantially' are used in patent documents when warranted by the nature of the invention, in order to accommodate the minor variations that may be appropriate to secure the invention . . . and indeed may be necessary in order to provide the inventor with the benefit of the invention." Verve, LLC v. Crane Cams, Inc., 311 F.3d 1116, 1120 (Fed. Cir. 2002). The range envisaged for the term "about" depends on the setting in which it is used: "its range must be interpreted in its technologic and stylistic context." Pall Corp. v. Micron Separations, Inc., 66 F.3d 1211, 1217 (Fed. Cir. 1995).

Both the Supreme Court and the Federal Circuit have suggested that guidance as to the meaning of terms of degree, such as "about" can be obtained in particular instances by looking to disclosures in the specification, the nature of the technological field, and the knowledge of persons of skill in that field. See Eibel Process Co. v. Minn. & Ont. Paper Co., 261 U.S. 45, 65 (1923) (meaning of patent terms "substantial" and "high" would be apparent to readers [of the patent] who were skilled in the art; "one versed in paper making could find in Eibel's specifications all he needed to know, to avail himself of the invention."); Modine Mfg. Co. v. U.S. Int'l Trade Comm'n, 75 F.3d 1545, 1554 (Fed. Cir. 1996) ("Although it is rarely feasible to attach a precise limit to 'about,' the usage can usually be understood in light of the technology embodied in the invention. When the claims are applied to an accused device, it is a question of technologic fact whether the accused device meets a reasonable meaning of 'about' in the particular circumstances."); Pall Corp., 66 F.3d at 1217 (The word "about" does not have "a universal meaning in patent claims" and the meaning "depends on the technological facts of the particular case."); Andrew Corp., 847 F.2d at 821 (The term "substantially equal" is a term of

degree, and "its acceptability depends on 'whether one of ordinary skill in the art would understand what is claimed . . . in light of the specification.").

The Federal Circuit addressed this issue in some detail more than 30 years ago, and its observations are still valid:

> Definiteness problems often arise when words of degree are used in a claim. That some claim language may not be precise, however, does not automatically render a claim invalid. When a word of degree is used the district court must determine whether the patent's specification provides some standard for measuring that degree. The trial court must decide, that is, whether one of ordinary skill in the art would understand what is claimed when the claim is read in light of the specification.

Seattle Box Co., 731 F.2d at 826.

That standard is satisfied in this case. Guidance as to the meaning of the term "about" in the patents in suit can be garnered from the intrinsic record, including both the specification and the prosecution history, as well as the nature of the technical field and the knowledge of persons of skill in that field. Those sources provide sufficient definiteness to the term "about," as it is used in the patent, to overcome the defendants' invalidity challenge. This is true for several reasons.

First, as noted, the applicants made clear throughout the prosecution of the applications that the recited concentrations of cyclosporin A and castor oil were critical to the invention, because it was at the recited levels of concentration that the unexpected advantages of the invention were observed. Although the Court has held that the criticality of the claimed values does not compel a construction limiting the claims to those precise values, the discussion of the criticality of the claimed values indicates that the range of those values is not intended to be large.

Given the nature of the pharmaceutical arts, a person of skill in that field would understand that concentration values that differ only slightly from the values recited in the patent would still be expected to exhibit the level of therapeutic effectiveness that is claimed for the values of 0.05% cyclosporin A and 1.25% castor oil. Just as it is unreasonable to expect that a real-world formulation could have precisely those values, it is equally unreasonable to think there is not any range around those values that would share the heightened level of therapeutic efficacy of those concentrations, even if the range is small.

Second, the scope of the term "about" is substantially confined by the prior art Ding reference. It is clear that the range cannot extend to the percentages of cyclosporin and castor oil disclosed in the compositions set forth in Ding, or even values close to the values in those compositions, since the applicants went to great lengths to emphasize that Ding did not disclose or make obvious the invention claimed in the patents in suit.

Ding teaches concentrations of cyclosporin A and castor oil that produce a cyclosporin A/castor oil ratio of 0.08 in four of Ding's compositions, and 0.04 in the fifth. One of those compositions contains the same concentration of cyclosporin A as in the patents in suit, but twice the concentration of castor oil. The fifth of Ding's compositions contains the same ratio of cyclosporin A to castor oil as in the asserted claims, but uses four times the amount of cyclosporin A and castor oil.[10] Thus, with regard to the concentration of both cyclosporin A and castor oil, and the ratio of the concentrations of those two components, Ding is close prior art.

