

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Acheampong, *et al.*

Serial No.: TBA

Filed: Herewith

For: METHODS OF PROVIDING
THERAPEUTIC EFFECTS USING
CYCLOSPORIN COMPONENTS

Examiner: TBA

Group Art Unit: TBA

Confirmation No. TBA

Customer No.: 51957

PRELIMINARY AMENDMENT

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

Prior to examining the above-referenced application, please amend the specification as described on page 2 of this paper, and please amend the claims as described on pages 3-6 of this paper. Remarks follow on page 7.

Amendments to the Specification

Please replace page 1, lines 5-10 of the specification filed herewith with the following amended paragraph:

This application is a continuation of copending U.S. Application Serial No. 13/961,808 filed August 7, 2013, which is a continuation of copending U.S. Application Serial No. 11/897,177, filed August 28, 2007, which is a continuation of U.S. Application Serial No. 10/927,857, filed August 27, 2004, now abandoned, which claimed the benefit of U.S. Provisional Application No. 60/503,137 filed September 15, 2003, which ~~is~~ are incorporated in ~~its~~ their entirety herein by reference.

Amendments to the claims

The following list of claims will replace all previous versions of claims presented in this application:

1. – 36. (Canceled)

37. (New) A topical ophthalmic emulsion for treating an eye of a human, wherein the topical ophthalmic emulsion comprises cyclosporin A in an amount of about 0.05% by weight, polysorbate 80, Pemulen, water, and castor oil in an amount of about 1.25% by weight; and

wherein the topical ophthalmic emulsion is therapeutically effective in treating dry eye disease.

38. (New) The topical ophthalmic emulsion of Claim 37, wherein the topical ophthalmic emulsion further comprises a tonicity agent or a demulcent component.

39. (New) The topical ophthalmic emulsion of Claim 38, wherein the tonicity agent or the demulcent component is glycerine.

40. (New) The topical ophthalmic emulsion of Claim 37, wherein the topical ophthalmic emulsion further comprises a buffer.

41. (New) The topical ophthalmic emulsion of Claim 40, wherein the buffer is sodium hydroxide.

42. (New) The topical ophthalmic emulsion of Claim 37, wherein the topical ophthalmic emulsion further comprises glycerine and a buffer.

43. (New) The topical ophthalmic emulsion of Claim 37, wherein the topical ophthalmic emulsion comprises polysorbate 80 in an amount of about 1.0% by weight.

44. (New) The topical ophthalmic emulsion of Claim 37, wherein the topical ophthalmic emulsion comprises Pemulen in an amount of about 0.05% by weight.
45. (New) The topical ophthalmic emulsion of Claim 37, wherein the topical ophthalmic emulsion further comprises glycerine in an amount of about 2.2% by weight and a buffer.
46. (New) The topical ophthalmic emulsion of Claim 45, wherein the buffer is sodium hydroxide.
47. (New) The topical ophthalmic emulsion of Claim 37, wherein, when the topical ophthalmic emulsion is administered to an eye of a human in an effective amount in treating dry eye disease, the blood of the human has substantially no detectable concentration of cyclosporin A.
48. (New) The topical ophthalmic emulsion of Claim 42, wherein the topical ophthalmic emulsion has a pH in the range of about 7.2 to about 7.6.
49. (New) The topical ophthalmic emulsion of Claim 37, wherein the topical ophthalmic emulsion is as substantially therapeutically effective as an emulsion comprising cyclosporin A in an amount of 0.1% by weight and castor oil in an amount of 1.25% by weight.
50. (New) The topical ophthalmic emulsion of Claim 37, wherein the topical ophthalmic emulsion achieves at least as much therapeutic effectiveness as an emulsion comprising cyclosporin A in an amount of 0.1% by weight and castor oil in an amount of 1.25% by weight.
51. (New) The topical ophthalmic emulsion of Claim 37, wherein the topical ophthalmic emulsion breaks down more quickly in the eye of a human, once administered to the eye of the human, thereby reducing vision distortion in the eye of the human as compared to an emulsion that contains only 50% as much castor oil.

52. (New) The topical ophthalmic emulsion of Claim 37, wherein the topical ophthalmic emulsion, when administered to the eye of a human, demonstrates a reduction in adverse events in the human, relative to an emulsion comprising cyclosporin A in an amount of 0.1% by weight and castor oil in an amount of 1.25% by weight.

53. (New) The topical ophthalmic emulsion of Claim 52, wherein the adverse events include side effects.

54. (New) A topical ophthalmic emulsion for treating an eye of a human, wherein the topical ophthalmic emulsion is therapeutically effective in treating dry eye and wherein the topical ophthalmic emulsion comprises:

- cyclosporin A in an amount of about 0.05% by weight;
- castor oil in an amount of about 1.25% by weight;
- polysorbate 80 in an amount of about 1.0% by weight;
- Pemulen in an amount of about 0.05% by weight;
- a tonicity component or a demulcent component in an amount of about 2.2% by weight;
- a buffer; and
- water.

55. (New) The topical ophthalmic emulsion of Claim 54, wherein the buffer is sodium hydroxide.

56. (New) The topical ophthalmic emulsion of Claim 54, wherein the tonicity component or the demulcent component is glycerine.

57. (New) The topical ophthalmic emulsion of Claim 54, wherein, when the topical ophthalmic emulsion is administered to an eye of a human in an effective amount in treating dry eye disease, the blood of the human has substantially no detectable concentration of the cyclosporin A.

58. (New) The topical ophthalmic emulsion of Claim 54, wherein the topical ophthalmic emulsion has a pH in the range of about 7.2 to about 7.6.

59. (New) A topical ophthalmic emulsion for treating an eye of a human, the topical ophthalmic emulsion comprising:

cyclosporin A in an amount of about 0.05% by weight;

castor oil in an amount of about 1.25% by weight;

polysorbate 80 in an amount of about 1.0% by weight;

Pemulen in an amount of about 0.05% by weight;

glycerine in an amount of about 2.2% by weight;

sodium hydroxide; and

water;

wherein the emulsion is therapeutically effective in treating dry eye disease.

60. (New) The topical ophthalmic emulsion of Claim 59, wherein the topical ophthalmic emulsion has a pH in the range of about 7.2 to about 7.6.

REMARKS

The applicants have canceled claims 1-36 and have added claims 37-60. Support for the limitations recited in the new claims may be found throughout the specification, and at least at page 5, lines 5-14, page 26, lines 5-19, and page 27, lines 4-31 of the application specification filed herewith. No new matter has been added.

The claims of the present application may vary in scope from the claims pursued in the parent applications. To the extent any prior amendments or characterizations of the scope of any claim, or the specification, or referenced art could be construed as a disclaimer of any subject matter supported by the present disclosure, the Applicants hereby rescind and retract such disclaimer.

Specifically, the Applicants would like to bring to the Examiner's attention comments made in the Response filed on June 15, 2009 in U.S. Patent Application Serial No. 10/927,857 (now abandoned) and comments made in the Amendment filed on June 15, 2009 in U.S. Patent Application Serial No. 11/897,177 (currently pending) regarding U.S. Patent No. 5,474,979 and the present application specification. Since these comments have been filed, the Applicants have collected evidence that supports the patentability of the pending claims.

The Commissioner is hereby authorized to charge any fees required or necessary for the filing, processing or entering of this paper or any of the enclosed papers, and to refund any overpayment, to deposit account 01-0885.

Respectfully submitted,

/Laura L. Wine/

Laura L. Wine
Attorney of Record
Registration Number 68,681

Date: August 14, 2013

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**CERTIFICATION AND REQUEST FOR PRIORITIZED EXAMINATION
 UNDER 37 CFR 1.102(e) (Page 1 of 1)**

First Named Inventor:	Andrew Acheampong	Nonprovisional Application Number (if known):	
Title of Invention:	METHODS OF PROVIDING THERAPEUTIC EFFECTS USING CYCLOSPORIN COMPONENTS		

APPLICANT HEREBY CERTIFIES THE FOLLOWING AND REQUESTS PRIORITIZED EXAMINATION FOR THE ABOVE-IDENTIFIED APPLICATION.

1. The processing fee set forth in 37 CFR 1.17(i)(1), the prioritized examination fee set forth in 37 CFR 1.17(c), and if not already paid, the publication fee set forth in 37 CFR 1.18(d) have been filed with the request. The basic filing fee, search fee, examination fee, and any required excess claims and application size fees are filed with the request or have been already been paid.
2. The application contains or is amended to contain no more than four independent claims and no more than thirty total claims, and no multiple dependent claims.
3. The applicable box is checked below:

I. Original Application (Track One) - Prioritized Examination under § 1.102(e)(1)

- i. (a) The application is an original nonprovisional utility application filed under 35 U.S.C. 111(a). This certification and request is being filed with the utility application via EFS-Web.
 ---OR---
 (b) The application is an original nonprovisional plant application filed under 35 U.S.C. 111(a). This certification and request is being filed with the plant application in paper.
- ii. The executed inventor's oath or declaration is filed with the application. (37 CFR 1.63 and 1.64)

II. Request for Continued Examination - Prioritized Examination under § 1.102(e)(2)

- i. A request for continued examination has been filed with, or prior to, this form.
- ii. If the application is a utility application, this certification and request is being filed via EFS-Web.
- iii. The application is an original nonprovisional utility application filed under 35 U.S.C. 111(a), or is a national stage entry under 35 U.S.C. 371.
- iv. This certification and request is being filed prior to the mailing of a first Office action responsive to the request for continued examination.
- v. No prior request for continued examination has been granted prioritized examination status under 37 CFR 1.102(e)(2).

Signature /Laura L. Wine/	Date August 14, 2013
Name (Print/Typed) Laura L. Wine	Practitioner Registration Number 68681

Note: This form must be signed in accordance with 37 CFR 1.33. See 37 CFR 1.4(d) for signature requirements and certifications. Submit multiple forms if more than one signature is required.*

*Total of 1 forms are submitted.

Privacy Act Statement

The **Privacy Act of 1974 (P.L. 93-579)** requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C. 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether disclosure of these records is required by the Freedom of Information Act.
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3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.
4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).
5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.
6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).
7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (*i.e.*, GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.
8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspection or an issued patent.
9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

Electronic Patent Application Fee Transmittal

Application Number:				
Filing Date:				
Title of Invention:	METHODS OF PROVIDING THERAPEUTIC EFFECTS USING CYCLOSPORIN COMPONENTS			
First Named Inventor/Applicant Name:	Andrew Acheampong			
Filer:	Laura Lee Wine/Lauren Barberena			
Attorney Docket Number:	17618CON2B (AP)			
Filed as Large Entity				
Track I Prioritized Examination - Nonprovisional Application under 35 USC 111(a) Filing Fees				
Description	Fee Code	Quantity	Amount	Sub-Total in USD(\$)
Basic Filing:				
Utility application filing	1011	1	280	280
Utility Search Fee	1111	1	600	600
Utility Examination Fee	1311	1	720	720
Request for Prioritized Examination	1817	1	4000	4000
Pages:				
Claims:				
Claims in Excess of 20	1202	3	80	240
Miscellaneous-Filing:				

Description	Fee Code	Quantity	Amount	Sub-Total in USD(\$)
Publ. Fee- Early, Voluntary, or Normal	1504	1	300	300
OTHER PUBLICATION PROCESSING FEE	1808	1	130	130
Petition:				
Patent-Appeals-and-Interference:				
Post-Allowance-and-Post-Issuance:				
Extension-of-Time:				
Miscellaneous:				
Total in USD (\$)				6270

Electronic Acknowledgement Receipt

EFS ID:	16593528
Application Number:	13967189
International Application Number:	
Confirmation Number:	4818
Title of Invention:	METHODS OF PROVIDING THERAPEUTIC EFFECTS USING CYCLOSPORIN COMPONENTS
First Named Inventor/Applicant Name:	Andrew Acheampong
Customer Number:	51957
Filer:	Laura Lee Wine/Lauren Barberena
Filer Authorized By:	Laura Lee Wine
Attorney Docket Number:	17618CON2B (AP)
Receipt Date:	14-AUG-2013
Filing Date:	
Time Stamp:	18:56:04
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	Deposit Account
Payment was successfully received in RAM	\$6270
RAM confirmation Number	6280
Deposit Account	010885
Authorized User	

The Director of the USPTO is hereby authorized to charge indicated fees and credit any overpayment as follows:

Charge any Additional Fees required under 37 C.F.R. Section 1.17 (Patent application and reexamination processing fees)

Charge any Additional Fees required under 37 C.F.R. Section 1.21 (Miscellaneous fees and charges)

File Listing:					
Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1		17618CON_SPEC.pdf	4360450 9b080e02f8cb41c5b767d994b15dca09f38dd180	yes	34
	Multipart Description/PDF files in .zip description				
	Document Description		Start	End	
	Specification		1	28	
	Claims		29	33	
Abstract		34	34		
Warnings:					
Information:					
2	Application Data Sheet	17618CON2B_ADS.pdf	1505486 76589eca6d26b270f1c4b8b6c19ac7f0c916afd9	no	8
Warnings:					
Information:					
3	Oath or Declaration filed	17618CON2B_DECS.pdf	628594 53d34ff82a0d42446d338021a29746cdcecb3bc75	no	6
Warnings:					
The page size in the PDF is too large. The pages should be 8.5 x 11 or A4. If this PDF is submitted, the pages will be resized upon entry into the Image File Wrapper and may affect subsequent processing					
Information:					
4	Power of Attorney	17618CON2B_POA.pdf	1931208 b399bf0ff4cef322968c0420686c4c8839483b79	no	2
Warnings:					
Information:					
5		17618CON2B_PRELIM_AMENDMENT.pdf	106412 581cda4dfcb4b3b1c241b35cd16682e00108f716	yes	7
	Multipart Description/PDF files in .zip description				
	Document Description		Start	End	
	Preliminary Amendment		1	1	
Specification		2	2		

	Claims	3	6
	Applicant Arguments/Remarks Made in an Amendment	7	7

Warnings:

Information:

6	TrackOne Request	17618CON2B_PRIORITIZED_EX AM.pdf	153236 <small>25dfacc03da02daa83f2ddb89a2c3ab62cc535b5</small>	no	2
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Warnings:

Information:

7	Fee Worksheet (SB06)	fee-info.pdf	42020 <small>9aa08e84c0b4ec795b5f25400b1798c19ba060eb</small>	no	2
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Warnings:

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Total Files Size (in bytes):			8727406
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This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

METHODS OF PROVIDING THERAPEUTIC EFFECTS
USING CYCLOSPORIN COMPONENTS

5 Related Application

This application is a continuation of U.S. Application
Serial No. 10/927,857, filed August 27, 2004, which claimed
the benefit of U.S. Provisional Application No. 60/503,137
filed September 15, 2003, which is incorporated in its
10 entirety herein by reference.

Background of the Invention

The present invention relates to methods of providing
desired therapeutic effects to humans or animals using
15 compositions including cyclosporin components. More
particularly, the invention relates to methods including
administering to an eye of a human or animal a
therapeutically effective amount of a cyclosporin component
to provide a desired therapeutic effect, preferably a
20 desired ophthalmic or ocular therapeutic effect.

The use of cyclosporin-A and cyclosporin A derivatives
to treat ophthalmic conditions has been the subject of
various patents, for example Ding et al U.S. Patent
5,474,979; Garst U.S. Patent 6,254,860; and Garst U.S.
25 6,350,442, this disclosure of each of which is incorporated
in its entirety herein by reference. In addition,
cyclosporin A compositions used in treating ophthalmic
conditions is the subject of a number of publications.
Such publications include, for example, "Blood
30 concentrations of cyclosporin a during long-term treatment
with cyclosporin a ophthalmic emulsions in patients with
moderate to severe dry eye disease," Small et al, *J Ocul*
Pharmacol Ther, 2002 Oct, 18(5):411-8; "Distribution of

cyclosporin A in ocular tissues after topical administration to albino rabbits and beagle dogs,"
Acheampong et al, *Curr Eye Res*, 1999 Feb, 18(2):91-103b;
"Cyclosporine distribution into the conjunctiva, cornea,
5 lacrimal gland, and systemic blood following topical dosing of cyclosporine to rabbit, dog, and human eyes," Acheampong et al, *Adv Exp Med Biol*, 1998, 438:1001-4; "Preclinical safety studies of cyclosporine ophthalmic emulsion,"
Angelov et al, *Adv Exp Med Biol*, 1998, 438:991-5;
10 "Cyclosporin & Emulsion & Eye," Stevenson et al, *Ophthalmology*, 2000 May, 107(5):967-74; and "Two multicenter, randomized studies of the efficacy and safety of cyclosporine ophthalmic emulsion in moderate to severe dry eye disease. CsA Phase 3 Study Group," Sall et al,
15 *Ophthalmology*, 2000 Apr, 107(4):631-9. Each of these publications is incorporated in its entirety herein by reference. In addition, cyclosporin A-containing oil-in-water emulsions have been clinically tested, under conditions of confidentiality, since the mid 1990's in
20 order to obtain U.S. Food and Drug Administration (FDA) regulatory approval.

Examples of useful cyclosporin A-containing emulsions are set out in Ding et al U.S. Patent 5,474,979. Example 1 of this patent shows a series of emulsions in which the
25 ratio of cyclosporin A to castor oil in each of these compositions was 0.08 or greater, except for Composition B, which included 0.2% by weight cyclosporin A and 5% by weight castor oil. The Ding et al patent placed no significance in Composition B relative to Compositions A, C
30 and D of Example 1.

Over time, it has become apparent that cyclosporin A emulsions for ophthalmic use preferably have less than 0.2%

by weight of cyclosporin A. With cyclosporin A concentrations less than 0.2%, the amount of castor oil employed has been reduced since one of the functions of the castor oil is to solubilize the cyclosporin A. Thus, if
5 reduced amounts of cyclosporin are employed, reduced amounts of castor oil are needed to provide effective solubilization of cyclosporin A.