[10] In particular, example 1 in Ding has four compositions that contain varying amounts of cyclosporin and castor oil. In all of those compositions, the ratio of cyclosporin A to castor oil is 0.08, twice the ratio in the asserted claims of the patents in suit. U.S. Pat. No. 5,474,979, col. 4, ll. 31-43 (example 1, compositions A, C, D, and E). In one of the compositions disclosed in Ding (example 1, composition B), the ratio of cyclosporin A to castor oil is 0.04 (the same ratio that is recited in the patents in suit), but that composition in Ding contains four times the concentration of both cyclosporin A and castor oil as in the compositions of the patents in suit.

Because the applicants emphasized throughout the prosecution that their invention achieved surprising results not achieved by the compositions described in Ding, the term "about" in the patents in suit cannot be interpreted so broadly as to read on a composition having concentrations of cyclosporin A and castor oil, and a ratio of cyclosporin A to castor oil, that approaches the values disclosed in the Ding compositions.

Third, some guidance can be derived from the degree of precision set forth in the claims themselves. The patentees chose the number of significant figures to use in the claimed percentages. Those numbers would naturally be assumed to include percentages that would round up or down to 0.05% and 1.25%—that is, roughly 0.045% to 0.054% for cyclosporin A and 1.245% to 1.254% for castor oil. In fact, given the number of significant figures used in the claims, those ranges of percentages would ordinarily be deemed fully equivalent to the claimed percentages, even without the need to add an additional range to account for the term "about." That range therefore establishes the floor, or minimum range, from which to determine the scope of the range to which Allergan is entitled by virtue of its use of the term "about."

Fourth, given that patents are written for persons of skill in the pertinent art, the term "about" must be interpreted as a person skilled in the pharmaceutical arts would understand it in the context of the invention. That is, whether a particular deviation from a fixed value is within the scope of the term "about" depends on whether a person of skill in the art would consider such a difference insignificant, i.e., whether such a person would consider the deviation sufficient to render the accused product a different product from the product recited in the claims. See Modine Mfg. Co., 75 F.3d at 1554 ("Such broadening usages as 'about' must be given reasonable scope; they must be viewed by the decisionmaker as they would be understood by persons experience in the field of the invention."); see also BJ Servs. Co., 338 F.3d at 1372

("The question becomes whether one of ordinary skill in the art would understand what is claimed when the claim is read in light of the specification."); Eiselstein v. Frank, 52 F.3d 1035, 1040 (Fed. Cir. 1995) ("The meaning of the word 'about' is dependent on the facts of a case, the nature of the invention, and the knowledge imparted by the totality of the earlier disclosure to those skilled in the art.").

Extrinsic evidence offered in this case indicates that a person of skill in the pharmaceutical arts would understand that generally accepted standards for the manufacture and sale of drugs tolerate small degrees of variations or ranges in component concentrations and small amounts of impurities, while regarding the drugs as still being the same product. Allergan points to guidelines issued in 1999 by the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use that characterize a drug as conforming to specifications if tests reveal that its components fall within appropriate numerical limits, ranges, or other criteria." Specifications: Test Procedures and Acceptance Criteria for New Drug Substances and New Drug Products: Chemical Substances Q6A," Dkt. No. 211-1, at 5. The evidence further showed that the new drug application for Restasis, the commercial embodiment of the patents in suit, contained tolerance ranges for the concentration of cyclosporin A in the formulation, both for the manufacturing process and for the product's shelf life. Those tolerances are five percent and ten percent variations, respectively. Allergan's Supplemental Claim Construction Brief, Dkt. No. 211, at 8. Moreover, Allergan introduced evidence that those tolerances are typical for many pharmaceutical products. One of Allergan's experts, Dr. Thorsteinn Loftsson, stated in his declaration that a person of skill in the art could look to regulatory guidance from the U.S. Food and Drug Administration. Since before the time of the invention, he explained, the FDA has said that "in order to be considered 'the same' by the

U.S. FDA, products may be up to 5% different from one another in active and inactive ingredients." Declaration of Thorsteinn Loftsson, Ph.D. in Support of Plaintiff Allergan's Claim Construction, Dkt. No. 211-2, at 8-9.

If all products falling within a prescribed range are considered to be equivalent to a person of skill in the art, that is evidence that at least those products having component values that fall within those ranges would be considered to have values that are "about" the same. Based on the evidence offered in the claim construction process, the Court concludes that a person of ordinary skill in the art would not consider a variation of less than ten percent in the concentrations of cyclosporin A and castor oil in the claimed emulsion to make a significant difference in the nature of the product.