There continues to be a need for providing enhanced methods of treating ophthalmic or ocular conditions with
10 cyclosporin-containing emulsions.

Summary of the Invention

New methods of treating a human or animal using cyclosporin component-containing emulsions have been
15 discovered. Such methods provide substantial overall efficacy in providing desired therapeutic effects. In addition, other important benefits are obtained employing the present methods. For example, patient safety is enhanced. In particular, the present methods provide for
20 reduced risks of side effects and/or drug interactions. Prescribing physicians advantageously have increased flexibility in prescribing such methods and the compositions useful in such methods, for example, because of the reduced risks of harmful side effects and/or drug
25 interactions. The present methods can be easily practiced.

In short, the present methods provide substantial and acceptable overall efficacy, together with other advantages, such as increased safety and/or flexibility.

In one aspect of the present invention, the present
30 methods comprise administering to an eye of a human or animal a composition in the form of an emulsion 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 is less than 0.08.

5 It has been found that the relatively increased amounts of hydrophobic component together with relatively reduced, yet therapeutically effective, amounts of cyclosporin component provide substantial and advantageous benefits. For example, the overall efficacy of the present
10 compositions, for example in treating dry eye disease, is substantially equal to an identical composition in which the cyclosporin component is present in an amount of 0.1% by weight. Further, a relatively high concentration of hydrophobic component is believed to provide for a more
15 quick or rapid breaking down or resolving of the emulsion in the eye, which reduces vision distortion which may be caused by the presence of the emulsion in the eye and/or facilitates the therapeutic effectiveness of the composition. Additionally, and importantly, using reduced
20 amounts of the active cyclosporin component mitigates against undesirable side effects and/or potential drug interactions.

In short, the present invention provides at least one advantageous benefit, and preferably a plurality of
25 advantageous benefits.

The present methods are useful in treating any suitable condition which is therapeutically sensitive to or treatable with cyclosporin components. Such conditions preferably are ophthalmic or ocular conditions, that is
30 relating to or having to do with one or more parts of an eye of a human or animal. Included among such conditions are, without limitation, dry eye syndrome,

phacoanaphylactic endophthalmitis, uveitis, vernal conjunctivitis, atopic kerapoconjunctivitis, corneal graft rejection and the like conditions. The present invention is particularly effective in treating dry eye syndrome.

5 Employing reduced concentrations of cyclosporin component, as in the present invention, is advantageously effective to provide the blood of the human or animal under treatment with reduced concentrations of cyclosporin component, preferably with substantially no detectable
10 concentration of the cyclosporin component. The cyclosporin component concentration of blood can be advantageously measured using a validated liquid chromatography/mass spectrometry-mass spectrometry (VLC/MS-MS) analytical method, such as described elsewhere herein.

15 In one embodiment, in the present methods the blood of the human or animal has concentrations of clyclosporin component of 0.1 ng/ml or less.

Any suitable cyclosporin component effective in the present methods may be used.

20 Cyclosporins are a group of nonpolar cyclic oligopeptides with known immunosuppressant activity. Cyclosporin A, along with several other minor metabolites, cyclosporin B through I, have been identified. In addition, a number of synthetic analogs have been prepared.

25 In general, commercially available cyclosporins may contain a mixture of several individual cyclosporins which all share a cyclic peptide structure consisting of eleven amino acid residues with a total molecular weight of about 1,200, but with different substituents or configurations of
30 some of the amino acids.

The term "cyclosporin component" as used herein is 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.

Particularly 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.

Any suitable hydrophobic component may be employed in the present invention. Advantageously, the cyclosporin component is solubilized in the hydrophobic component. The hydrophobic component may be considered as comprising a discontinuous phase in the presently useful cyclosporin component-containing emulsions.

The hydrophobic component preferably is present in the emulsion compositions in an amount greater than about 0.625% by weight. For example, the hydrophobic component may be present in an amount of up to about 1.0% by weight or about 1.5% by weight or more of the composition.

Preferably, the hydrophobic component comprises one or more oily materials. Examples of useful oil materials include, without limitation, vegetable oils, animal oils, mineral oils, synthetic oils and the like and mixtures thereof. In a very useful embodiment, the hydrophobic component comprises one or more higher fatty acid glycerides. Excellent results are obtained when the hydrophobic component comprises castor oil.

The presently useful compositions may include one or more other components in amounts effective to facilitate the usefulness and effectiveness of the compositions. Examples of such other components include, without limitation, emulsifier components, tonicity components,

polyelectrolyte components, surfactant components, viscosity inducing components, acids and/or bases to adjust the pH of the composition, buffer components, preservative components and the like. Components may be employed which are effective to perform two or more functions in the presently useful compositions. For example, components which are effective as both emulsifiers and surfactants may be employed, and/or components which are effective as both polyelectrolyte components and viscosity inducing components may be employed. The specific composition chosen for use in the present invention advantageously is selected taking into account various factors present in the specific application at hand, for example, the desired therapeutic effect to be achieved, the desired properties of the compositions to be employed, the sensitivities of the human or animal to whom the composition is to be administered, and the like factors.

The presently useful compositions advantageously are ophthalmically acceptable. A composition, component or material is ophthalmically acceptable when it is compatible with ocular tissue, that is, it does not cause significant or undue detrimental effects when brought into contact with ocular tissues.

Such compositions have pH's within the physiological range of about 6 to about 10, preferably in a range of about 7.0 to about 8.0 and more preferably in a range of about 7.2 to about 7.6.

The present methods preferably provide for an administering step comprising topically administering the presently useful compositions to the eye or eyes of a human or animal.

Each and every feature described herein, and each and

every combination of two or more of such features, is included within the scope of the present invention provided that the features included in such a combination are not mutually inconsistent.

5 These and other aspects and advantages of the present invention are apparent in the following detailed description, example and claims.

Detailed Description

10 The present methods are effective for treating an eye of a human or animal. Such methods, in general, comprise administering, preferably topically administering, to an eye of a human or animal a cyclosporin component-containing emulsion. The emulsion contains water, for example U.S.
15 pure water, a hydrophobic component and a cyclosporin component in a therapeutically effective amount of less than 0.1% by weight of the emulsion. In addition, beneficial results have been found when the weight ratio of the cyclosporin component to the hydrophobic component is
20 less than 0.08.

 As noted above, the present administering step preferably includes topically administering the emulsion to the eye of a patient of a human or animal. Such administering may involve a single use of the presently
25 useful compositions, or repeated or periodic use of such compositions, for example, as required or desired to achieve the therapeutic effect to be obtained. The topical administration of the presently useful composition may involve providing the composition in the form of eye drops
30 or similar form or other form so as to facilitate such topical administration.

 The present methods have been found to be very

effective in providing the desired therapeutic effect or effects while, at the same time, substantially reducing, or even substantially eliminating, side effects which may result from the presence of the cyclosporin component in the blood of the human or animal being treated, and eye irritation which, in the past, has been caused by the presence of certain components in prior art cyclosporin-containing emulsions. Also, the use of the present compositions which include reduced amounts of the cyclosporin components allow for more frequent administration of the present compositions to achieve the desired therapeutic effect or effects without substantially increasing the risk of side effects and/or eye irritation.

The present methods are useful in treating any condition which is therapeutically sensitive to or treatable with cyclosporin components. Such conditions preferably are ophthalmic or ocular conditions, that is relating to or having to do with one or more parts of an eye of a human or animal. Included among such conditions are, without limitation, dry eye syndrome, phacoanaphylactic endophthalmitis, uveitis, vernal conjunctivitis, atopic kerapoconjunctivitis, corneal graft rejection and the like conditions. The present invention is particularly effective in treating dry eye syndrome.

The frequency of administration and the amount of the presently useful composition to use during each administration varies depending upon the therapeutic effect to be obtained, the severity of the condition being treated and the like factors. The presently useful compositions are designed to allow the prescribing physician substantial flexibility in treating various ocular conditions to achieve the desired therapeutic effect or effects with

reduced risk of side effects and/or eye irritation. Such administration may occur on an as needed basis, for example, in treating or managing dry eye syndrome, on a one time basis or on a repeated or periodic basis once, twice, 5 thrice or more times daily depending on the needs of the human or animal being treated and other factors involved in the application at hand.

One of the important advantages of the present invention is the reduced concentration of the cyclosporin component in the blood of the human or animal as a result 10 of administering the present composition as described herein. One very useful embodiment of the present administering step provides no substantial detectable concentration of cyclosporin component in the blood of the 15 human or animal. Cyclosporin component concentration in blood preferably is determined using a liquid chromatography-mass spectroscopy-mass spectroscopy (LC-MS/MS), which test has a cyclosporin component detection limit of 0.1 ng/ml. Cyclosporin component concentrations 20 below or less than 0.1 ng/ml are therefore considered substantially undetectable.

The LC-MS/MS test is advantageously run as follows.

One ml of blood is acidified with 0.2 ml of 0.1 N HCl solution, then extracted with 5 ml of methyl t-butyl ether. 25 After separation from the acidified aqueous layer, the organic phase is neutralized with 2 ml of 0.1 N NaOH, evaporated, reconstituted in a water/acetonitrile-based mobil phase, and injected onto a 2.1 x 50 mm, 3 μ m pore size C-8 reverse phase high pressure liquid chromatography 30 (HPLC) column (Keystone Scientific, Bellefonte, PA). Compounds are gradient-eluted at 0.2 mL/min and detected using an API III triple quadrupole mass spectrometer with a

turbo-ionspray source (PE-Sciex, Concord, Ontario, Canada).

Molecular reaction monitoring enhances the sensitivity and selectivity of this assay. Protonated molecules for the analyte and an internal standard are collisionally dissociated and product ions at m/z 425 are monitored for the analyte and the internal standard. Under these conditions, cyclosporin A and the internal standard cyclosporin G elute with retention times of about 3.8 minutes. The lower limit of quantitation is 0.1 ng/mL, at which concentration the coefficient of variation and deviation from nominal concentration is <15%.

As noted previously, any suitable cyclosporin component effective in the present methods may be employed.

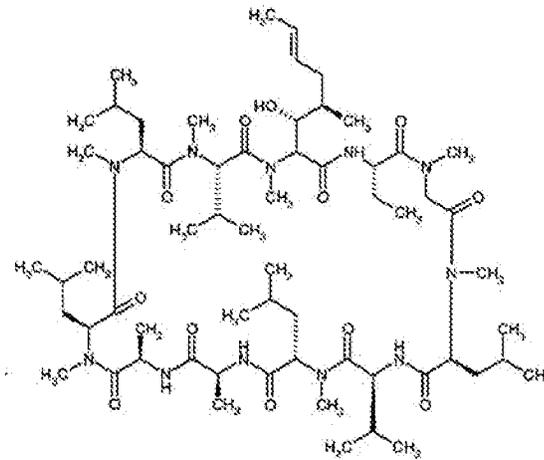
Very useful cyclosporin components include, without limitation, cyclosporin A, derivatives of cyclosporin A and the like and mixtures thereof.

The chemical structure for cyclosporin A is represented by Formula 1

Formula I

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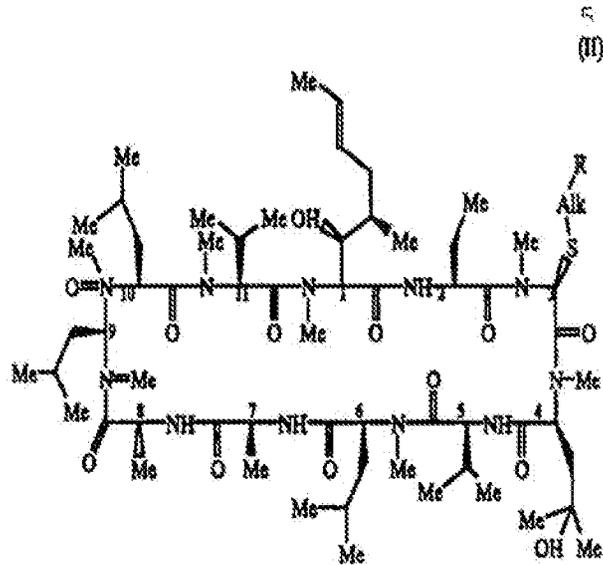


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As used herein the term "derivatives" of a cyclosporin refer to compounds having structures sufficiently similar to the cyclosporin so as to function in a manner substantially similar to or substantially identical to the cyclosporin, for example, cyclosporin A, in the present methods. Included, without limitation, within the useful cyclosporin A derivatives are those selected from ((R)-methylthio-Sar)³-(4'-hydroxy-MeLeu) cyclosporin A, ((R)-
 20 (Cyclo)alkylthio-Sar)³-(4'-hydroxy-MeLeu)⁴-cyclosporin A, and ((R)-(Cyclo)alkylthio-Sar)³-cyclosporin A derivatives described below.

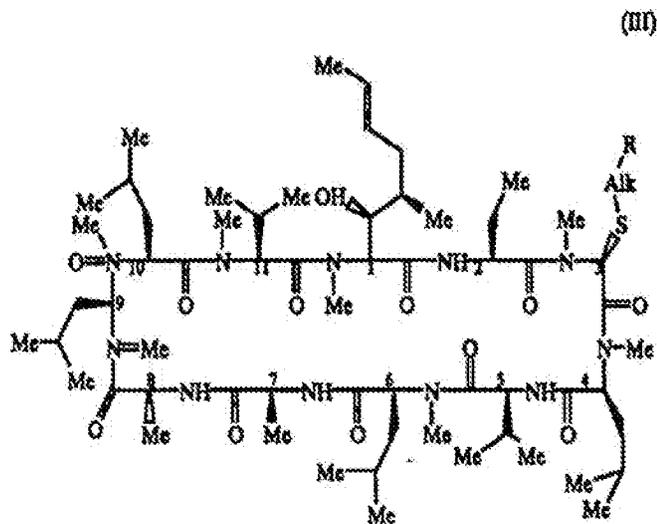
These cyclosporin derivatives are represented by the following general formulas (II), (III), and (IV)
 30 respectively:

Formula II



20

Formula III



25

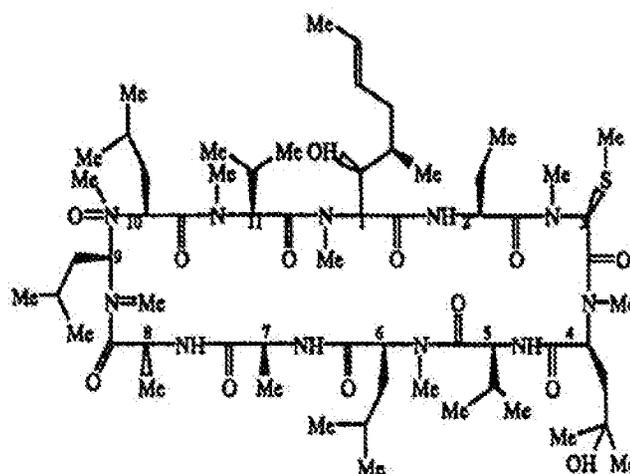
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Formula IV

5

(f)

10



15

wherein Me is methyl; Alk is 2-6C alkylene or 3-6C cycloalkylene; R is OH, COOH, alkoxy carbonyl, $-NR_1R_2$ or $N(R_3)-(CH_2)_n-NR_1R_2$; wherein R_1, R_2 is H, alkyl, 3-6C cycloalkyl, phenyl (optionally substituted by halo, alkoxy, alkoxy carbonyl, amino, alkylamino or dialkylamino), benzyl or saturated or unsaturated heterocyclyl having 5 or 6 members and 1-3 heteroatoms; or NR_1R_2 is a 5 or 6 membered heterocycle which may contain a further N, O or S heteroatom and may be alkylated; R_3 is H or alkyl and n is 2-4; and the alkyl moieties contain 1-4C.

In one embodiment, the cyclosporin component is effective as an immunosuppressant. 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.

One important feature of the present invention is that the presently useful compositions contain less than 0.1% by weight of the cyclosporin component. The advantages of such low-concentrations of cyclosporin components have been discussed in some detail elsewhere herein. Low concentrations of cyclosporin component, together with concentrations of the hydrophobic component such that the weight ratio of cyclosporin component to hydrophobic component is greater than 0.08, provides one or more substantial advantages in the present methods.

Any suitable hydrophobic component may be employed in the present invention. Such hydrophobic component may be considered as comprising a discontinuous phase in the presently useful cyclosporin component-containing emulsions, with the water or aqueous phase being considered the continuous phase in such emulsion. The hydrophobic component is preferably selected so as to solubilize the cyclosporin component, which is often substantially insoluble in the aqueous phase. Thus, with a suitable hydrophobic component included in the presently useful emulsions, the cyclosporin component is preferably solubilized in the emulsions.

In one very useful embodiment, the hydrophobic component comprises an oily material, in particular, a material which is substantially not miscible in water. Examples of useful oily materials include, without limitation, vegetable oils, animal oils, mineral oils, synthetic oils, and the like and mixtures thereof. Thus, the present hydrophilic components may comprise naturally occurring oils, including, without limitation refined naturally occurring oils, or naturally occurring oils which

have been processed to alter their chemical structures to some extent or oils which are substantially entirely synthetic. One very useful hydrophobic component includes higher fatty acid glycerides.

5 Examples of useful hydrophobic components include, without limitation, olive oil, arachis oil, castor oil, mineral oil, silicone fluid and the like and mixtures thereof. Higher fatty acid glycerides such as olive oil, peanut oil, castor oil and the like and mixtures thereof
10 are particularly useful in the present invention. Excellent results are obtained using a hydrophobic component comprising castor oil. Without wishing to limit the invention to any particular theory of operation, it is believed that castor oil includes a relatively high
15 concentration of ricinoleic acid which itself may be useful in benefitting ocular tissue and/or in providing one or more therapeutic effects when administered to an eye.