The ten percent variation in the concentration of the components is greater than the variation that would be reached by simply rounding the values in the claims up or down, but it is not great enough to approach the concentration levels set forth in the examples disclosed in Ding. For purposes of determining indefiniteness, the Court concludes that the evidence as to the meaning of the term "about" in the patents in suit shows that the meaning of the term is sufficiently clear to avoid a finding of indefiniteness.

In pressing the issue of indefiniteness, the defendants have relied heavily on the Federal Circuit's decision in Amgen, Inc. v. Chugai Pharmaceutical Co., 927 F.2d 1200 (Fed. Cir. 1991). That case is similar to this one in some respects and different in others. While Amgen is the strongest authority for the defendants, the Court concludes, in light of the foregoing analysis of the evidence bearing on indefiniteness in this case, that Amgen is sufficiently different from this case that it does not call for a finding of indefiniteness here.

Amgen involved patents on a process of using recombinant technology to produce Erythropoietin ("EPO"), a protein that stimulates the production of red blood cells. The claim language at issue in Amgen related to the potency of EPO products. EPO potency is measured by the product's specific activity, which is calculated as the ratio of international units to absorbance units (IU/AU). The disputed claim language recited a ratio of "about 160,000" IU/AU, and the question before the court was whether the use of the term "about" rendered the claims indefinite.

The court of appeals held that it did. It noted that the district court had found that the term "about 160,000" gave "no hint" as to what value between the prior art (128,620) and 160,000 constitutes infringement. 927 F.2d at 1218. The district court's holding, the appellate court explained, "was further supported by the fact that nothing in the specification, prosecution history, or prior art provides any indication as to what range of specific activity is covered by the term 'about' and by the fact that no expert testified as to a definite meaning for the term in the context of the prior art." Id. In light of the close prior art and the lack of clear meaning to the claim language, the court held the term "about" rendered the claims indefinite. The court was careful, however, to caution that its ruling "should not be understood as ruling out any and all uses of this term ["about"] in patent claims." Id.

The court in Amgen found nothing in the specification or in the art that gave any hint as to how broadly the term "about" should be interpreted in the context of the patents before it. In this case, by contrast, the specification and the nature of the art suggest limits to the term "about" that are defined by the understandings of persons of skill in the art as to the general range of variation of components such as those in this case that are permissible in the industry and not considered so great as to alter the nature of the product.

Based on the evidence submitted in connection with the claim construction proceedings, the Court is able to make a preliminary determination that the claims containing the term "about" are not indefinite. It may be that evidence will be offered at trial that will provide more enlightenment as to the scope of the term "about" as used in the patents in suit. That evidence may be pertinent to (1) the proper construction of the term "about"; (2) the question whether the term "about" is indefinite; and (3) whether the accused products infringe under the proper construction of the term "about."

Because the Court's construction of the term "about" is based only on the evidence offered by the parties in the claim construction proceedings, it is by its nature tentative. The Federal Circuit has made clear that a district court may adopt an "evolving" or "rolling" claim construction, in which the Court's construction of claims evolves as the Court better understands the technology and the patents at issue. See Wi-Lan USA, Inc. v. Apple Inc., 830 F.3d 1374, 1385 (Fed. Cir. 2016) ("We have long held that a district court may "engage in rolling claim construction in which the court revisits and alters its interpretation of the claim terms as its understanding of the technology evolves.") quoting Conoco, Inc. v. Energy & Envtl. Int'l, L.C., 460 F.3d 1349, 1359 (Fed. Cir. 2006); Pressure Prods. Med. Supplies, Inc. v. Greatbatch Ltd., 599 F.3d 1308, 1316 (Fed. Cir. 2010) (quoting Pfizer, Inc. v. Teva Pharms. USA, Inc., 429 F.3d 1364, 1377 (Fed. Cir. 2005)) ("[D]istrict courts may engage in a rolling claim construction, in which the court revisits and alters its interpretation of the claim terms as its understanding of the technology evolves."); Utah Med. Prods., Inc. v. Graphic Controls Corp., 350 F.3d 1376, 1381-82 (Fed. Cir. 2003) (same); Jack Guttman, Inc. v. Kopykake Enters., Inc., 302 F.3d 1352, 1361 (Fed. Cir. 2002) (same).