 The hydrophobic component is preferably present in the presently useful cyclosporin component-containing emulsion
20 compositions in an amount greater than about 0.625% by weight. For example, the hydrophobic component may be present in an amount up to about 0.75% by weight or about 1.0% by weight or about 1.5% by weight or more of the presently useful emulsion compositions.

25 The presently useful compositions may include one or more other components in amounts effective to facilitate the usefulness and effectiveness of the present methods and/or the presently useful compositions. Examples of such other components include, without limitation, emulsifier
30 components, surfactant components, tonicity components, poly electrolyte components, emulsion stability components, viscosity inducing components, demulcent components, acid

and/or bases to adjust the pH of the composition, buffer components, preservative components and the like.

In one very useful embodiment, the presently useful compositions are substantially free of preservatives. Thus, the presently useful compositions may be sterilized and maintained in a sterile condition prior to use, for example, provided in a sealed package or otherwise maintained in a substantially sterile condition.

Any suitable emulsifier component may be employed in the presently useful compositions, provided, that such emulsifier component is effective in forming maintaining the emulsion and/or in the hydrophobic component in emulsion, while having no significant or undue detrimental effect or effects on the compositions during storage or use.

In addition, the presently useful compositions, as well as each of the components of the present compositions in the concentration present in the composition advantageously are ophthalmically acceptable.

Useful emulsifier components may be selected from such component which are conventionally used and well known in the art. Examples of such emulsifier components include, without limitation, surface active components or surfactant components which may be anionic, cationic, nonionic or amphoterteric in nature. In general, the emulsifier component includes a hydrophobic constituent and a hydrophilic constituent. Advantageously, the emulsifier component is water soluble in the presently useful compositions. Preferably, the emulsifier component is nonionic. Specific examples of suitable emulsifier components include, without limitation, polysorbate 80, polyoxyalkylene alkylene ethers, polyalkylene oxide ethers

of alkyl alcohols, polyalkylene oxide ethers of alkylphenols, other emulsifiers/surfactants, preferably nonionic emulsifiers/surfactants, useful in ophthalmic compositions, and the like and mixtures thereof.

5 The emulsifier component is present in an amount effective in forming the present emulsion and/or in maintaining the hydrophobic component in emulsion with the water or aqueous component. In one preferred embodiment, the emulsifier component is present in an amount in a range
10 of about 0.1% to about 5%, more preferably about 0.2% to about 2% and still more preferably about 0.5% to about 1.5% by weight of the presently useful compositions.

 Polyelectrolyte or emulsion stabilizing components may be included in the presently useful compositions. Such
15 components are believed to be effective in maintaining the electrolyte balance in the presently useful emulsions, thereby stabilizing the emulsions and preventing the emulsions from breaking down prior to use. In one embodiment, the presently useful compositions include a
20 polyanionic component effective as an emulsion stabilizing component. Examples of suitable polyanionic components useful in the presently useful compositions include, without limitation, anionic cellulose derivatives, anionic acrylic acid-containing polymers, anionic methacrylic acid-
25 containing polymers, anionic amino acid-containing polymers and the like and mixtures thereof.

 A particularly useful class of polyanionic components include one or more polymeric materials having multiple anionic charges. Examples include, but are not limited to:

30

metal carboxy methylcelluloses
metal carboxy methylhydroxyethylcelluloses

metal carboxy methylstarchs
metal carboxy methylhydroxyethylstarchs
hydrolyzed polyacrylamides and polyacrylonitriles
heparin
5 gucoaminoglycans
hyaluronic acid
chondroitin sulfate
dermatan sulfate
peptides and polypeptides
10 alginic acid
metal alginates
homopolymers and copolymers of one or more of:
 acrylic and methacrylic acids
 metal acrylates and methacrylates
15 vinylsulfonic acid
 metal vinylsulfonate
 amino acids, such as aspartic acid, glutamic
 acid and the like
 metal salts of amino acids
20 p-styrenesulfonic acid
 metal p-styrenesulfonate
 2-methacryloyloxyethylsulfonic acids
 metal 2-methacryloyloxethylsulfonates
 3-methacryloyloxy-2-hydroxypropylsulfonic acids
25 metal 3-methacryloyloxy-2-
 hydroxypropylsulfonates
 2-acrylamido-2-methylpropanesulfonic acids
 metal 2-acrylamido-2-methylpropanesulfonates
 allylsulfonic acid
30 metal allylsulfonate and the like.

One particularly useful emulsion stabilizing component

includes crosslinked polyacrylates, such as carbomers and Pemulen® materials. Pemulen® is a registered trademark of B.F. Goodrich for polymeric emulsifiers and are commercially available from B.F. Goodrich Company, Specialty Polymers & Chemicals Division, Cleveland, Ohio. Pemulen® materials include acrylate/C10-30 alkyl acrylate cross-polymers, or high molecular weight co-polymers of acrylic acid and a long chain alkyl methacrylate cross-linked with allyl ethers of pentaerythritol.

10 The presently useful polyanionic components may also be used to provide a suitable viscosity to the presently useful compositions. Thus, the polyanionic components may be useful in stabilizing the presently useful emulsions and in providing a suitable degree of viscosity to the
15 presently useful compositions.

The polyelectrolyte or emulsion stabilizing component advantageously is present in an amount effective to at least assist in stabilizing the cyclosporin component-containing emulsion. For example, the
20 polyelectrolyte/emulsion stabilizing component may be present in an amount in a range of about 0.01% by weight or less to about 1% by weight or more, preferably about 0.02% by weight to about 0.5% by weight, of the composition.

Any suitable tonicity component may be employed in
25 accordance with the present invention. Preferably, such tonicity component is non-ionic, for example, in order to avoid interfering with the other components in the presently useful emulsions and to facilitate maintaining the stability of the emulsion prior to use. Useful
30 tonicity agents include, without limitation, glycerine, mannitol, sorbitol and the like and mixtures thereof. The presently useful emulsions are preferably within the range

of plus or minus about 20% or about 10% from being isotonic.

Ophthalmic demulcent components may be included in effective amounts in the presently useful compositions. For example, ophthalmic demulcent components such as carboxymethylcellulose, other cellulose polymers, dextran 70, gelatin, glycerine, polyethylene glycols (e.g., PEG 300 and PEG 400), polysorbate 80, propylene glycol, polyvinyl alcohol, povidone and the like and mixtures thereof, may be used in the present ophthalmic compositions, for example, compositions useful for treating dry eye.

The demulcent components are preferably present in the compositions, for example, in the form of eye drops, in an amount effective in enhancing the lubricity of the presently useful compositions. The amount of demulcent component in the present compositions may be in a range of at least about 0.01% or about 0.02% to about 0.5% or about 1.0% by weight of the composition.

Many of the presently useful polyelectrolyte/emulsion stabilizing components may also be effective as demulcent components, and vice versa. The emulsifier/surfactant components may also be effective as demulcent components and vice versa.

The pH of the emulsions can be adjusted in a conventional manner using sodium hydroxide and/or hydrochloric acid to a physiological pH level. The pH of the presently useful emulsions preferably is in the range of about 6 to about 10, more preferably about 7.0 to about 8.0 and still more preferably about 7.2 to about 7.6.

Although buffer components are not required in the presently useful compositions, suitable buffer components, for example, and without limitation, phosphates, citrates,

acetates, borates and the like and mixtures thereof, may be employed to maintain a suitable pH in the presently useful compositions.

5 The presently useful compositions may include an effective amount of a preservative component. Any suitable preservative or combination of preservatives may be employed. Examples of suitable preservatives include, without limitation, benzalkonium chloride, methyl and ethyl parabens, hexetidine, phenyl mercuric salts and the like
10 and mixtures thereof. The amounts of preservative components included in the present compositions are such to be effective in preserving the compositions and can vary based on the specific preservative component employed, the specific composition involved, the specific application
15 involved, and the like factors. Preservative concentrations often are in the range of about 0.00001% to about 0.05% or about 0.1% (w/v) of the composition, although other concentrations of certain preservatives may be employed.

20 Very useful examples of preservative components in the present invention include, but are not limited to, chlorite components. Specific examples of chlorite components useful as preservatives in accordance with the present invention include stabilized chlorine dioxide (SCD), metal
25 chlorites such as alkali metal and alkaline earth metal chlorites, and the like and mixtures thereof. Technical grade (or USP grade) sodium chlorite is a very useful preservative component. The exact chemical composition of many chlorite components, for example, SCD, is not
30 completely understood. The manufacture or production of certain chlorite components is described in McNicholas U.S. Patent 3,278,447, which is incorporated in its entirety by

reference herein. Specific examples of useful SCD products include that sold under the trademark Dura Klor by Rio Linda Chemical Company, Inc., and that sold under the trademark Anthium Dioxide® by International Dioxide, Inc.

5 An especially useful SCD is a product sold under the trademark Bio-Cide® by Bio-Cide International, Inc., as well as a product identified by Allergan, Inc. by the trademark Purite®.

10 Other useful preservatives include antimicrobial peptides. Among the antimicrobial peptides which may be employed include, without limitation, defensins, peptides related to defensins, cecropins, peptides related to cecropins, magainins and peptides related to magainins and other amino acid polymers with antibacterial, antifungal
15 and/or antiviral activities. Mixtures of antimicrobial peptides or mixtures of antimicrobial peptides with other preservatives are also included within the scope of the present invention.

The compositions of the present invention may include
20 viscosity modifying agents or components, such as cellulose polymers, including hydroxypropyl methyl cellulose (HPMC), hydroxyethyl cellulose (HEC), ethyl hydroxyethyl cellulose, hydroxypropyl cellulose, methyl cellulose and carboxymethyl cellulose; carbomers (e.g. carbopol, and the like);
25 polyvinyl alcohol; polyvinyl pyrrolidone; alginates; carrageenans; and guar, karaya, agarose, locust bean, tragacanth and xanthan gums. Such viscosity modifying components are employed, if at all, in an amount effective to provide a desired viscosity to the present compositions.
30 The concentration of such viscosity modifiers will typically vary between about 0.01 to about 5 % w/v of the

total composition, although other concentrations of certain viscosity modifying components may be employed.

The presently useful compositions may be produced using conventional and well known methods useful in
5 producing ophthalmic products including oil-in-water emulsions.

In one example, the oily phase of the emulsion can be combined with the cyclosporin component to solubilize the cyclosporin component in the oily material phase. The oily
10 phase and the water may be separately heated to an appropriate temperature. This temperature may be the same in both cases, generally a few degrees to about 10°C above the melting temperature of the ingredient(s) having the highest melting point in the case of a solid or semi-solid
15 oily phase for emulsifier components in the oily phase. Where the oily phase is a liquid at room temperature, a suitable temperature for preparation of a composition may be determined by routine experimentation in which the melting point of the ingredients aside from the oily phase
20 is determined. In cases where all components of either the oily phase or the water phase are soluble at room temperature, no heating may be necessary. Non-emulsifying agents which are water soluble are dissolved in the water and oil soluble components including the surfactant
25 components are dissolved in the oily phase.

To create an oil-in-water emulsion, the final oil phase is gently mixed into either an intermediate, preferably de-ionized water, phase or into the final water phase to create a suitable dispersion and the product is
30 allowed to cool with or without stirring. In the case where the final oil phase is first gently mixed into an intermediate water phase, the resulting emulsion

concentrate is thereafter mixed in the appropriate ratio with the final aqueous phase. In such cases, the emulsion concentrate and the final aqueous phase may not be at the same temperature or heated above room temperature, as the emulsion may be already formed at this point.

The oil-in-water emulsions of the present invention can be sterilized after preparation using heat, for example, autoclave steam sterilization or can be sterile filtered using, for example, a 0.22 micron sterile filter. Sterilization employing a sterilization filter can be used when the emulsion droplet (or globule or particle) size and characteristics allows this. The droplet size distribution of the emulsion need not be entirely below the particle size cutoff of the 0.22 micron sterile filtration membrane to be sterile-filtratable. In cases wherein the droplet size distribution of the emulsion is above the particle size cutoff of the 0.22 micron sterile filtration membrane, the emulsion needs to be able to deform or change while passing through the filtration membrane and then reform after passing through. This property is easily determined by routine testing of emulsion droplet size distributions and percent of total oil in the compositions before and after filtration. Alternatively, a loss of a small amount of larger droplet sized material may be acceptable.

The present oil-in-water emulsions preferably are thermodynamically stable, much like microemulsions, and yet may not be isotropic transparent compositions as are microemulsions. The emulsions of the present invention advantageously have a shelf life exceeding one year at room temperature.

The following non-limiting examples illustrate certain aspects of the present invention.

EXAMPLE 1

Two compositions are selected for testing. These compositions are produced in accordance with well known techniques and have the following make-ups:

	<u>Composition I</u>	<u>Composition II</u>
	wt%	wt%
5		
10		
15		

20 These compositions are employed in a Phase 3, double-masked, randomized, parallel group study for the treatment of dry eye disease.

The results of this study indicate that Composition II, in accordance with the present invention, which has a reduced concentration of cyclosporin A and a cyclosporin A to castor oil ratio of less than 0.08, provides overall efficacy in treating dry eye disease substantially equal to that of Composition I. This is surprising for a number of reasons. For example, the reduced concentration of cyclosporin A in Composition II would have been expected to result in reduced overall efficacy in treating dry eye disease. Also, the large amount of castor oil relative to the amount of cyclosporin A in Composition II might have been expected to cause increased eye irritation relative to

Composition I. However, both Composition I and Composition II are found to be substantially non-irritating in use.

Using relatively increased amounts of castor oil, with reduced amounts of cyclosporin component, as in Composition II, is believed to take advantage of the benefits, for example the ocular lubrication benefits, of castor oil, as well as the presence of ricinoleic acid in the castor oil, to at least assist in treating dry eye syndrome in combination with cyclosporin A.

In addition, it is found that the high concentration of castor oil relative to cyclosporin component, as in Composition II, provides the advantage of more quickly or rapidly (for example, relative to a composition which includes only 50% as much castor oil) breaking down or resolving the emulsion in the eye, for example, as measured by split-lamp techniques to monitor the composition in the eye for phase separation. Such rapid break down of the emulsion in the eye reduces vision distortion as the result of the presence of the emulsion in the eye, as well as facilitating the therapeutic effectiveness of the composition in treating dry eye disease.

Using reduced amounts of cyclosporin A, as in Composition II, to achieve therapeutic effectiveness mitigates even further against undesirable side effects and potential drug interactions. Prescribing physicians can provide (prescribe) Composition II to more patients and/or with fewer restrictions and/or with reduced risk of the occurrence of adverse events, e.g., side effects, drug interactions and the like, relative to providing Composition I.

While this invention has been described with respect to various specific examples and embodiments, it is to be

understood that the invention is not limited thereto and that it can be variously practiced within the scope of the following claims.

WHAT IS CLAIMED IS:

1. A method of treating an eye of a human or animal comprising:

administering to an eye of a human or animal a composition in the form of an emulsion 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 is less than 0.08.

2. The method of claim 1 wherein the administering step is effective in treating a condition selected from the group consisting of dry eye syndrome, phacoanaphylactic endophthalmitis, uveitis, vernal conjunctivitis, atopic keratoconjunctivitis and corneal graft rejection.

3. The method of claim 1 wherein the administering step is effective in treating dry eye syndrome.

4. The method of claim 1 wherein the blood of the human or animal has substantially no detectable concentration of the cyclosporin component.

5. The method of claim 1 wherein the blood of the human or animal has substantially no detectable concentration of the cyclosporin component as measured using a validated liquid chromatography/mass spectrometry-mass spectrometry analytical method.

6. The method of claim 1 wherein the blood of the human or animal has a concentration of the cyclosporin component of 0.1 ng/ml or less.

7. The method of claim 1 wherein the cyclosporin component comprises a material selected from cyclosporin A, derivatives of cyclosporin A and mixtures thereof.

8. The method of claim 1 wherein the cyclosporin component comprises cyclosporin A.

9. The method of claim 1 wherein the cyclosporin component is solubilized in the hydrophobic component present in the composition.

10. The method of claim 1 wherein the hydrophobic component is present in the composition in an amount greater than 0.625% by weight of the composition.

11. The method of claim 1 wherein the hydrophobic component comprises an oily material.

12. The method of claim 1 wherein the hydrophobic component comprises an ingredient selected from the group consisting of vegetable oils, animal oils, mineral oils, synthetic oils and mixtures thereof.

13. The method of claim 1 wherein the hydrophobic component comprises castor oil.

14. The method of claim 1 wherein the administering step comprises topically administering the composition to the eye of the human.

15. The method of claim 1 wherein the composition comprises an effective amount of an emulsifier component.

16. The method of claim 1 wherein the composition comprises an effective amount of a tonicity component.

17. The method of claim 1 wherein the composition comprises an effective amount of an organic tonicity component.

18. The method of claim 1 wherein the composition comprises a polyelectrolyte component in an amount effective in stabilizing the composition.

19. The method of claim 1 wherein the composition has a pH in the range of about 7.0 to about 8.0.

20. The method of claim 1 wherein the composition has a pH in the range of about 7.2 to about 7.6.

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.

22. The composition of claim 21 having a make-up so that when the composition is administered to an eye of a

human in an effective amount in treating dry eye syndrome, the blood of the human has substantially no detectable concentration of the cyclosporin component.

23. The composition of claim 21 wherein the cyclosporin component comprises a material selected from cyclosporin A, derivatives of cyclosporin A and mixtures thereof.

24. The composition of claim 21 wherein the cyclosporin component comprises cyclosporin A.

25. The composition of claim 21 in the form of an emulsion.

26. The composition of claim 21 wherein the hydrophobic component is present in an amount greater than 0.625% by weight of the composition.

27. The composition of claim 21 wherein the hydrophobic component is an oily material.

28. The composition of claim 21 wherein the hydrophobic component comprises an ingredient selected from the group consisting of vegetable oils, animal oils, mineral oils, synthetic oils, and mixtures thereof.

29. The composition of claim 21 wherein the hydrophobic component comprises castor oil.

30. The composition of claim 21 wherein the administering step comprises topically administering the composition to the eye of the human.

31. The composition of claim 21 wherein the composition comprises an effective amount of an emulsifier component.

32. The composition of claim 21 wherein the composition comprises an effective amount of a tonicity component.

33. The composition of claim 21 wherein the composition comprises an effective amount of an organic tonicity component.

34. The composition of claim 21 wherein the composition comprises a polyelectrolytic component in an amount effective in stabilizing the composition.

35. The composition of claim 21 wherein the composition includes water and has a pH in the range of about 7.0 to about 8.0.

36. The composition of claim 21 wherein the composition includes water and has a pH in the range of about 7.2 to about 7.6.

METHODS OF PROVIDING THERAPEUTIC EFFECTS
USING CYCLOSPORIN COMPONENTS

Abstract of the Disclosure

5

Methods of treating an eye of a human or animal include administering to an eye of a human or animal a composition in the form of an emulsion including 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 is less than 0.8.

10

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Application Data Sheet 37 CFR 1.76		Attorney Docket Number	17618CON2B (AP)
		Application Number	
Title of Invention	METHODS OF PROVIDING THERAPEUTIC EFFECTS USING CYCLOSPORIN COMPONENTS		
The application data sheet is part of the provisional or nonprovisional application for which it is being submitted. The following form contains the bibliographic data arranged in a format specified by the United States Patent and Trademark Office as outlined in 37 CFR 1.76. This document may be completed electronically and submitted to the Office in electronic format using the Electronic Filing System (EFS) or the document may be printed and included in a paper filed application.			

Secrecy Order 37 CFR 5.2

<input type="checkbox"/>	Portions or all of the application associated with this Application Data Sheet may fall under a Secrecy Order pursuant to 37 CFR 5.2 (Paper filers only. Applications that fall under Secrecy Order may not be filed electronically.)
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Address 1	3726 Las Vegas Blvd S. Unit 3303 W				
Address 2					
City	Las Vegas	State/Province	NV		
Postal Code	89158	Country i	US		

Inventor 3					<input type="button" value="Remove"/>
Legal Name					
Prefix	Given Name	Middle Name	Family Name	Suffix	
	James	N.	Chang		
Residence Information (Select One) <input checked="" type="radio"/> US Residency <input type="radio"/> Non US Residency <input type="radio"/> Active US Military Service					

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Application Data Sheet 37 CFR 1.76		Attorney Docket Number	17618CON2B (AP)	
		Application Number		
Title of Invention	METHODS OF PROVIDING THERAPEUTIC EFFECTS USING CYCLOSPORIN COMPONENTS			

City	Newport Beach	State/Province	CA	Country of Residence i	US
-------------	---------------	-----------------------	----	-------------------------------	----

Mailing Address of Inventor:

Address 1	36 Cervantes				
Address 2					
City	Newport Beach	State/Province	CA		
Postal Code	92660	Country i	US		

Inventor 4	<input type="button" value="Remove"/>
-------------------	---------------------------------------

Legal Name

Prefix	Given Name	Middle Name	Family Name	Suffix
	David	F.	Power	

Residence Information (Select One) US Residency Non US Residency Active US Military Service

City	Hubert	State/Province	NC	Country of Residence i	US
-------------	--------	-----------------------	----	-------------------------------	----

Mailing Address of Inventor:

Address 1	202 Fox Way N				
Address 2					
City	Hubert	State/Province	NC		
Postal Code	28539	Country i	US		

All Inventors Must Be Listed - Additional Inventor Information blocks may be generated within this form by selecting the **Add** button.

Correspondence Information:

Enter either Customer Number or complete the Correspondence Information section below. For further information see 37 CFR 1.33(a).

 An Address is being provided for the correspondence information of this application.

Customer Number	51957		
Email Address	patents_ip@allergan.com	<input type="button" value="Add Email"/>	<input type="button" value="Remove Email"/>

Application Information:

Title of the Invention	METHODS OF PROVIDING THERAPEUTIC EFFECTS USING CYCLOSPORIN COMPONENTS		
Attorney Docket Number	17618CON2B (AP)	Small Entity Status Claimed	<input type="checkbox"/>
Application Type	Nonprovisional		
Subject Matter	Utility		
Total Number of Drawing Sheets (if any)		Suggested Figure for Publication (if any)	

Application Data Sheet 37 CFR 1.76	Attorney Docket Number	17618CON2B (AP)
	Application Number	
Title of Invention	METHODS OF PROVIDING THERAPEUTIC EFFECTS USING CYCLOSPORIN COMPONENTS	

Publication Information:
 Request Early Publication (Fee required at time of Request 37 CFR 1.219)

 Request Not to Publish. I hereby request that the attached application not be published under 35 U.S.C. 122(b) and certify that the invention disclosed in the attached application **has not and will not** be the subject of an application filed in another country, or under a multilateral international agreement, that requires publication at eighteen months after filing.
Representative Information:

Representative information should be provided for all practitioners having a power of attorney in the application. Providing this information in the Application Data Sheet does not constitute a power of attorney in the application (see 37 CFR 1.32). Either enter Customer Number or complete the Representative Name section below. If both sections are completed the customer Number will be used for the Representative Information during processing.

Please Select One:	<input checked="" type="radio"/> Customer Number	<input type="radio"/> US Patent Practitioner	<input type="radio"/> Limited Recognition (37 CFR 11.9)
Customer Number	51597		

Domestic Benefit/National Stage Information:

This section allows for the applicant to either claim benefit under 35 U.S.C. 119(e), 120, 121, or 365(c) or indicate National Stage entry from a PCT application. Providing this information in the application data sheet constitutes the specific reference required by 35 U.S.C. 119(e) or 120, and 37 CFR 1.78.

Prior Application Status	Pending	Remove	
Application Number	Continuity Type	Prior Application Number	Filing Date (YYYY-MM-DD)
	Continuation of	13961808	2013-08-07
Prior Application Status	Pending	Remove	
Application Number	Continuity Type	Prior Application Number	Filing Date (YYYY-MM-DD)
13961808	Continuation of	11897177	2007-08-28
Prior Application Status	Abandoned	Remove	
Application Number	Continuity Type	Prior Application Number	Filing Date (YYYY-MM-DD)
11897177	Continuation of	10927857	2004-08-27
Prior Application Status	Expired	Remove	
Application Number	Continuity Type	Prior Application Number	Filing Date (YYYY-MM-DD)
10927857	non provisional of	60503137	2003-09-15
Additional Domestic Benefit/National Stage Data may be generated within this form by selecting the Add button.			Add

Foreign Priority Information:

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Application Data Sheet 37 CFR 1.76	Attorney Docket Number	17618CON2B (AP)
	Application Number	
Title of Invention	METHODS OF PROVIDING THERAPEUTIC EFFECTS USING CYCLOSPORIN COMPONENTS	

This section allows for the applicant to claim priority to a foreign application. Providing this information in the application data sheet constitutes the claim for priority as required by 35 U.S.C. 119(b) and 37 CFR 1.55(d). When priority is claimed to a foreign application that is eligible for retrieval under the priority document exchange program (PDX) the information will be used by the Office to automatically attempt retrieval pursuant to 37 CFR 1.55(h)(1) and (2). Under the PDX program, applicant bears the ultimate responsibility for ensuring that a copy of the foreign application is received by the Office from the participating foreign intellectual property office, or a certified copy of the foreign priority application is filed, within the time period specified in 37 CFR 1.55(g)(1).

Remove

Application Number	Country ⁱ	Filing Date (YYYY-MM-DD)	Access Code ^j (if applicable)

Additional Foreign Priority Data may be generated within this form by selecting the Add button.

Add

Statement under 37 CFR 1.55 or 1.78 for AIA (First Inventor to File) Transition Applications

This application (1) claims priority to or the benefit of an application filed before March 16, 2013 and (2) also contains, or contained at any time, a claim to a claimed invention that has an effective filing date on or after March 16, 2013.

NOTE: By providing this statement under 37 CFR 1.55 or 1.78, this application, with a filing date on or after March 16, 2013, will be examined under the first inventor to file provisions of the AIA.

Authorization to Permit Access:

Authorization to Permit Access to the Instant Application by the Participating Offices

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Application Data Sheet 37 CFR 1.76	Attorney Docket Number	17618CON2B (AP)
	Application Number	
Title of Invention	METHODS OF PROVIDING THERAPEUTIC EFFECTS USING CYCLOSPORIN COMPONENTS	

If checked, the undersigned hereby grants the USPTO authority to provide the European Patent Office (EPO), the Japan Patent Office (JPO), the Korean Intellectual Property Office (KIPO), the World Intellectual Property Office (WIPO), and any other intellectual property offices in which a foreign application claiming priority to the instant patent application is filed access to the instant patent application. See 37 CFR 1.14(c) and (h). This box should not be checked if the applicant does not wish the EPO, JPO, KIPO, WIPO, or other intellectual property office in which a foreign application claiming priority to the instant patent application is filed to have access to the instant patent application.

In accordance with 37 CFR 1.14(h)(3), access will be provided to a copy of the instant patent application with respect to: 1) the instant patent application-as-filed; 2) any foreign application to which the instant patent application claims priority under 35 U.S.C. 119(a)-(d) if a copy of the foreign application that satisfies the certified copy requirement of 37 CFR 1.55 has been filed in the instant patent application; and 3) any U.S. application-as-filed from which benefit is sought in the instant patent application.

In accordance with 37 CFR 1.14(c), access may be provided to information concerning the date of filing this Authorization.

Applicant Information:

Providing assignment information in this section does not substitute for compliance with any requirement of part 3 of Title 37 of CFR to have an assignment recorded by the Office.

Applicant 1	<input type="button" value="Remove"/>
<p>If the applicant is the inventor (or the remaining joint inventor or inventors under 37 CFR 1.45), this section should not be completed. The information to be provided in this section is the name and address of the legal representative who is the applicant under 37 CFR 1.43; or the name and address of the assignee, person to whom the inventor is under an obligation to assign the invention, or person who otherwise shows sufficient proprietary interest in the matter who is the applicant under 37 CFR 1.46. If the applicant is an applicant under 37 CFR 1.46 (assignee, person to whom the inventor is obligated to assign, or person who otherwise shows sufficient proprietary interest) together with one or more joint inventors, then the joint inventor or inventors who are also the applicant should be identified in this section.</p>	
<input type="button" value="Clear"/>	

<input checked="" type="radio"/> Assignee	<input type="radio"/> Legal Representative under 35 U.S.C. 117	<input type="radio"/> Joint Inventor
<input type="radio"/> Person to whom the inventor is obligated to assign.	<input type="radio"/> Person who shows sufficient proprietary interest	

If applicant is the legal representative, indicate the authority to file the patent application, the inventor is:

Name of the Deceased or Legally Incapacitated Inventor :	
--	--

If the Applicant is an Organization check here.

Organization Name	Allergan, Inc.
-------------------	----------------

Mailing Address Information:

Address 1	2525 Dupont Drive		
Address 2			
City	Irvine	State/Province	CA
Country	US	Postal Code	92612
Phone Number		Fax Number	

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Application Data Sheet 37 CFR 1.76		Attorney Docket Number	17618CON2B (AP)	
		Application Number		
Title of Invention	METHODS OF PROVIDING THERAPEUTIC EFFECTS USING CYCLOSPORIN COMPONENTS			
Email Address	patent_ip@allergan.com			
Additional Applicant Data may be generated within this form by selecting the Add button.				<input type="button" value="Add"/>

Non-Applicant Assignee Information:

Providing assignment information in this section does not substitute for compliance with any requirement of part 3 of Title 37 of CFR to have an assignment recorded by the Office.

Assignee 1				
Complete this section only if non-applicant assignee information is desired to be included on the patent application publication in accordance with 37 CFR 1.215(b). Do not include in this section an applicant under 37 CFR 1.46 (assignee, person to whom the inventor is obligated to assign, or person who otherwise shows sufficient proprietary interest), as the patent application publication will include the name of the applicant(s).				
				<input type="button" value="Remove"/>
If the Assignee is an Organization check here. <input type="checkbox"/>				
Prefix	Given Name	Middle Name	Family Name	Suffix
Mailing Address Information:				
Address 1				
Address 2				
City		State/Province		
Country i	Postal Code			
Phone Number		Fax Number		
Email Address				
Additional Assignee Data may be generated within this form by selecting the Add button.				<input type="button" value="Add"/>

Signature:

NOTE: This form must be signed in accordance with 37 CFR 1.33. See 37 CFR 1.4 for signature requirements and certifications				
Signature	/Laura L. Wine/		Date (YYYY-MM-DD)	2013-08-14
First Name	Laura	Last Name	Wine	Registration Number
				68681
Additional Signature may be generated within this form by selecting the Add button.				<input type="button" value="Add"/>

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Application Data Sheet 37 CFR 1.76	Attorney Docket Number	17618CON2B (AP)
	Application Number	
Title of Invention	METHODS OF PROVIDING THERAPEUTIC EFFECTS USING CYCLOSPORIN COMPONENTS	

This collection of information is required by 37 CFR 1.76. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 23 minutes to complete, including gathering, preparing, and submitting the completed application data sheet form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

Privacy Act Statement

The Privacy Act of 1974 (P.L. 93-579) requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C. 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether the Freedom of Information Act requires disclosure of these records.
2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.
3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.
4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).
5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.
6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).
7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.
8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspections or an issued patent.
9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

DECLARATION (37 CFR 1.63) FOR UTILITY OR DESIGN APPLICATION USING AN APPLICATION DATA SHEET (37 CFR 1.76)

Title of Invention	METHODS OF PROVIDING THERAPEUTIC EFFECTS USING CYCLOSPORIN COMPONENTS Docket No.: 17618CON2(AP)
---------------------------	--

As the below named inventor, I hereby declare that:

This declaration is directed to: The attached application, or
 United States application or PCT international application number 13/961,808
filed on 8/7/2013

The above-identified application was made or authorized to be made by me.

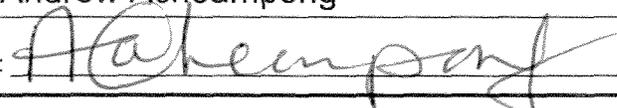
I believe that I am the original inventor or an original joint inventor of a claimed invention in the application.

I hereby acknowledge that any willful false statement made in this declaration is punishable under 18 U.S.C. 1001 by fine or imprisonment of not more than five (5) years, or both.

WARNING:

Petitioner/applicant is cautioned to avoid submitting personal information in documents filed in a patent application that may contribute to identity theft. Personal information such as social security numbers, bank account numbers, or credit card numbers (other than a check or credit card authorization form PTO-2038 submitted for payment purposes) is never required by the USPTO to support a petition or an application. If this type of personal information is included in documents submitted to the USPTO, petitioners/applicants should consider redacting such personal information from the documents before submitting them to the USPTO. Petitioner/applicant is advised that the record of a patent application is available to the public after publication of the application (unless a non-publication request in compliance with 37 CFR 1.213(a) is made in the application) or issuance of a patent. Furthermore, the record from an abandoned application may also be available to the public if the application is referenced in a published application or an issued patent (see 37 CFR 1.14). Checks and credit card authorization forms PTO-2038 submitted for payment purposes are not retained in the application file and therefore are not publicly available.

LEGAL NAME OF INVENTOR

Inventor: Andrew Acheampong Date (Optional) : _____
Signature: 

Note: An application data sheet (PTO/AIA/14 or equivalent), including naming the entire inventive entity, must accompany this form. Use an additional PTO/SB/AIA01 form for each additional inventor.

This collection of information is required by 35 U.S.C. 115 and 37 CFR 1.63. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11 and 1.14. This collection is estimated to take 1 minute to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

DECLARATION (37 CFR 1.63) FOR UTILITY OR DESIGN APPLICATION USING AN APPLICATION DATA SHEET (37 CFR 1.76)

Title of Invention	METHODS OF PROVIDING THERAPEUTIC EFFECTS USING CYCLOSPORIN COMPONENTS Docket No.: 17618CON2(AP)
---------------------------	--

As the below named inventor, I hereby declare that:

This declaration is directed to: The attached application, or
 United States application or PCT international application number 13/961,808
 filed on 8/7/2013

The above-identified application was made or authorized to be made by me.

I believe that I am the original inventor or an original joint inventor of a claimed invention in the application.

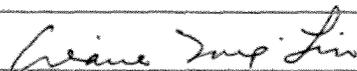
I hereby acknowledge that any willful false statement made in this declaration is punishable under 18 U.S.C. 1001 by fine or imprisonment of not more than five (5) years, or both.

WARNING:

Petitioner/applicant is cautioned to avoid submitting personal information in documents filed in a patent application that may contribute to identity theft. Personal information such as social security numbers, bank account numbers, or credit card numbers (other than a check or credit card authorization form PTO-2038 submitted for payment purposes) is never required by the USPTO to support a petition or an application. If this type of personal information is included in documents submitted to the USPTO, petitioners/applicants should consider redacting such personal information from the documents before submitting them to the USPTO. Petitioner/applicant is advised that the record of a patent application is available to the public after publication of the application (unless a non-publication request in compliance with 37 CFR 1.213(a) is made in the application) or issuance of a patent. Furthermore, the record from an abandoned application may also be available to the public if the application is referenced in a published application or an issued patent (see 37 CFR 1.14). Checks and credit card authorization forms PTO-2038 submitted for payment purposes are not retained in the application file and therefore are not publicly available.