When the Court is satisfied that the term "about" has been defined with whatever specificity the pertinent evidence allows, and if the Court concludes that the term as so construed, is not indefinite, what remains is for the Court to determine infringement. See PPG Indus. v. Guardian Indus. Corp., 156 F.3d 1351, 1355 (Fed. Cir. 1998) ("Claims are often drafted using terminology that is not as precise or specific as it might be. . . . That does not mean, however, that a court, under the rubric of claim construction, may give a claim whatever additional precision or specificity is necessary to facilitate a comparison between the claim and the accused product. Rather, after the court has defined the claim with whatever specificity and precision is warranted by the language of the claim and the evidence bearing on the proper construction, the task of determining whether the construed claim reads on the accused product is for the finder of fact."); W.L. Gore & Assocs., Inc. v. Garlock, Inc., 842 F.2d 1275, 1280 (Fed. Cir. 1988) ("Whether an imprecise claim limitation, such as the phrase 'about 100% per second' is literally met, is a question of fact for the trial court."); Seattle Box Co., 731 F.2d at 829 ("[T]he trier of fact must determine the scope of an imprecise phrase such as 'substantially equal to,' which, by its very nature, has a fact-dependent meaning.").

Accordingly, **the term "about" will be construed to have its ordinary meaning, which is "approximately"; in deciding whether that limitation is satisfied as a factual matter, the Court will consider whether the variation between the recited values and the values of an accused product has a material effect on the properties of the composition.** The Court concludes that the term "about," as used in the patents in suit, is not indefinite.

7. **"cyclosporin A is the only peptide present"**

This phrase is found in independent claims 1, 13, and 17 of the '111 patent and in all of the claims depending from those three claims (claims 2-12, claims 14-17, and claims 19-27).

Each of the independent claims recites that the topical ophthalmic emulsion comprises "cyclosporin A in an amount of about 0.05% by weight"; the disputed phrase appears in the final limitation of each claim, which recites "wherein cyclosporin A is the only peptide present in the topical ophthalmic emulsion."

Both sides argue that this phrase should be given its plain and ordinary meaning, but they disagree about what the plain and ordinary meaning is. The defendants argue that the plain and ordinary meaning of the phrase is that no peptides can be present in the emulsion except for cyclosporin A. That is, the defendants argue that the phrase excludes metabolites and derivatives of cyclosporin A; some impurities can be included in the claimed emulsion, according to the defendants, but not peptide impurities.

Allergan's position is a little more complex. In the initial briefing on claim construction, Allergan argued that the phrase "cyclosporin A is the only peptide present" excludes peptides other than cyclosporin A, but that it does not exclude metabolites or derivatives of cyclosporin A, nor does it exclude impurities that happen to be peptides. In its supplemental brief, Allergan no longer urged that the phrase does not exclude "metabolites" of cyclosporin A, but argued only that the phrase does not exclude "at least derivatives of cyclosporin A and impurities." Allergan's Supplemental Claim Construction Brief, Dkt. No. 211, at 10. In its supplemental reply brief, Allergan seemed to take an even narrower position, not mentioning derivatives of cyclosporin A, but simply urging the Court to "find that an emulsion containing impurities, regardless of what those impurities are, falls within the scope of the claims." Allergan's Supplemental Reply Claim Construction Brief, Dkt. No. 212, at 10.

Claim 1 of the original '857 application recited a method of treatment comprising administering to an eye of a human or animal "a composition comprising water, a hydrophobic

component and a cyclosporin component in a therapeutically effective amount of less than 0.1% by weight of the composition, the weight ratio of the cyclosporin component to the hydrophobic component" being less than 0.08. Claim 21 in that application recited a composition for treating an eye of a human or animal "comprising an emulsion comprising water, a hydrophobic component, and a cyclosporin component in a therapeutically effective amount of less than 0.1% by weight, the weight ratio of the cyclosporin component to the hydrophobic component being less than 0.08." Dkt. No. 165-7, at 30, 33. The specification for the '857 application, which has remained essentially unchanged throughout the prosecution, defined the term "cyclosporin component" as "intended to include any individual member of the cyclosporin group and derivatives thereof, as well as mixtures of two or more individual cyclosporins and derivatives thereof." Dkt. No. 165-7, at 6-7. The specification added that "[p]articularly preferred cyclosporin components include, without limitation, cyclosporin A, derivatives of cyclosporin A and the like and mixtures thereof. Cyclosporin A is an especially useful cyclosporin component." Id. at 7.

The examiner rejected the claims of the '857 application for, inter alia, lack of an adequate written description. The examiner noted that the "hydrophobic component" is not limited to particular compounds, but includes any compound with hydrophobicity. Office Action (Jan. 17, 2007), Dkt. No. 165-14, at 9. As for the "cyclosporin component," the examiner pointed out that that component was "not limited to cyclosporine but to any cyclosporin A derivatives and mixtures thereof having similar functionality to cyclosporine." Id. The examiner added that "one of skill in the art would not know how to find and use all the instantly claimed derivatives of cyclosporine based on the guidance presented," id. at 10, as the specification provided only a single example of a composition within the claims, i.e., a composition containing

cyclosporin A and castor oil. In addition, the examiner found claim 21 to be vague and indefinite because it was unclear what kinds of derivatives of cyclosporin were covered by the claim. Id. at 11.

In response, the applicants withdrew claim 1 and amended claim 21 to read: "A composition for treating an eye of a human or animal comprising an emulsion comprising water, castor oil, and cyclosporin A in a therapeutically effective amount of less than 0.1% by weight, the weight ratio of the cyclosporin A to the castor oil being less than 0.08." Amendment A (Mar. 27, 2007), Dkt. No. 165-15, at 7-8. As the applicants explained, claim 21 was amended to refer specifically to castor oil rather than to a "hydrophobic component" and that it was amended to refer to "cyclosporin A" instead of "a cyclosporin component." Id. at 11. The applicants added new claims to compositions containing 1.25% by weight of castor oil (claim 37), 0.05% by weight of cyclosporin A (claim 38), and 0.05% by weight of cyclosporin A together with 1.25% by weight of castor oil (claims 39 and 40). Id. at 10.

Although the '857 application was ultimately abandoned, the continuation applications that matured into the '111 patent continued to recite the combination of cyclosporin A and castor oil, rather than the combination of a cyclosporin component and a hydrophobic component. See Application Serial Number 13/961,828, Preliminary Amendment (Aug. 7, 2013), Dkt. No. 165-12; Application Serial Number 13/967,163, Preliminary Amendment (Aug. 14, 2013), Dkt. No. 165-8.

In addition, in the course of the prosecution of the '163 application, which ultimately became the '111 patent, the applicants agreed to amend the application in order, as the examiner put it, "to avoid issues of anticipation or obviousness" with respect to U.S. Patent No. 6,984,628 to Bakhit, which disclosed a combination of peptides, including cyclosporin. That was the point

at which the applicants added the limitation "wherein cyclosporin A is the only peptide present in the topical ophthalmic emulsion" to the claims that ultimately became claims 1, 13, and 18 of the '111 patent. Dkt. No. 155-18, at 9; Application Serial Number 13/967,163, Comments on Examiner's Statement of Reasons for Allowance and Interview Summary (Nov. 21, 2013), at 2; see also Applicant-Initiated Interview Summary, Dkt. No. 190-2.

The prosecution history provides substantial guidance as to the proper scope of the "only peptide present" amendment that was added to claims 1, 13, and 18 of the '111 patent. In its brief, Allergan relies heavily on the definition of "cyclosporin component" in the specification, see '111 patent, col. 3, ll. 38-41. But that definition plainly does not govern the meaning of the term "cyclosporin A" in the claims. The term "cyclosporin component" was initially used in the '857 application claims, but that term was dropped in favor of the term "cyclosporin A" in response to the rejection in which the examiner found that the term "cyclosporin component" rendered the claims unpatentable.

Allergan's reliance on the specification (and the opinion of its expert, as expressed in a declaration submitted with Allergan's supplemental brief) overlooks the fact that the definition of "cyclosporin component" referred to a broad term that was in the original claims but was narrowed in response to the examiner's objection that the term "cyclosporin component" was vague and indefinite. The term "cyclosporin component" was jettisoned for the very reason that the replacement term, "cyclosporin A," was narrower and more precise. Therefore, the fact that the specification defined the term "cyclosporin components" to include cyclosporin derivatives is of no help to Allergan.

The specification also makes clear that the term cyclosporin A is a different peptide from the other cyclosporins in the cyclosporin series, i.e., cyclosporins B through I. The specification

refers to cyclosporins as "a group of nonpolar cyclic oligopeptides with known immunosuppressant activity." '111 patent, col. 3, ll. 27-28. It then states that "Cyclosporin A, along with several other minor metabolites, cyclosporin B through I, have been identified." Id. at col. 3, ll. 28-30. That distinction in the specification between cyclosporin A and the "other minor metabolites" makes it clear that cyclosporins B through I are excluded from the scope of the claim term "cyclosporin A." Given that the metabolites cyclosporin B through I are excluded, and that there is nothing in the specification or elsewhere that suggests that other metabolites of cyclosporin A are included within the scope of the claims, the Court agrees with the defendants that the claim language does not implicitly include cyclosporin A metabolites.