LEGAL NAME OF INVENTOR

Inventor: DIANE D. TANG-LIU Date (Optional): _____

Signature: 

Note: An application data sheet (PTO/AIA/14 or equivalent), including naming the entire inventive entity, must accompany this form. Use an additional PTO/SB/AIA/01 form for each additional inventor.

This collection of information is required by 35 U.S.C. 115 and 37 CFR 1.63. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11 and 1.14. This collection is estimated to take 1 minute to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

DECLARATION (37 CFR 1.63) FOR UTILITY OR DESIGN APPLICATION USING AN APPLICATION DATA SHEET (37 CFR 1.76)

Title of Invention	METHODS OF PROVIDING THERAPEUTIC EFFECTS USING CYCLOSPORIN COMPONENTS Docket No.: 17618CON2(AP)
---------------------------	--

As the below named inventor, I hereby declare that:

This declaration is directed to: The attached application, or
 United States application or PCT international application number 13/961,808
filed on 8/7/2013

The above-identified application was made or authorized to be made by me.

I believe that I am the original inventor or an original joint inventor of a claimed invention in the application.

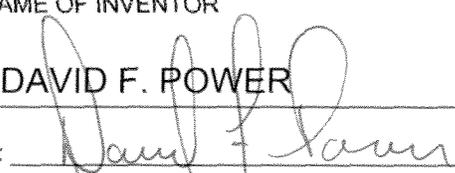
I hereby acknowledge that any willful false statement made in this declaration is punishable under 18 U.S.C. 1001 by fine or imprisonment of not more than five (5) years, or both.

WARNING:

Petitioner/applicant is cautioned to avoid submitting personal information in documents filed in a patent application that may contribute to identity theft. Personal information such as social security numbers, bank account numbers, or credit card numbers (other than a check or credit card authorization form PTO-2038 submitted for payment purposes) is never required by the USPTO to support a petition or an application. If this type of personal information is included in documents submitted to the USPTO, petitioners/applicants should consider redacting such personal information from the documents before submitting them to the USPTO. Petitioner/applicant is advised that the record of a patent application is available to the public after publication of the application (unless a non-publication request in compliance with 37 CFR 1.213(a) is made in the application) or issuance of a patent. Furthermore, the record from an abandoned application may also be available to the public if the application is referenced in a published application or an issued patent (see 37 CFR 1.14). Checks and credit card authorization forms PTO-2038 submitted for payment purposes are not retained in the application file and therefore are not publicly available.

LEGAL NAME OF INVENTOR

Inventor: DAVID F. POWER Date (Optional): 8-12-2013

Signature: 

Note: An application data sheet (PTO/AIA/14 or equivalent), including naming the entire inventive entity, must accompany this form. Use an additional PTO/SB/AIA01 form for each additional inventor.

This collection of information is required by 35 U.S.C. 115 and 37 CFR 1.63. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11 and 1.14. This collection is estimated to take 1 minute to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

SUBSTITUTE STATEMENT IN LIEU OF AN OATH OR DECLARATION FOR UTILITY OR DESIGN PATENT APPLICATION (35 U.S.C. 115(d) AND 37 CFR 1.64)

Title of Invention	Methods of Providing Therapeutic Effects Using Cyclosporin Components Docket No.: 17618CON2(AP)		
This statement is directed to:			
<input type="checkbox"/> The attached application,			
OR			
<input checked="" type="checkbox"/> United States application or PCT international application number <u>13/961,808</u> filed on <u>8-7-13</u>			
LEGAL NAME of inventor to whom this substitute statement applies: (E.g., Given Name (first and middle (if any)) and Family Name or Surname)			
James N. Chang			
Residence (except for a deceased or legally incapacitated inventor):			
City	Newport Beach	State	CA US
Mailing Address (except for a deceased or legally incapacitated inventor):			
36 Cervantes			
City	Newport Beach	State	CA 92660 US
I believe the above-named inventor or joint inventor to be the original inventor or an original joint inventor of a claimed invention in the application.			
The above-identified application was made or authorized to be made by me.			
I hereby acknowledge that any willful false statement made in this statement is punishable under 18 U.S.C. 1001 by fine or imprisonment of not more than five (5) years, or both.			
Relationship to the inventor to whom this substitute statement applies:			
<input type="checkbox"/> Legal Representative (for deceased or legally incapacitated inventor only),			
<input checked="" type="checkbox"/> Assignee,			
<input type="checkbox"/> Person to whom the inventor is under an obligation to assign,			
<input type="checkbox"/> Person who otherwise shows a sufficient proprietary interest in the matter (petition under 37 CFR 1.46 is required), or			
<input type="checkbox"/> Joint inventor.			

This collection of information is required by 35 U.S.C. 115 and 37 CFR 1.63. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11 and 1.14. This collection is estimated to take 1 minute to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

SUBSTITUTE STATEMENT

Circumstances permitting execution of this substitute statement:

- Inventor is deceased,
 Inventor is under legal incapacity,
 Inventor cannot be found or reached after diligent effort, or
 Inventor has refused to execute the oath or declaration under 37 CFR 1.63.

If there are joint inventors, please check the appropriate box below:

- An application data sheet under 37 CFR 1.76 (PTO/AIA/14 or equivalent) naming the entire inventive entity has been or is currently submitted.

OR

- An application data sheet under 37 CFR 1.76 (PTO/AIA/14 or equivalent) has not been submitted. Thus, a Substitute Statement Supplemental Sheet (PTO/AIA/11 or equivalent) naming the entire inventive entity and providing inventor information is attached. See 37 CFR 1.64(b).

WARNING:

Petitioner/applicant is cautioned to avoid submitting personal information in documents filed in a patent application that may contribute to identity theft. Personal information such as social security numbers, bank account numbers, or credit card numbers (other than a check or credit card authorization form PTO-2038 submitted for payment purposes) is never required by the USPTO to support a petition or an application. If this type of personal information is included in documents submitted to the USPTO, petitioners/applicants should consider redacting such personal information from the documents before submitting them to the USPTO. Petitioner/applicant is advised that the record of a patent application is available to the public after publication of the application (unless a non-publication request in compliance with 37 CFR 1.213(a) is made in the application) or issuance of a patent. Furthermore, the record from an abandoned application may also be available to the public if the application is referenced in a published application or an issued patent (see 37 CFR 1.14). Checks and credit card authorization forms PTO-2038 submitted for payment purposes are not retained in the application file and therefore are not publicly available.

PERSON EXECUTING THIS SUBSTITUTE STATEMENT:

Name: **Debra D. Condino** TITLE: ASSISTANT SECRETARY
 COMPANY: ALLEGAN, INC. (ASSIGNED)
 Date (Optional):

Signature: *D Condino*

Residence (unless provided in an application data sheet, PTO/AIA/14 or equivalent):

City	Irvine	State	CA	Country	US
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Mailing Address (unless provided in an application data sheet, PTO/AIA/14 or equivalent)

2525 Dupont Drive-T2-7H

City	Irvine	State	CA	Zip	92612	Country	US
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Note: Use an additional PTO/AIA/02 form for each inventor who is deceased, legally incapacitated, cannot be found or reached after diligent effort, or has refused to execute the oath or declaration under 37 CFR 1.63.

Privacy Act Statement

The Privacy Act of 1974 (P.L. 93-579) requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C. 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether disclosure of these records is required by the Freedom of Information Act.
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5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.
6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).
7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.
8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspection or an issued patent.
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NOTE: This form is to be submitted with the Power of Attorney by Applicant form (PTO/AIA/82B or equivalent) to identify the application to which the Power of Attorney is directed, in accordance with 37 CFR 1.5. If the Power of Attorney by Applicant form is not accompanied by this transmittal form or an equivalent, the Power of Attorney will not be recognized in the application.

Application Number	unknown
Filing Date	herewith
First Named Inventor	Andrew Acheampong
Title	METHODS OF PROVIDING THERAPEUTIC EFFECTS USING CYCLOSPORIN COMPONENTS
Art Unit	
Examiner Name	
Attorney Docket Number	17618CON2B (AP)

SIGNATURE of Applicant or Patent Practitioner

Signature	/Laura L. Wine/	Date	August 14, 2013
Name	Laura L. Wine	Telephone	714-246-6996
Registration Number	68,681		

NOTE: This form must be signed in accordance with 37 CFR 1.33. See 37 CFR 1.4(d) for signature requirements and certifications.

*Total of 1 forms are submitted.

This collection of information is required by 37 CFR 1.31, 1.32 and 1.33. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11 and 1.14. This collection is estimated to take 3 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

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POWER OF ATTORNEY BY APPLICANT

I hereby revoke all previous powers of attorney given in the application identified in the attached transmittal letter.

I hereby appoint Practitioner(s) associated with the following Customer Number as my/our attorney(s) or agent(s), and to transact all business in the United States Patent and Trademark Office connected therewith for the application referenced in the attached transmittal letter (form PTO/AIA/82A or equivalent):

51957

OR

I hereby appoint Practitioner(s) named below as my/our attorney(s) or agent(s), and to transact all business in the United States Patent and Trademark Office connected therewith for the application referenced in the attached transmittal letter (form PTO/AIA/82A or equivalent):

Name	Registration Number	Name	Registration Number

Please recognize or change the correspondence address for the application identified in the attached transmittal letter to:

The address associated with the above-mentioned Customer Number.

OR

The address associated with Customer Number:

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City State Zip

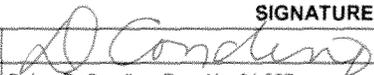
Country

Telephone Email

I am the Applicant:

- Inventor or Joint Inventor
- Legal Representative of a Deceased or Legally Incapacitated Inventor
- Assignee or Person to Whom the Inventor is Under an Obligation to Assign
- Person Who Otherwise Shows Sufficient Proprietary Interest (e.g., a petition under 37 CFR 1.46(b)(2) was granted in the application or is concurrently being filed with this document)

SIGNATURE of Applicant for Patent

Signature		Date	
Name	Debra D. Condino, Reg. No. 31,007	Telephone	714-246-2388
Title and Company	Assistant Secretary, Allergan, Inc.		

NOTE: Signature - This form must be signed by the applicant in accordance with 37 CFR 1.33. See 37 CFR 1.4 for signature requirements and certifications. Submit multiple forms for more than one signature, see below *.

*Total of _____ forms are submitted.

This collection of information is required by 37 CFR 1.31, 1.32 and 1.33. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11 and 1.14. This collection is estimated to take 3 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.

Electronic Patent Application Fee Transmittal

Application Number:	13967189
Filing Date:	
Title of Invention:	METHODS OF PROVIDING THERAPEUTIC EFFECTS USING CYCLOSPORIN COMPONENTS
First Named Inventor/Applicant Name:	Andrew Acheampong
Filer:	Laura Lee Wine/Lauren Barberena
Attorney Docket Number:	17618CON2B (AP)

Filed as Large Entity

Utility under 35 USC 111(a) Filing Fees

Description	Fee Code	Quantity	Amount	Sub-Total in USD(\$)
Basic Filing:				
Pages:				
Claims:				
Claims in Excess of 20	1202	1	80	80

Miscellaneous-Filing:

Petition:

Patent-Appeals-and-Interference:

Post-Allowance-and-Post-Issuance:

Extension-of-Time:

Description	Fee Code	Quantity	Amount	Sub-Total in USD(\$)
Miscellaneous:				
Total in USD (\$)				80

Electronic Acknowledgement Receipt

EFS ID:	16594189
Application Number:	13967189
International Application Number:	
Confirmation Number:	4818
Title of Invention:	METHODS OF PROVIDING THERAPEUTIC EFFECTS USING CYCLOSPORIN COMPONENTS
First Named Inventor/Applicant Name:	Andrew Acheampong
Customer Number:	51957
Filer:	Laura Lee Wine/Lauren Barberena
Filer Authorized By:	Laura Lee Wine
Attorney Docket Number:	17618CON2B (AP)
Receipt Date:	14-AUG-2013
Filing Date:	
Time Stamp:	19:56:57
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	Deposit Account
Payment was successfully received in RAM	\$80
RAM confirmation Number	6828
Deposit Account	010885
Authorized User	

The Director of the USPTO is hereby authorized to charge indicated fees and credit any overpayment as follows:

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File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Fee Worksheet (SB06)	fee-info.pdf	30698 <small>5ca960e737fe250aaf1a5f4557295ff39ac9e1dd</small>	no	2

Warnings:**Information:****Total Files Size (in bytes):**

30698

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New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)	Application Number		13967189
	Filing Date		2013-08-14
	First Named Inventor	ACHEAMPONG, ANDREW	
	Art Unit		1653
	Examiner Name	TBD	
	Attorney Docket Number		17618-US-BCON2-AP

U.S.PATENTS						
Examiner Initial*	Cite No	Patent Number	Kind Code ¹	Issue Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1	3278447		1966-10-11	Thomas McNicholas	
	2	4388229		1983-06-14	Cherng-Chyi Fu	
	3	4388307		1983-06-14	Thomas Cavanak	
	4	4614736		1986-09-30	Devallee et al	
	5	4649047		1987-03-10	Renee Kaswan	
	6	4764503		1988-08-16	Roland Wenger	
	7	4814323		1989-03-21	Andrieu et al	
	8	4839342		1989-06-13	Renee Kaswan	

**INFORMATION DISCLOSURE
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Art Unit	1653	
Examiner Name	TBD	
Attorney Docket Number	17618-US-BCON2-AP	

	9	4970076		1990-11-13	David Horrobin	
	10	4990337		1991-02-05	Kurihara et al	
	11	4996193		1991-02-26	Hewitt et al	
	12	5047396		1991-09-10	Orban et al	
	13	5051402		1991-09-24	Kurihara et al	
	14	5053000		1991-10-01	Booth et al	
	15	5286730		1994-02-15	Caufield et al	
	16	5286731		1994-02-15	Caufield et al	
	17	5294604		1994-03-15	Nussenblatt et al	
	18	5296158		1994-03-22	MacGilp et al	
	19	5342625		1994-08-30	Hauer et al	

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Examiner Name	TBD	
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	20	5368854		1994-11-29	Donna Rennick	
	21	5411952		1995-05-02	Renee Kaswan	
	22	5424078		1995-06-13	Anthony Dziabo	
	23	5474919		1995-12-12	Chartrain et al	
	24	5474979		1995-12-12	Ding et al	U.S. Application No. 08/243,279 and its entire prosecution history**
	25	5504068		1996-04-02	Komiya et al	
	26	5540931		1996-07-30	Hewitt et al	
	27	5543393		1996-08-06	Kim et al	
	28	5589455		1996-12-31	Jong Woo	
	29	5591971		1997-01-07	Shahar et al	
	30	5614491		1997-03-25	Walch et al	

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Attorney Docket Number	17618-US-BCON2-AP

31	5639724		1997-06-17	Thomas Cavanak	
32	5652212		1997-07-29	Cavanak et al	
33	5719123		1998-02-17	Morley et al	
34	5739105		1998-04-14	Kim et al	
35	5753166		1998-05-19	Dalton et al	
36	5766629		1998-06-16	Cho et al	
37	5798333		1998-08-25	Bernard Sherman	
38	5807820		1998-09-15	Elias et al	
39	5827822		1998-10-27	Floch'h et al	
40	5827862		1998-10-27	Yoshitaka Yamamura	
41	5834017		1998-11-10	Cho et al	

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Attorney Docket Number	17618-US-BCON2-AP

	42	5843452		1998-12-01	Wiedmann et al	
	43	5843891		1998-12-01	Bernard Sherman	
	44	5858401		1999-01-12	Bhalani et al	
	45	5866159		1999-02-02	Hauer et al	
	46	5891846		1999-04-06	Ishida et al	
	47	5916589		1999-06-29	Hauer et al	
	48	5929030		1999-07-27	Hamied et al	
	49	5951971		1999-09-14	Kawashima et al	
	50	5962014		1999-10-05	Hauer et al	
	51	5962017		1999-10-05	Hauer et al	
	52	5962019		1999-10-05	Cho et al	

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Art Unit	1653	
Examiner Name	TBD	
Attorney Docket Number	17618-US-BCON2-AP	

	53	5977066		1999-11-02	Thomas Cavanak	
	54	5981479		1999-11-09	Ko et al	
	55	5981607		1999-11-09	Ding et al	U.S. Application No. 09/008,924 and its entire prosecution history**
	56	5998365		1999-12-07	Bernard Sherman	
	57	6004566		1999-12-21	Friedman et al	
	58	6007840		1999-12-28	Hauer et al	
	59	6008191		1999-12-28	Amarjit Singh	
	60	6008192		1999-12-28	Al-Razzak et al	
	61	6022852		2000-02-08	Klokkers et al	
	62	6024978		2000-02-15	Hauer et al	
	63	6046163		2000-04-04	Stuchlik et al	

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Examiner Name	TBD
Attorney Docket Number	17618-US-BCON2-AP

64	6057289		2000-05-02	Nirmal Mulye	
65	6159933		2000-12-12	Bernard Sherman	
66	6197335		2001-03-06	Bernard Sherman	
67	6254860		2001-07-03	Michael Garst	
68	6254885		2001-07-03	Cho et al	
69	6267985		2001-07-31	Chen et al	
70	6284268		2001-09-04	Mishra et al	
71	6294192		2001-09-25	Patel et al	
72	6306825		2001-10-23	Thomas Cavanak	
73	6323204		2001-11-27	James Burke	
74	6346511		2002-02-12	Singh et al	

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Attorney Docket Number	17618-US-BCON2-AP

75	6350442		2002-02-26	Michael Garst	
76	6413547		2002-07-02	Bennett et al	
77	6420355		2002-07-16	Richter et al	
78	6468968		2002-10-22	Cavanak et al	
79	6475519		2002-11-05	Meinzer et al	
80	6486124		2002-11-26	Olbrich et al	
81	6544953		2003-04-08	Tsuzuki et al	
82	6555526		2003-04-29	Toshihiko Matsuo	
83	6562873		2003-05-13	Olejniak et al	
84	6569463		2003-03-27	Patel et al	
85	6582718		2003-06-24	Yoichi Kawashima	

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Attorney Docket Number	17618-US-BCON2-AP

	86	6656460		2003-12-02	Benita et al	
	87	6872705		2005-03-29	Robert Lyons	
	88	7202209		2007-04-10	James N. Chang	U.S. Application No. 11/181,428 and its entire prosecution history**
	89	7276476		2007-10-02	Chang et al	U.S. Application No. 11/181,187 and its entire prosecution history**
	90	7288520		2007-10-30	Chang et al	U.S. Application No. 11/255,821 and its entire prosecution history**
	91	7297679		2007-11-20	James Chang	U.S. Application No. 11/181,178 and its entire prosecution history**
	92	7501393		2009-03-10	Tien et al	U.S. Application No. 11/161,218 and its entire prosecution history**
	93	8211855		2012-07-03	Chang et al	U.S. Application No. 11/857,223 and its entire prosecution history**
	94	8288348		2012-10-16	Chang et al	U.S. Application No. 11/917,448 and its entire prosecution history**

If you wish to add additional U.S. Patent citation information please click the Add button.