The specification (both in the original '857 application and in the issued '111 patent) also makes it clear that "derivatives" of cyclosporin A do not fall within the meaning of "cyclosporin A" as that term is used in the '111 patent. In addressing the term "cyclosporin components," the specification states that "[p]articularly preferred cyclosporin components include, without limitation, cyclosporin A, derivatives of cyclosporin A and the like and mixtures thereof. Cyclosporin A is an especially useful cyclosporin component." '111 patent, col. 3, ll. 42-45. The specification later states that the term "derivatives" of a cyclosporin refers to "compounds having structures sufficiently similar to the cyclosporin so as to function in a manner substantially similar to or substantially identical to the cyclosporin, for example, cyclosporin A, in the present methods." Id., col. 5, ll. 59-64.

Those passages from the specification make clear that the term "derivatives" refers to a category of compounds separate from the compound identified as "cyclosporin A," and that derivatives are not a subset of a group of compounds that the patent refers to as "cyclosporin A." The Court therefore agrees with the defendants that the term "cyclosporin A" does not include

derivatives of cyclosporin A as the patent uses those terms. For that reason, the Court construes the phrase "wherein cyclosporin A is the only peptide present in the topical ophthalmic emulsion" to exclude derivatives of cyclosporin A as well as metabolites of cyclosporin A.

The remaining question is whether that claim limitation also excludes impurities that happen to be peptides (other than cyclosporin A), as the defendants contend. On this point, the Court agrees with Allergan that such impurities are not excluded by the phrase "wherein cyclosporin A is the only peptide present in the topical ophthalmic emulsion."

Through its expert, Dr. Berkland, Allergan has introduced evidence that a person of ordinary skill would understand that natural impurities are present in every pharmaceutical formulation. Declaration of Cory J. Berkland, Ph.D., in Support of Plaintiff Allergan's Claim Construction, Dkt. No. 211-10, at 11. In addition, Dr. Berkland explained, the Food and Drug Administration recognizes that impurities exist in all chemical compositions as a result of manufacturing issues or product degradation. Id. at 11-12; see U.S. Dept. of Health and Human Services, Guidance for Industry, ANDAs: Impurities in Drug Products 3-5 (Nov. 2010) ("FDA Guidance") (discussing "qualification thresholds" for "degradation products" in drugs), Dkt. No. 155-29; Dkt. No. 156-2.

While Dr. Berkland did not specifically state that such impurities include peptides, it is apparent to the Court that impurities in a composition containing the peptide cyclosporin A will include at least trace amounts of peptides as the degradation products of the cyclosporin A. See id. at 13. Indeed, the FDA Guidance regarding allowable drug impurities includes "degradation products" as among those impurities, FDA Guidance at 3, and it notes that "degradation product[s]" may include a "significant metabolite of the drug substance," id. at 5.

Although the defendants offer the declaration of their expert, Dr. Erning Xia, in support of their argument that the claim language does not allow for peptide impurities in any amount, Dr. Xia states only that "other peptides can be present in a formulation depending on the efforts to purify the formulation, but the claims literally exclude them." Declaration of Erning Xia, Ph.D., Dkt. No. 165-25, at 16. He does not go so far as to say that it is possible, as a practical matter, to purify a cyclosporin A composition to the point that it can be confidently said to be wholly free of any peptide impurity whatsoever.

Patents are drafted for real world applications, not as theoretical constructs. In the real world, impurities are inevitable. In any pharmaceutical product, especially one that may be stored for some period of time before use, there are likely to be trace amounts of impurities that result from the manufacturing process and the gradual degradation of product purity over time. Therefore any characterization of a pharmaceutical product in a patent claim must be assumed to include impurities, unless the claim very clearly prohibits the presence of all such impurities. For that reason, it would require the clearest possible drafting to persuade the Court that the claims asserted in this case were meant to be limited to compositions that were entirely free of any peptide impurities. There is no such clarity in the '111 patent. The Court therefore will not read the phrase "wherein cyclosporin A is the only peptide present in the topical ophthalmic emulsion" to exclude all compositions that have any peptide impurities whatsoever.

One further point of clarification is that, in accordance with Dr. Berkland's declaration and the FDA Guidance, peptides that qualify as metabolites or derivatives of cyclosporin A but that are present as impurities constitute impurities within the meaning of the Court's construction. The exclusions from the construction of "cyclosporin A" discussed above apply to derivatives and metabolites as ingredients of the claimed emulsion, not to impurities otherwise

occurring in the emulsion. The inventors initially claimed cyclosporin metabolites and derivatives as the drug substance—i.e., an ingredient that would function to treat the disease—but amended the claims to name only cyclosporin A, in order to overcome the Examiner's indefiniteness challenge. This was not, however, a disclaimer of emulsions in which such metabolites and derivatives are present as impurities, which a person of skill would understand to be an inevitable byproduct. See In re Marosi, 710 F.2d 799, 803 (Fed. Cir. 1983) (finding "essentially free of alkali metal" not indefinite despite patent's silence as to "particular number" (minimum amount of alkali metal) allowed because "a person [of skill in the art] would draw the line between unavoidable impurities in starting materials and essential ingredients"). In other words, "wherein cyclosporin A is the only peptide present in the topical ophthalmic emulsion" means that metabolites of cyclosporin A (e.g., cyclosporin B), derivatives of cyclosporin A, or other peptides that are included as additional ingredients, rather than introduced as impurities, would create an emulsion that falls outside the scope of the claims.

That does not entirely resolve the issue of the meaning of the phrase "cyclosporin A is the only peptide present," however. While the disputed phrase does not exclude compositions that have trace amounts of peptide impurities, it does exclude any compositions containing peptide impurities that materially affect the character and function of the composition. But in the absence of any such material effect, the Court concludes that small amounts of impurities, such as metabolites of the active ingredient, will not take a composition outside the scope of the claims. The "only peptide present" language is not sufficiently explicit to exclude such inevitable impurities and metabolites.

The Court therefore concludes that the phrase "cyclosporin A is the only peptide present" **should be given its plain and ordinary meaning, which is that the active ingredient of the composition is limited to cyclosporin A, but that impurities, including peptide impurities, may be present."**

8. "administered to an/the eye of a human; administered to a human; administering an emulsion topically to the eye of a human; administering to a human eye a second topical ophthalmic emulsion"

Allergan argues that these phrases should be given their plain and ordinary meaning; Allergan contends that the word "administered" means prescribing, dispensing, giving, or taking. The defendants also argue that these phrases should be given their plain and ordinary meaning, but they contend that the plain and ordinary meaning of the terms is "delivering into or onto the eye of a human." Defendants' Responsive Claim Construction Brief, Dkt. No. 165, at 27. The defendants regard Allergan's definition" to be too broad, as it would not be limited to those persons who actually place the drug in the patient's eye, but could be extended to include persons who prescribe the drug (such as physicians), those who dispense the drug (such as pharmacists), or even persons who give the drug to the patient, which could include persons such as a postal carrier who delivers the drug to the patient's home.

When referring to the administration of medical treatment, the term "administer," by itself, may include persons who participate in the patient's treatment, such as a doctor who prescribes medicine and directs the patient in its use. Thus, a doctor may be said to administer a course of treatment upon prescribing medicines and directing the patient in their use, even if the doctor does not actually, for example, put pills in the patient's mouth. It was in that context that this Court ruled, in Erfindergemeinschaft UroPep, GmbH v. Eli Lilly & Co., No. 2:15-cv-1202

(E.D. Tex. Aug. 11, 2016), that "administering" treatment to a person in need thereof could include actions by persons other than the individual who is either taking a pill or directly placing the pill in the patient's mouth. See also Gilead Scis., Inc. v. Merck & Co., No. 5:13-cv-4057, 2015 WL 2062575, at *7 (N.D. Cal. May 1, 21015) (in a method of treatment case, construing "administering" to mean "providing a compound of the invention . . . to the individual in need"); Janssen Prods. L.P. v. Lupin Ltd., C.A. No. 10-cv-5954, 2013 U.S. Dist. Lexis 189016, at *36-38 (D.N.J. Oct. 9, 2013) (construing "administering" to include "the activities of doctors and other medical professionals who are involved in prescribing the claimed compounds" or otherwise supervising patients' care); Iovate Health Scis., Inc. v. Bio-Engineered Supplements & Nutrition, Inc., No. 9:07-cv-46, 2008 WL 2359961, at *2-3 (E.D. Tex. June 5, 2008) (construing "administering" to mean "delivery into a body, or the management or supervision of the process whereby something is delivered into a body").