U.S.PATENT APPLICATION PUBLICATIONS

Examiner Initial*	Cite No	Publication Number	Kind Code ¹	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
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Application Number		13967189
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Art Unit	1653	
Examiner Name	TBD	
Attorney Docket Number	17618-US-BCON2-AP	

1	20010003589		2001-06-14	Neuer et al	
2	20010014665		2001-08-16	Fischer et al	
3	20010036449		2001-11-01	Michael Garst	
4	20020012680		2002-01-31	Patel et al	
5	20020013272		2002-01-31	Cavanak et al	
6	20020016290		2002-02-07	Floc'h et al	
7	20020016292		2002-02-07	Richter et al	
8	20020025927		2002-02-28	Olbrich et al	
9	20020045601		2002-04-18	Yoichi Kawashima	
10	20020107183		2002-08-08	Petszulat et al	
11	20020119190		2002-08-29	Meinzer et al	

**INFORMATION DISCLOSURE
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First Named Inventor	ACHEAMPONG, ANDREW
Art Unit	1653
Examiner Name	TBD
Attorney Docket Number	17618-US-BCON2-AP

12	20020165134		2002-11-07	Richter et al	
13	20030021816		2003-01-30	Kang et al	
14	20030044452		2003-03-06	Ryuji Ueno	
15	20030055028		2003-03-20	Stergiopoulos et al	
16	20030059470		2003-03-27	Rainer Muller	
17	20030060402		2003-03-27	Cavanak et al	
18	20030087813		2003-05-08	Or et al	
19	20030104992		2003-06-05	Or et al	
20	20030108626		2003-06-12	Benita et al	
21	20030109425		2003-06-12	Or et al	
22	20030109426		2003-06-12	Or et al	

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**

(Not for submission under 37 CFR 1.99)

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Art Unit	1653	
Examiner Name	TBD	
Attorney Docket Number	17618-US-BCON2-AP	

23	20030133984		2003-07-17	Ambuhl et al	
24	20030143250		2003-07-31	Hauer et al	
25	20030147954		2003-08-07	Yang et al	
26	20030166517		2003-09-04	Fricker et al	
27	20050014691		2005-01-20	Bakhit et al	
28	20050059583		2005-03-17	Andrew Acheampong	U.S. Application No. 10/927,857 and its entire prosecution history**
29	20070015691		2007-01-18	James Chang	U.S. Application No. 11/181,409 and its entire prosecution history**
30	20070027072		2007-02-01	Tien et al	
31	20070087962		2007-04-19	Tien et al	
32	20070149447		2007-06-28	Chang et al	U.S. Application No. 11/679,934 and its entire prosecution history**
33	20070299004		2007-12-27	Acheampong et al	U.S. Application No. 11/897,177 and its entire prosecution history**

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34	20080039378		2008-02-14	Graham et al	U.S. Application No. 11/781,095 and its entire prosecution history**
35	20080070834		2008-03-20	Chang et al	U.S. Application No. 11/940,652 and its entire prosecution history**
36	20080146497		2008-06-19	Graham et al	U.S. Application No. 11/858,200 and its entire prosecution history**
37	20080207495		2008-08-28	Graham et al	U.S. Application No. 12/035,698 and its entire prosecution history**
38	20090131307		2009-05-21	Tien et al	U.S. Application No. 12/361,335 and its entire prosecution history**
39	20100279951		2010-11-04	Morgan et al	U.S. Application No. 12/771,952 and its entire prosecution history**
40	20110009339		2011-01-13	Rhett Schiffman	U.S. Application No. 12/759,431 and its entire prosecution history**
41	20110294744		2011-12-01	Morgan et al	U.S. Application No. 13/115,764 and its entire prosecution history**
42	20120270805		2012-10-25	Chang et al	U.S. Application No. 13/536,479 and its entire prosecution history**
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Examiner Initial*	Cite No	Foreign Document Number ³	Country Code ²	Kind Code ⁴	Publication Date	Name of Patentee or Applicant of cited Document	Pages, Columns, Lines where Relevant Passages or Relevant Figures Appear	T ⁵
	1	19810655	DE		1999-09-16	Eberhard-Karis- Universitat Tubingen Universitatskl		<input type="checkbox"/>
	2	0471293	EP		1992-02-19	ABBOTT LABORATORIES		<input type="checkbox"/>
	3	0547229	EP		1993-01-07	LLT Institute Co., Ltd.		<input type="checkbox"/>
	4	0760237	EP		1997-03-05	Cipla Limited		<input type="checkbox"/>
	5	1995-031211	WO		1995-11-23	Allergan Inc.		<input type="checkbox"/>
	6	2000-000179	WO		2000-01-06	Won Jin Biopharma Co., Ltd		<input type="checkbox"/>
	7	2001-032142	WO		2001-05-10	Cipla Limited		<input type="checkbox"/>
	8	2001-041671	WO		2001-06-14	Transneuronix, Inc.		<input type="checkbox"/>
	9	2002-009667	WO		2002-02-07	Pharmasol GMBH		<input type="checkbox"/>
	10	2002-049603	WO		2002-06-27	LG Household & Health Care Ltd.		<input type="checkbox"/>

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11	2003-030834	WO		2003-04-17	Enanta Pharmaceuticals, Inc.	<input type="checkbox"/>
12	2003-053405	WO		2003-07-03	Yissum Research Development Company of the Hebrew	<input type="checkbox"/>

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	1	ABDULRAZIK, M. ET AL, Ocular Delivery of Cyclosporin A II. Effect of Submicron Emulsion's Surface Charge on Ocular Distribution of Topical Cyclosporin A, S.T.P. Pharma Sciences, Dec. 2001, 427-432, 11(6)	<input type="checkbox"/>
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19	DONNENFELD, ERIC D., The Economics Of Using Restasis, Ophthalmology Management, 10/2003, 3 pages, US	<input type="checkbox"/>
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65	U.S. Pending Application: 13/961,808 Filed on August 07, 2013	<input type="checkbox"/>
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Signature	/Laura L. Wine/	Date (YYYY-MM-DD)	2013-09-04
Name/Print	Laura L. Wine	Registration Number	68,681

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International Application Number:	
Confirmation Number:	4818
Title of Invention:	METHODS OF PROVIDING THERAPEUTIC EFFECTS USING CYCLOSPORIN COMPONENTS
First Named Inventor/Applicant Name:	Andrew Acheampong
Customer Number:	51957
Filer:	Laura Lee Wine/Ken Dinh
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Attorney Docket Number:	17618CON2B (AP)
Receipt Date:	04-SEP-2013
Filing Date:	14-AUG-2013
Time Stamp:	21:16:24
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	no
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File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Information Disclosure Statement (IDS) Form (SB08)	17618CON2B-IDS_09_04_2013.pdf	541590 <small>9f394d44a6793efa377b6aed3106a35c65a9adc9</small>	no	24

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59	Non Patent Literature	Restasis_Increasing_tear_Production_2009.pdf	332259 0a1285bcf642f927562ba180ba3ba5446eb 2afe4	no	3
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Total Files Size (in bytes):			92386808		
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Electronic Acknowledgement Receipt

EFS ID:	16766268
Application Number:	13967189
International Application Number:	
Confirmation Number:	4818
Title of Invention:	METHODS OF PROVIDING THERAPEUTIC EFFECTS USING CYCLOSPORIN COMPONENTS
First Named Inventor/Applicant Name:	Andrew Acheampong
Customer Number:	51957
Filer:	Laura Lee Wine/Ken Dinh
Filer Authorized By:	Laura Lee Wine
Attorney Docket Number:	17618CON2B (AP)
Receipt Date:	04-SEP-2013
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Time Stamp:	21:36:02
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	no
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File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
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Table with 7 columns: APPLICATION NUMBER, FILING or 371(c) DATE, GRP ART UNIT, FIL FEE REC'D, ATTY. DOCKET NO, TOT CLAIMS, IND CLAIMS. Row 1: 13/967,189, 08/14/2013, 1653, 2220, 17618CON2B (AP), 24, 3

CONFIRMATION NO. 4818

51957
ALLERGAN, INC.
2525 DUPONT DRIVE, T2-7H
IRVINE, CA 92612-1599

FILING RECEIPT



Date Mailed: 09/05/2013

Receipt is acknowledged of this non-provisional patent application. The application will be taken up for examination in due course. Applicant will be notified as to the results of the examination. Any correspondence concerning the application must include the following identification information: the U.S. APPLICATION NUMBER, FILING DATE, NAME OF APPLICANT, and TITLE OF INVENTION. Fees transmitted by check or draft are subject to collection. Please verify the accuracy of the data presented on this receipt. If an error is noted on this Filing Receipt, please submit a written request for a Filing Receipt Correction. Please provide a copy of this Filing Receipt with the changes noted thereon. If you received a "Notice to File Missing Parts" for this application, please submit any corrections to this Filing Receipt with your reply to the Notice. When the USPTO processes the reply to the Notice, the USPTO will generate another Filing Receipt incorporating the requested corrections

Inventor(s)

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Applicant(s)

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Assignment For Published Patent Application

Allergan, Inc., Irvine, CA

Power of Attorney: The patent practitioners associated with Customer Number 51957

Domestic Priority data as claimed by applicant

This application is a CON of 13/961,808 08/07/2013
which is a CON of 11/897,177 08/28/2007
which is a CON of 10/927,857 08/27/2004 ABN
which claims benefit of 60/503,137 09/15/2003

Foreign Applications for which priority is claimed (You may be eligible to benefit from the Patent Prosecution Highway program at the USPTO. Please see http://www.uspto.gov for more information.) - None.

Foreign application information must be provided in an Application Data Sheet in order to constitute a claim to foreign priority. See 37 CFR 1.55 and 1.76.

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If Required, Foreign Filing License Granted: 08/29/2013

The country code and number of your priority application, to be used for filing abroad under the Paris Convention, is **US 13/967,189**

Projected Publication Date: 12/12/2013

Non-Publication Request: No

Early Publication Request: No

Title

METHODS OF PROVIDING THERAPEUTIC EFFECTS USING CYCLOSPORIN COMPONENTS

Preliminary Class

435

Statement under 37 CFR 1.55 or 1.78 for AIA (First Inventor to File) Transition Applications: No

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The grant of a license does not in any way lessen the responsibility of a licensee for the security of the subject matter as imposed by any Government contract or the provisions of existing laws relating to espionage and the national security or the export of technical data. Licensees should apprise themselves of current regulations especially with respect to certain countries, of other agencies, particularly the Office of Defense Trade Controls, Department of State (with respect to Arms, Munitions and Implements of War (22 CFR 121-128)); the Bureau of Industry and Security, Department of Commerce (15 CFR parts 730-774); the Office of Foreign Assets Control, Department of Treasury (31 CFR Parts 500+) and the Department of Energy.

NOT GRANTED

No license under 35 U.S.C. 184 has been granted at this time, if the phrase "IF REQUIRED, FOREIGN FILING LICENSE GRANTED" DOES NOT appear on this form. Applicant may still petition for a license under 37 CFR 5.12, if a license is desired before the expiration of 6 months from the filing date of the application. If 6 months has lapsed from the filing date of this application and the licensee has not received any indication of a secrecy order under 35 U.S.C. 181, the licensee may foreign file the application pursuant to 37 CFR 5.15(b).

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The United States represents the largest, most dynamic marketplace in the world and is an unparalleled location for business investment, innovation, and commercialization of new technologies. The U.S. offers tremendous resources and advantages for those who invest and manufacture goods here. Through SelectUSA, our nation works to promote and facilitate business investment. SelectUSA provides information assistance to the international investor community; serves as an ombudsman for existing and potential investors; advocates on behalf of U.S. cities, states, and regions competing for global investment; and counsels U.S. economic development organizations on investment attraction best practices. To learn more about why the United States is the best country in the world to develop technology, manufacture products, deliver services, and grow your business, visit <http://www.SelectUSA.gov> or call +1-202-482-6800.



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NUMBER	FILING OR 371(C) DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO./TITLE
13/967,189	08/14/2013	Andrew Acheampong	17618CON2B (AP)

CONFIRMATION NO. 4818

POA ACCEPTANCE LETTER

51957
ALLERGAN, INC.
2525 DUPONT DRIVE, T2-7H
IRVINE, CA 92612-1599



Date Mailed: 09/05/2013

NOTICE OF ACCEPTANCE OF POWER OF ATTORNEY

This is in response to the Power of Attorney filed 08/14/2013.

The Power of Attorney in this application is accepted. Correspondence in this application will be mailed to the above address as provided by 37 CFR 1.33.

/btsebhatu/

Office of Data Management, Application Assistance Unit (571) 272-4000, or (571) 272-4200, or 1-888-786-0101

Electronic Acknowledgement Receipt

EFS ID:	16593528
Application Number:	13967189
International Application Number:	
Confirmation Number:	4818
Title of Invention:	METHODS OF PROVIDING THERAPEUTIC EFFECTS USING CYCLOSPORIN COMPONENTS
First Named Inventor/Applicant Name:	Andrew Acheampong
Customer Number:	51957
Filer:	Laura Lee Wine/Lauren Barberena
Filer Authorized By:	Laura Lee Wine
Attorney Docket Number:	17618CON2B (AP)
Receipt Date:	14-AUG-2013
Filing Date:	
Time Stamp:	18:56:04
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes		
Payment Type	Deposit Account	Adjustment date: 09/20/2013 CKHLOK 08/15/2013 INTEFSW 00006280 010885 13967189 07 FC:1800 130.00 CR	
Payment was successfully received in RAM	\$6270		
RAM confirmation Number	6280	09/20/2013 CKHLOK 00000002 010885 13967189	
Deposit Account	010885	01 FC:1830 140.00 DA	
Authorized User			

The Director of the USPTO is hereby authorized to charge indicated fees and credit any overpayment as follows:

- Charge any Additional Fees required under 37 C.F.R. Section 1.17 (Patent application and reexamination processing fees)
- Charge any Additional Fees required under 37 C.F.R. Section 1.21 (Miscellaneous fees and charges)

	Claims	3	6
	Applicant Arguments/Remarks Made in an Amendment	7	7

Warnings:

Information:

6	TrackOne Request	17618CON2B_PRIORITIZED_EX AM.pdf	153236 <small>26d1acc03da02daa83f2ddb09a2c3ab62cc535b5</small>	no	2
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Warnings:

Information:

7	Fee Worksheet (SB06)	fee-info.pdf	42020 <small>9aa08e84c0b4cc795b5f25400b1798c19ba060eb</small>	no	2
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Warnings:

Information:

Total Files Size (in bytes):			8727406
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This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

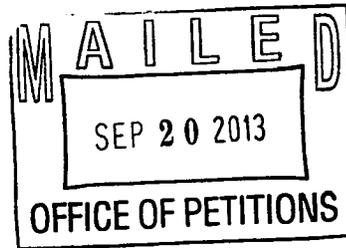
If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.



ALLERGAN, INC.
2525 DUPONT DRIVE, T2-7H
IRVINE CA 92612-1599

Doc Code: TRACK1.GRANT

<p>Decision Granting Request for Prioritized Examination (Track I or After RCE)</p>	<p>Application No.: 13/967,189</p>
<p>1. THE REQUEST FILED <u>August 14, 2013</u> IS GRANTED.</p> <p>The above-identified application has met the requirements for prioritized examination</p> <p>A. <input checked="" type="checkbox"/> for an original nonprovisional application (Track I). B. <input type="checkbox"/> for an application undergoing continued examination (RCE).</p> <p>2. The above-identified application will undergo prioritized examination. The application will be accorded special status throughout its entire course of prosecution until one of the following occurs:</p> <p>A. filing a <u>petition for extension of time</u> to extend the time period for filing a reply; B. filing an <u>amendment to amend the application to contain more than four independent claims, more than thirty total claims</u>, or a multiple dependent claim; C. filing a <u>request for continued examination</u>; D. filing a notice of appeal; E. filing a request for suspension of action; F. mailing of a notice of allowance; G. mailing of a final Office action; H. completion of examination as defined in 37 CFR 41.102; or I. abandonment of the application.</p> <p>Telephone inquiries with regard to this decision should be directed to <u>Michelle R. Eason</u> at (571) 272-4231. In his/her absence, calls may be directed to Brian W. Brown at (571) 272-5338.</p> <p><u>/Michelle R. Eason/</u> (Signature) <u>Paralegal Specialist, Office of Petitions</u> (Title)</p>	

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)	Application Number		13967189	
	Filing Date		2013-08-14	
	First Named Inventor	ACHEAMPONG, ANDREW		
	Art Unit	1653		
	Examiner Name	TBD		
	Attorney Docket Number	17618-US-BCON2-AP		

U.S.PATENTS						
Examiner Initial*	Cite No	Patent Number	Kind Code ¹	Issue Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1					

If you wish to add additional U.S. Patent citation information please click the Add button.

U.S.PATENT APPLICATION PUBLICATIONS						
Examiner Initial*	Cite No	Publication Number	Kind Code ¹	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1					

If you wish to add additional U.S. Published Application citation information please click the Add button.

FOREIGN PATENT DOCUMENTS								
Examiner Initial*	Cite No	Foreign Document Number ³	Country Code ²	Kind Code ⁴	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear	T ⁵
	1							<input type="checkbox"/>

If you wish to add additional Foreign Patent Document citation information please click the Add button

NON-PATENT LITERATURE DOCUMENTS			
Examiner Initials*	Cite No	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc), date, pages(s), volume-issue number(s), publisher, city and/or country where published.	T ⁵

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)	Application Number	13967189
	Filing Date	2013-08-14
	First Named Inventor	ACHEAMPONG, ANDREW
	Art Unit	1653
	Examiner Name	TBD
	Attorney Docket Number	17618-US-BCON2-AP

1	U.S. Re-Examination Application: 90/009,944 and its entire prosecution history, Filed on August, 27, 2011 **	<input type="checkbox"/>
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If you wish to add additional non-patent literature document citation information please click the Add button

EXAMINER SIGNATURE

Examiner Signature		Date Considered	
--------------------	--	-----------------	--

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through a citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ See Kind Codes of USPTO Patent Documents at www.USPTO.GOV or MPEP 901.04. ² Enter office that issued the document, by the two-letter code (WIPO Standard ST.3). ³ For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁴ Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. ⁵ Applicant is to place a check mark here if English language translation is attached.

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)	Application Number	13967189
	Filing Date	2013-08-14
	First Named Inventor	ACHEAMPONG, ANDREW
	Art Unit	1653
	Examiner Name	TBD
	Attorney Docket Number	17618-US-BCON2-AP

CERTIFICATION STATEMENT

Please see 37 CFR 1.97 and 1.98 to make the appropriate selection(s):

That each item of information contained in the information disclosure statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(1).

OR

That no item of information contained in the information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application, and, to the knowledge of the person signing the certification after making reasonable inquiry, no item of information contained in the information disclosure statement was known to any individual designated in 37 CFR 1.56(c) more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(2).

** Signature indicates consideration of publication and file history. The Examiner has access to these materials through the PTO computer systems. If additional copies are desired, please notify the Applicants through their attorneys.

- See attached certification statement.
- Fee set forth in 37 CFR 1.17 (p) has been submitted herewith.
- None

SIGNATURE

A signature of the applicant or representative is required in accordance with CFR 1.33, 10.18. Please see CFR 1.4(d) for the form of the signature.

Signature	/Laura L. Wine/	Date (YYYY-MM-DD)	2013-09-24
Name/Print	Laura L. Wine	Registration Number	68,681

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 1 hour to complete, including gathering, preparing and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. **DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

Privacy Act Statement

The Privacy Act of 1974 (P.L. 93-579) requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C. 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether the Freedom of Information Act requires disclosure of these records.
2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.
3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.
4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).
5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.
6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).
7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.
8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspections or an issued patent.
9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

Electronic Acknowledgement Receipt

EFS ID:	16951660
Application Number:	13967189
International Application Number:	
Confirmation Number:	4818
Title of Invention:	METHODS OF PROVIDING THERAPEUTIC EFFECTS USING CYCLOSPORIN COMPONENTS
First Named Inventor/Applicant Name:	Andrew Acheampong
Customer Number:	51957
Filer:	Laura Lee Wine/Ken Dinh
Filer Authorized By:	Laura Lee Wine
Attorney Docket Number:	17618CON2B (AP)
Receipt Date:	25-SEP-2013
Filing Date:	14-AUG-2013
Time Stamp:	14:00:05
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	no
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File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Information Disclosure Statement (IDS) Form (SB08)	17618CON2B-IDS_09_24_2013.pdf	493644 <small>9bea8e0d9774981a910a583f8c42412d852a9239</small>	no	4

Warnings:

Information:

This is not an USPTO supplied IDS fillable form

2	Non Patent Literature	90009944.pdf	1904560	no	39
			4b5aa1ab68a1940d5930d4265e9053cf67203dc9		

Warnings:

Information:

Total Files Size (in bytes): 2398204

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New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Acheampong, *et al.*

Serial No.: 13/967,189

Filed: August 14, 2013

For: METHODS OF PROVIDING
THERAPEUTIC EFFECTS USING
CYCLOSPORIN COMPONENTS

Examiner: Marcela M. Cordero Garcia

Group Art Unit: 1658

Confirmation No. 4818

Customer No.: 51957

COMMUNICATION UNDER MPEP 502.03

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

Recognizing that Internet communications are not secure, I hereby authorize the USPTO to communicate with me concerning any subject matter of this application by electronic mail. I understand that a copy of these communications will be made of record in the application file.

Respectfully submitted,

/Laura L. Wine/

Date: October 1, 2013

Laura L. Wine
Attorney of Record
Registration Number 68,681

Please direct all inquiries and correspondence to:
Laura L. Wine, Esq.
Allergan, Inc.
2525 Dupont Drive, T2-7H
Irvine, California 92612
Tel: (714) 246-6996 Fax: (714) 246-4249

Electronic Acknowledgement Receipt

EFS ID:	17013203
Application Number:	13967189
International Application Number:	
Confirmation Number:	4818
Title of Invention:	METHODS OF PROVIDING THERAPEUTIC EFFECTS USING CYCLOSPORIN COMPONENTS
First Named Inventor/Applicant Name:	Andrew Acheampong
Customer Number:	51957
Filer:	Laura Lee Wine/Alexis Swan
Filer Authorized By:	Laura Lee Wine
Attorney Docket Number:	17618CON2B (AP)
Receipt Date:	01-OCT-2013
Filing Date:	14-AUG-2013
Time Stamp:	19:14:47
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	no
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File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Miscellaneous Incoming Letter	17618CON2B-Comm-Under-502.pdf	104511 <small>027353835e952daccdef6cea5ab134b2fb923e692</small>	no	1

Warnings:

Information:

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

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New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

Doc Code: DIST.E.FILE Document Description: Electronic Terminal Disclaimer - Filed	PTO/SB/25 U.S. Patent and Trademark Office Department of Commerce
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Electronic Petition Request	TERMINAL DISCLAIMER TO OBLIATE A PROVISIONAL DOUBLE PATENTING REJECTION OVER A PENDING "REFERENCE" APPLICATION
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Application Number	13967189
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Filing Date	14-Aug-2013
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First Named Inventor	Andrew Acheampong
----------------------	-------------------

Attorney Docket Number	17618CON2B (AP)
------------------------	-----------------

Title of Invention	METHODS OF PROVIDING THERAPEUTIC EFFECTS USING CYCLOSPORIN COMPONENTS
--------------------	---

<input checked="" type="checkbox"/> Filing of terminal disclaimer does not obviate requirement for response under 37 CFR 1.111 to outstanding Office Action <input checked="" type="checkbox"/> This electronic Terminal Disclaimer is not being used for a Joint Research Agreement.
--

Owner	Percent Interest
Allergan, Inc.	100%

The owner(s) of percent interest listed above in the instant application hereby disclaims, except as provided below, the terminal part of the statutory term of any patent granted on the instant application which would extend beyond the expiration date of the full statutory term of any patent granted on pending reference Application Number(s)

- 13961808 filed on 08/07/2013
- 13961818 filed on 08/07/2013
- 13961828 filed on 08/07/2013
- 13961835 filed on 08/07/2013
- 13967179 filed on 08/14/2013
- 13967163 filed on 08/14/2013
- 13967168 filed on 08/14/2013

as the term of any patent granted on said reference application may be shortened by any terminal disclaimer filed prior to the grant of any patent on the pending reference application. The owner hereby agrees that any patent so granted on the instant application shall be enforceable only for and during such period that it and any patent granted on the reference application are commonly owned. This agreement runs with any patent granted on the instant application and is binding upon the grantee, its successors or assigns.

In making the above disclaimer, the owner does not disclaim the terminal part of any patent granted on the instant application that would extend to the expiration date of the full statutory term of any patent granted on said reference application, "as the term of any patent granted on said reference application may be shortened by any terminal disclaimer filed prior to the grant of any patent on the pending reference application," in the event that any such patent granted on the pending reference application: expires for failure to pay a maintenance fee, is held unenforceable, is found invalid by a court of competent jurisdiction, is statutorily disclaimed in whole or terminally disclaimed under 37 CFR 1.321, has all claims canceled by a reexamination certificate, is reissued, or is in any manner terminated prior to the expiration of its full statutory term as shortened by any terminal disclaimer filed prior to its grant.

- Terminal disclaimer fee under 37 CFR 1.20(d) is included with Electronic Terminal Disclaimer request.
- I certify, in accordance with 37 CFR 1.4(d)(4), that the terminal disclaimer fee under 37 CFR 1.20(d) required for this terminal disclaimer has already been paid in the above-identified application.

- Applicant claims SMALL ENTITY status. See 37 CFR 1.27.
- Applicant is no longer claiming SMALL ENTITY status. See 37 CFR 1.27(g)(2).
- Applicant(s) status remains as SMALL ENTITY.
- Applicant(s) status remains as other than SMALL ENTITY.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

THIS PORTION MUST BE COMPLETED BY THE SIGNATORY OR SIGNATORIES

I certify, in accordance with 37 CFR 1.4(d)(4) that I am:

- An attorney or agent registered to practice before the Patent and Trademark Office who is of record in this application
Registration Number 68681
- A sole inventor
- A joint inventor; I certify that I am authorized to sign this submission on behalf of all of the inventors
- A joint inventor; all of whom are signing this request
- The assignee of record of the entire interest that has properly made itself of record pursuant to 37 CFR 3.71

Signature	/Laura Wine/
Name	Laura Wine

*Statement under 37 CFR 3.73(b) is required if terminal disclaimer is signed by the assignee (owner).
Form PTO/SB/96 may be used for making this certification. See MPEP § 324.

Electronic Patent Application Fee Transmittal

Application Number:	13967189			
Filing Date:	14-Aug-2013			
Title of Invention:	METHODS OF PROVIDING THERAPEUTIC EFFECTS USING CYCLOSPORIN COMPONENTS			
First Named Inventor/Applicant Name:	Andrew Acheampong			
Filer:	Laura Lee Wine/Lauren Barberena			
Attorney Docket Number:	17618CON2B (AP)			
Filed as Large Entity				
Utility under 35 USC 111(a) Filing Fees				
Description	Fee Code	Quantity	Amount	Sub-Total in USD(\$)
Basic Filing:				
Statutory or Terminal Disclaimer	1814	1	160	160
Pages:				
Claims:				
Miscellaneous-Filing:				
Petition:				
Patent-Appeals-and-Interference:				
Post-Allowance-and-Post-Issuance:				
Extension-of-Time:				

Description	Fee Code	Quantity	Amount	Sub-Total in USD(\$)
Miscellaneous:				
Total in USD (\$)				160

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Applicant/Patent under Reexamination: Acheampong et al.

Electronic Terminal Disclaimer filed on October 7, 2013

APPROVED

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U.S. Patent and Trademark Office

Electronic Acknowledgement Receipt

EFS ID:	17062246
Application Number:	13967189
International Application Number:	
Confirmation Number:	4818
Title of Invention:	METHODS OF PROVIDING THERAPEUTIC EFFECTS USING CYCLOSPORIN COMPONENTS
First Named Inventor/Applicant Name:	Andrew Acheampong
Customer Number:	51957
Filer:	Laura Lee Wine/Lauren Barberena
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File Listing:					
Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Electronic Terminal Disclaimer-Filed	eTerminal-Disclaimer.pdf	39377 e57b54e68b01cc1fb6a28b7b31bc520e3843ed09	no	3
Warnings:					
Information:					
2	Fee Worksheet (SB06)	fee-info.pdf	30732 1d7282f4dae13a260a3de13ebef3eae1729695a1	no	2
Warnings:					
Information:					
Total Files Size (in bytes):			70109		
<p>This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.</p> <p><u>New Applications Under 35 U.S.C. 111</u> If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.</p> <p><u>National Stage of an International Application under 35 U.S.C. 371</u> If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.</p> <p><u>New International Application Filed with the USPTO as a Receiving Office</u> If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.</p>					



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Table with 5 columns: APPLICATION NO., FILING DATE, FIRST NAMED INVENTOR, ATTORNEY DOCKET NO., CONFIRMATION NO.
Row 1: 13/967,189, 08/14/2013, Andrew Acheampong, 17618CON2B (AP), 4818
Row 2: 51957, 7590, 10/10/2013, ALLERGAN, INC., 2525 DUPONT DRIVE, T2-7H, IRVINE, CA 92612-1599
Row 3: EXAMINER, CORDERO GARCIA, MARCELA M
Row 4: ART UNIT, PAPER NUMBER, 1658
Row 5: NOTIFICATION DATE, DELIVERY MODE, 10/10/2013, ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patents_ip@allergan.com
pair_allergan@firsttofile.com

<i>Applicant-Initiated Interview Summary</i>	Application No. 13/967,189	Applicant(s) ACHEAMPONG ET AL.	
	Examiner MARCELA M. CORDERO GARCIA	Art Unit 1658	

All participants (applicant, applicant's representative, PTO personnel):

(1) MARCELA M. CORDERO GARCIA. (3)_____.

(2) LAURA WINE. (4)_____.

Date of Interview: 27 September 2013.

Type: Telephonic Video Conference
 Personal [copy given to: applicant applicant's representative]

Exhibit shown or demonstration conducted: Yes No.
If Yes, brief description: _____.

Issues Discussed 101 112 102 103 Others
(For each of the checked box(es) above, please describe below the issue and detailed description of the discussion)

Claim(s) discussed: 37 and 59.

Identification of prior art discussed: Ding et al. (US 5,474,979).

Substance of Interview

(For each issue discussed, provide a detailed description and indicate if agreement was reached. Some topics may include: identification or clarification of a reference or a portion thereof, claim interpretation, proposed amendments, arguments of any applied references etc...)

See Continuation Sheet.

Applicant recordation instructions: The formal written reply to the last Office action must include the substance of the interview. (See MPEP section 713.04). If a reply to the last Office action has already been filed, applicant is given a non-extendable period of the longer of one month or thirty days from this interview date, or the mailing date of this interview summary form, whichever is later, to file a statement of the substance of the interview

Examiner recordation instructions: Examiners must summarize the substance of any interview of record. A complete and proper recordation of the substance of an interview should include the items listed in MPEP 713.04 for complete and proper recordation including the identification of the general thrust of each argument or issue discussed, a general indication of any other pertinent matters discussed regarding patentability and the general results or outcome of the interview, to include an indication as to whether or not agreement was reached on the issues raised.

Attachment

Summary of Record of Interview Requirements

Manual of Patent Examining Procedure (MPEP), Section 713.04, Substance of Interview Must be Made of Record

A complete written statement as to the substance of any face-to-face, video conference, or telephone interview with regard to an application must be made of record in the application whether or not an agreement with the examiner was reached at the interview.

Title 37 Code of Federal Regulations (CFR) § 1.133 Interviews

Paragraph (b)

In every instance where reconsideration is requested in view of an interview with an examiner, a complete written statement of the reasons presented at the interview as warranting favorable action must be filed by the applicant. An interview does not remove the necessity for reply to Office action as specified in §§ 1.111, 1.135. (35 U.S.C. 132)

37 CFR §1.2 Business to be transacted in writing.

All business with the Patent or Trademark Office should be transacted in writing. The personal attendance of applicants or their attorneys or agents at the Patent and Trademark Office is unnecessary. The action of the Patent and Trademark Office will be based exclusively on the written record in the Office. No attention will be paid to any alleged oral promise, stipulation, or understanding in relation to which there is disagreement or doubt.

The action of the Patent and Trademark Office cannot be based exclusively on the written record in the Office if that record is itself incomplete through the failure to record the substance of interviews.

It is the responsibility of the applicant or the attorney or agent to make the substance of an interview of record in the application file, unless the examiner indicates he or she will do so. It is the examiner's responsibility to see that such a record is made and to correct material inaccuracies which bear directly on the question of patentability.

Examiners must complete an Interview Summary Form for each interview held where a matter of substance has been discussed during the interview by checking the appropriate boxes and filling in the blanks. Discussions regarding only procedural matters, directed solely to restriction requirements for which interview recordation is otherwise provided for in Section 812.01 of the Manual of Patent Examining Procedure, or pointing out typographical errors or unreadable script in Office actions or the like, are excluded from the interview recordation procedures below. Where the substance of an interview is completely recorded in an Examiners Amendment, no separate Interview Summary Record is required.

The Interview Summary Form shall be given an appropriate Paper No., placed in the right hand portion of the file, and listed on the "Contents" section of the file wrapper. In a personal interview, a duplicate of the Form is given to the applicant (or attorney or agent) at the conclusion of the interview. In the case of a telephone or video-conference interview, the copy is mailed to the applicant's correspondence address either with or prior to the next official communication. If additional correspondence from the examiner is not likely before an allowance or if other circumstances dictate, the Form should be mailed promptly after the interview rather than with the next official communication.