Courts that have addressed this issue have noted that the meaning of the term "administering" or "administered" often depends on the context in which the term is used. In Tobinick v. Olmarker, 753 F.3d 1220, 1225 (Fed. Cir. 2014), for example, the Federal Circuit upheld the construction of the term "administered locally" as "administered directly to the site where it is intended to act" (internal quotation marks omitted). The use of the term "locally" in conjunction with "administered" was clearly important to the court's construction of the term "administered." Similarly, in Takeda Pharm. Co. v. Actavis Labs FL, Inc., Civil Action No. 15-451, 2015 WL 3193188 (D. Del. June 6, 2016), the district court explained that the way the term "administering" was used in the claims and specifications of the patents in suit guided the court's construction of that term; in particular, the court observed, the patents consistently used that term "solely to describe the physical act of delivering the drug into or onto the body," id. at *3, and

the court therefore construed the term in that manner, id. at *4. See also Andrulis Pharms Corp., 2015 WL 3978578, at *2-3 (D. Del. June 26, 2015) (construing the term "administering" to mean "delivering into or onto a [mammal's] body," particularly in light of the specification, which refers to "any type of administration including oral administration, topical administration, intramuscular injection and intravenous infusion"); AstraZeneca AB v. Hanmi USA, Inc., Civil Action No. 11-760, 2012 WL 6203602 (D.N.J. Dec. 12, 2012) (holding that a person of ordinary skill in the art would understand the term "oral administration" to refer to "the means of delivering the medication to an individual" and not "the prescription by a physician or other licensed healthcare professional, dispensing and ingestion").[11]

In this case, the context in which the terms "administering" and "administered" are used is quite different from the context in which the term "administering" was used in the Erfindergemeinschaft UroPep case and others like it. Here, the context in which the terms "administering" and "administered" are used strongly supports the interpretation of "administering" as meaning "delivering into or onto the eye."

As in some of the cases cited above, the term "administer" does not stand alone in the claims of the patents in suit, but consistently appears in connection with a reference to the direct placement of the emulsion in the eye. In addressing the administration of the drug, the claims use phrases such as "topically administering to the eye of the human in need thereof," see, e.g., '162 patent, claims 1 and 23; '048 patent, claims 1, 18, and 22; and '191 patent, claims 1, 13, 17, and 21, and "the topical ophthalmic emulsion is administered to an eye of a human," see, e.g.,

[11] Allergan argues that the definition of "administering" in the context of medical treatment should not depend on the method used to deliver the treatment. As the cited cases indicate, however, the context in which the term "administering" is used, including any references to the mode of treatment employed, is important in determining whether the term is limited to the actual delivery of a drug or applies more broadly to the process of prescribing medicines and supervising the patient's treatment.

’556 patent, claim 11; and ’930 patent, claims 11 and 23. The phrase “topically administering to the eye of the human in need thereof” and like phrases found in the patents in suit carry the meaning of placing or inserting the emulsion directly into the eye.

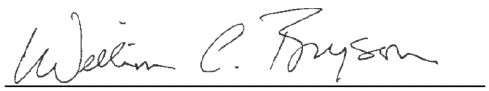
The person who places the emulsion in his or her own eye is the person who is “topically administering [the drug] to the eye of a human,” and in practice that will most often be the patient. A doctor who merely prescribes the drug or instructs the patient to administer the emulsion, or a pharmacist who merely provides the emulsion to the patient, is not “topically administering [the drug] to the eye of the human” or administering “the topical ophthalmic emulsion” to the patient’s eye in the ordinary sense of those terms.

Allergan points out that a few of the claims of three of the patents in suit refer to “administration to a human” rather than “administering to the eye of a human.” See ’162 patent, claims 13, 14, and 16, and ’048 patent, claims 13, 14, and 16. But those are all dependent claims that depend from independent claims that recite “the method comprising topically administering [the emulsion] to the eye of a human in need thereof.” See ’162 patent, claim 1; ’048 patent, claim 1. In light of the relationship between those dependent and independent claims, it is clear that the phrase “administered to a human” must be given the same construction as the phrase “administered to the eye of a human,” and thus that the administration referred to is the act of placing the drug in the eye.

Accordingly, the Court construes the phrases referring to administration to the eye of a human, or to a human, to mean **“delivering into or onto the eye of a human.”**

IT IS SO ORDERED.

SIGNED this 13th of December, 2016.



WILLIAM C. BRYSON
UNITED STATES CIRCUIT JUDGE