The Form provides for recordation of the following information:

- Application Number (Series Code and Serial Number)
- Name of applicant
- Name of examiner
- Date of interview
- Type of interview (telephonic, video-conference, or personal)
- Name of participant(s) (applicant, attorney or agent, examiner, other PTO personnel, etc.)
- An indication whether or not an exhibit was shown or a demonstration conducted
- An identification of the specific prior art discussed
- An indication whether an agreement was reached and if so, a description of the general nature of the agreement (may be by attachment of a copy of amendments or claims agreed as being allowable). Note: Agreement as to allowability is tentative and does not restrict further action by the examiner to the contrary.
- The signature of the examiner who conducted the interview (if Form is not an attachment to a signed Office action)

It is desirable that the examiner orally remind the applicant of his or her obligation to record the substance of the interview of each case. It should be noted, however, that the Interview Summary Form will not normally be considered a complete and proper recordation of the interview unless it includes, or is supplemented by the applicant or the examiner to include, all of the applicable items required below concerning the substance of the interview.

A complete and proper recordation of the substance of any interview should include at least the following applicable items:

- 1) A brief description of the nature of any exhibit shown or any demonstration conducted,
- 2) an identification of the claims discussed,
- 3) an identification of the specific prior art discussed,
- 4) an identification of the principal proposed amendments of a substantive nature discussed, unless these are already described on the Interview Summary Form completed by the Examiner,
- 5) a brief identification of the general thrust of the principal arguments presented to the examiner,
(The identification of arguments need not be lengthy or elaborate. A verbatim or highly detailed description of the arguments is not required. The identification of the arguments is sufficient if the general nature or thrust of the principal arguments made to the examiner can be understood in the context of the application file. Of course, the applicant may desire to emphasize and fully describe those arguments which he or she feels were or might be persuasive to the examiner.)
- 6) a general indication of any other pertinent matters discussed, and
- 7) if appropriate, the general results or outcome of the interview unless already described in the Interview Summary Form completed by the examiner.

Examiners are expected to carefully review the applicant's record of the substance of an interview. If the record is not complete and accurate, the examiner will give the applicant an extendable one month time period to correct the record.

Examiner to Check for Accuracy

If the claims are allowable for other reasons of record, the examiner should send a letter setting forth the examiner's version of the statement attributed to him or her. If the record is complete and accurate, the examiner should place the indication, "Interview Record OK" on the paper recording the substance of the interview along with the date and the examiner's initials.

Continuation of Substance of Interview including description of the general nature of what was agreed to if an agreement was reached, or any other comments: Applicants' representative contacted Examiner to request an in-person interview to discuss the case and also indicated that Applicants would be willing to amend the trademark Pemulen in the claims for acrylate/C10-30 alkyl acrylate cross-polymer (see attachment). This potential amendment was not deemed sufficient to make the claims allowable. During the in-person interview on 10/3/2013 the following attendees were present: Laura Wine, Debra Condino, Dr. Rhett Schiffman, Dr. Maysa Attar and Examiner Cordero Garcia. Applicant's representatives described the backround of dry eye disease, the process of arriving at the claimed invention and discussed: a) unexpected results, b) commercial success and c) long felt need. Further, the Ding et al. patent (US 5,474,979) was discussed with regards to its contents and relation to the claimed invention. With regards to the presented unexpected results, Examiner indicated that it would be necessary to include in a 37 CFR 1.32 declaration all the experimental conditions for the various clinical trials used in the 'unexpected results' evidence, in order to determine whether these clinical trials can be effectively used in the comparison of therapeutic effects of the cyclosporin compositions of Ding et al. with the claimed invention. Examiner also indicated that a first Office Action on the merits would be provided shortly after the interview since the proposed amendment would not obviate all rejections deemed necessary (see attached Office Action) and also briefly discussed potential statutory and non-statutory double patenting issues for the instant application. A courtesy draft of the Office Action was provided to Applicants' representatives.

DETAILED ACTION

1. The present application is being examined under the pre-AIA first to invent provisions.

Status of the claims

2. Claims 37-60 are pending in the application. Claims 37-60 are presented for examination on the merits.

Claim Rejections - 35 USC § 112

The following is a quotation of 35 U.S.C. 112(a):

(a) IN GENERAL.—The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and shall set forth the best mode contemplated by the inventor or joint inventor of carrying out the invention.

The following is a quotation of 35 U.S.C. 112 (pre-AIA), first paragraph:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of 35 U.S.C. 112(b):

(b) CONCLUSION.—The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the inventor or a joint inventor regards as the invention.

The following is a quotation of 35 U.S.C. 112 (pre-AIA), second paragraph:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claim 37, 54 and 59 (and dependent claims thereof, i.e., 38-53, 55-58 and 60) are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention for containing the trademark/trade name Pemulen®. Where a trademark

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or trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 U.S.C. 112, second paragraph (see MPEP 2173.05 (u)). The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the present case, the trademark/trade name is used to identify/describe acrylate/C10-30 alkyl acrylate cross-polymers, or high molecular weight co-polymers of acrylic acid and a long chain alkyl methacrylate cross-linked with allyl ethers of pentaerythritol (see paragraph bridging pages 19-20 of the disclosure) and, accordingly, the identification/description is indefinite.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

5. Claims 37-60 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ding et al. (US 5,474,979, cited in the IDS dated 12/27/2004).

Ding et al. disclose topical ophthalmic emulsions for treating an eye of human having KCS (dry eye disease):

<u>Example 1</u>					
	A	B	C	D	E
Cyclosporin A	0.40%	0.20%	0.20%	0.10%	0.05%
Castor oil	5.00%	5.00%	2.50%	1.25%	0.625%
Polysorbate 80	1.00%	1.00%	1.00%	1.00%	1.00%
Pemulen ®	0.05%	0.05%	0.05%	0.05%	0.05%
Glycerine	2.20%	2.20%	2.20%	2.20%	2.20%
NaOH	qs	qs	qs	qs	qs
Purified water	qs	qs	qs	qs	qs
pH	7.2-7.6	7.2-7.6	7.2-7.6	7.2-7.6	7.2-7.6

Thus, a comparison of the instantly claimed and some of the Ding et al. embodiments is presented below:

	DING et al. 1-D	instant invention	DING et al. 1-E
Cyclosporin	0.10%	0.05%	0.05%
Castor oil	1.25%	1.25%	0.625%
Polysorbate 80	1.00%	1.00%	1.00%
Pemulen	0.05%	0.05%	0.05%
Glycerine	2.20%	2.20%	2.20%
NaOH	qs	qs	qs
Purified water	qs	qs	qs
pH	7.2-7.6	7.2-7.6	7.2-7.6

Furthermore, the claims of Ding et al. disclose ranges for the components (e.g., claims 1-8). For example, Ding et al. discloses a pharmaceutical emulsion comprising

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cyclosporin A, castor oil, Pemulen, glycerine, polysorbate 80, water in amounts sufficient to prevent crystallization of cyclosporin A for a period of up to about nine months, said pharmaceutical emulsion being suitable for topical application to ocular tissue, wherein the cyclosporin A is present in an amount between about 0.05 to and about 0.40%, by weight, the castor oil is present in an amount of between about 0.625%, by weight, and about 5.0%, by weight, the polysorbate 80 is present in an amount of about 1.0%, by weight, the Pemulen is present in an amount of about 0.05%, by weight, and the glycerine is present in an amount of about 2.2%, by weight (e.g., claims 7-8).

The formulations set forth in Examples 1-4 were made for treatment of keratoconjunctivitis sicca (dry eye) syndrome with Examples 2, 3 and 4 without the active ingredient cyclosporin utilized to determine the toxicity of the emulsified components.

Ding et al. teach that the formulations in Examples 1-4 were applied to rabbit eyes eight times a day for seven days and were found to cause only slight to mild discomfort and slight hyperemia in the rabbit eyes. Slit lamp examination revealed no changes in the surface tissue. In addition, the cyclosporin containing castor oil emulsion, as hereinabove set forth in Examples 1A-1D, was also tested for ocular bioavailability in rabbits; and the therapeutic level of cyclosporin was found in the tissues of interest after dosage. Ding et al. go on to teach that this substantiates that cyclosporin in an ophthalmic delivery system is useful for treating dry eye.

One of ordinary skill in the art at the time the invention was made would have been motivated to modify the invention of Ding et al., e.g., Example 1E, by making any composition encompassed by the ranges disclosed in Ding et al. One of ordinary skill in the art at the time the invention was made would have been motivated to do so given the guidance provided by Ding et al., i.e., the amount of castor oil in the emulsions is taught to be cyclosporin to castor oil is between 0.12 and 0.02, which, for 0.05% corresponds to 0.4% to 2.5% of castor oil (which encompasses 1.25%). See, e.g., col. 3. One of ordinary skill in the art, at the time the invention was made, would have had a reasonable expectation of success for doing so because 1.25% was known to be non-irritating as shown in Example 1D, because such modifications are routinely determined and optimized in the art through routine experimentation [see MPEP 2144.05 (I) regarding optimization of ranges] and because the active ingredients, cyclosporin A and castor oil were present at overlapping concentrations between the instant invention and the invention of Ding et al. [see MPEP 2144.05 (I) regarding overlapping ranges]. Moreover, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical [see MPEP 2144.05 (II)]. Furthermore, to establish **unexpected results** over a claimed range, applicants should compare a sufficient number of tests both inside and outside the claimed range to show the criticality of the claimed range (MPEP 716.02).

Claim scope is not limited by claim language that suggests or makes optional but does not require steps to be performed, or by claim language that does not limit a claim

to a particular structure. However, examples of claim language, although not exhaustive, that may raise a question as to the limiting effect of the language in a claim are:

- (A) “adapted to” or “adapted for” clauses;
- (B) “wherein” clauses; and
- (C) “whereby” clauses.

The determination of whether each of these clauses is a limitation in a claim depends on the specific facts of the case. In the instant case, the limitations “, [...] the blood of the human has substantially no detectable concentration of cyclosporin A”, “wherein the emulsion breaks down more quickly in the eye of a human, once administered to the eye of the human, thereby reducing vision distortion in the eye of the human as compare to an emulsion that contains only 50% as much castor oil”, “wherein the ophthalmic emulsion, when administered to the eye of a human, demonstrates a reduction in adverse events in the human” and “wherein the adverse events include side effects”; it is noted that such functional effects would necessarily flow from the compositions of Ding et al. which comprise all the claimed components and amounts as set forth above.

From the teaching of the reference, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Double Patenting

6. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the “right to exclude” granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory double patenting rejection is appropriate where the claims at issue are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the reference application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement. A terminal disclaimer must be signed in compliance with 37 CFR 1.321(b).

The USPTO internet Web site contains terminal disclaimer forms which may be used. Please visit <http://www.uspto.gov/forms/>. The filing date of the application will determine what form should be used. A web-based eTerminal Disclaimer may be filled

out completely online using web-screens. An eTerminal Disclaimer that meets all requirements is auto-processed and approved immediately upon submission. For more information about eTerminal Disclaimers, refer to

<http://www.uspto.gov/patents/process/file/efs/guidance/eTD-info-I.jsp>.

7. Claims 37-60 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-8 of U.S. Patent No. 5,474,979. Although the conflicting claims are not identical, they are not patentably distinct from each other because Ding et al. (US 5,474,979) claims pharmaceutical emulsions comprising of cyclosporine A, castor oil, Pemulen ® (crosslinked polyacrylate stabilizer), glycerine and water as instantly claimed (see claims 6-8 of Ding et al.) for topical application comprising to ocular tissue wherein the cyclosporine A is presents in an amount of between about 0.05 to and about 0.40% by weight (which encompasses about 0.05% cyclosporin A), castor oil from about 0.625% to about 5.0% (which encompasses 1.25% of castor oil), Pemulen ® at about 0.05%, and glycerin at about 2.2%. (see, e.g., claim 8). Additionally, a different emulsifier, i.e., polysorbate 80, is taught at about 1.0% (see also claim 8). The emulsion contains water as set forth in claims 6-8 of Ding et al.

Furthermore, the instant specification was used to determine what is encompassed in the compositions claimed by Ding et al. and examination of Examples 1A-E shows that composition 1E comprises all the components and ranges instantly claimed except for the castor oil, which is encompassed by the claimed ranges to cyclosporin to castor oil.

One of ordinary skill in the art at the time the invention was made would have been motivated to modify the invention of Ding et al. by making any compositions encompassed by the ranges taught by Ding et al. One of ordinary skill in the art would have been motivated to do so in order to create nonirritating emulsions of cyclosporin suitable for topical application to ocular tissue. One of ordinary skill in the art, at the time the invention was made, would have had a reasonable expectation of success for doing so because such modifications are routinely determined and optimized in the art through routine experimentation [see MPEP 2144.05 (I) regarding optimization of ranges] and because the active ingredients, cyclosporin A and castor oil were present at overlapping concentrations between the instant invention and the invention of Ding et al. [see MPEP 2144.05 (I) regarding overlapping ranges]. Moreover, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical [see MPEP 2144.05 (II)]. Furthermore, to establish unexpected results over a claimed range, applicants should compare a sufficient number of tests both inside and outside the claimed range to show the criticality of the claimed range (MPEP 716.02).

Claim scope is not limited by claim language that suggests or makes optional but does not require steps to be performed, or by claim language that does not limit a claim to a particular structure. However, examples of claim language, although not exhaustive, that may raise a question as to the limiting effect of the language in a claim are:

- (A) “adapted to” or “adapted for” clauses;
- (B) “wherein” clauses; and
- (C) “whereby” clauses.

The determination of whether each of these clauses is a limitation in a claim depends on the specific facts of the case. In the instant case, the limitations “wherein the topical ophthalmic emulsion is therapeutically effective in treating KCS”, “wherein, when the topical ophthalmic emulsion is administered to an eye of a human, [...] the blood of the human has substantially no detectable concentration of cyclosporin A”, “wherein the emulsion breaks down more quickly in the eye of a human, once administered to the eye of the human, thereby reducing vision distortion in the eye of the human as compare to an emulsion that contains only 50% as much castor oil”, “wherein the ophthalmic emulsion, when administered to the eye of a human, demonstrates a reduction in adverse events in the human” and “wherein the adverse events include side effects”; it is noted that such functional effects would necessarily flow from the compositions claimed and exemplified by Ding et al. which comprise all the claimed components and amounts as set forth above.

From the teaching of the reference, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

8. Claims 37-60 are provisionally rejected on the ground of nonstatutory double patenting as being unpatentable over claims 37-61 of copending Application No. 13/967,179. Although the claims at issue are not identical, they are not patentably distinct from each other because US '179 is drawn to a method which encompasses the administration of the instantly claimed compositions and thus inherently disclose such compositions, e.g., claim 37 is drawn to a method of treating dry eye disease, the method comprising topically administering to the eye of the human an emulsion at a frequency of twice a day, wherein the emulsion comprises cyclosporin A in an amount of about 0.05% by weight, polysorbate 80, Pemulen, water, and castor oil in an amount of about 1.25% by weight; and wherein the topical ophthalmic emulsion is effective in treating dry eye disease. Thus, it inherently discloses a topical ophthalmic emulsion for treating an eye of a human, wherein the topical ophthalmic emulsion comprises cyclosporin A in an amount of about 0.05% by weight, polysorbate 80, Pemulen, water, and castor oil in an amount of about 1.25% by weight; and wherein the topical ophthalmic emulsion is therapeutically effective in treating dry eye disease (claim 37 of the instant application). The other claims in US '179 are also drawn to the corresponding use of the claimed compositions.

This is a provisional nonstatutory double patenting rejection because the patentably indistinct claims have not in fact been patented.

9. Claims 37-60 are provisionally rejected on the ground of nonstatutory double patenting as being unpatentable over claims 37-61 of copending Application No. 13/961,835. Although the claims at issue are not identical, they are not patentably

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distinct from each other because US '835 is drawn to a method of increasing tear production in the eye of a human, the method comprising topically administering to the eye of the human an emulsion at a frequency of twice a day, wherein the emulsion comprises cyclosporin A in an amount of about 0.05% by weight, polysorbate 80, Pemulen, water, and castor oil in an amount of about 1.25% by weight; and wherein the topical ophthalmic emulsion is effective in increasing tear production.

Thus, it inherently discloses a topical ophthalmic emulsion for treating an eye of a human, wherein the topical ophthalmic emulsion comprises cyclosporin A in an amount of about 0.05% by weight, polysorbate 80, Pemulen, water, and castor oil in an amount of about 1.25% by weight; and wherein the topical ophthalmic emulsion is therapeutically effective in treating dry eye disease (claim 37 of the instant application).

The other claims in US '179 are also drawn to the corresponding use of the claimed compositions. Moreover, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical [see MPEP 2144.05 (II)].

Furthermore, to establish **unexpected results** over a claimed range, applicants should compare a sufficient number of tests both inside and outside the claimed range to show the criticality of the claimed range (MPEP 716.02).

This is a provisional nonstatutory double patenting rejection because the patentably indistinct claims have not in fact been patented.

10. Claims 37-60 are provisionally rejected on the ground of nonstatutory double patenting as being unpatentable over claims 37-61 of copending Application No.

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13/961,818. Although the claims at issue are not identical, they are not patentably distinct from each other because US '818 is drawn to a method which encompasses the administration of the instantly claimed compositions and thus inherently disclose such compositions, e.g., claim 37 is drawn to a method of treating dry eye disease, the method comprising topically administering to the eye of the human an emulsion at a frequency of twice a day, wherein the emulsion comprises cyclosporin A in an amount of about 0.05% by weight, polysorbate 80, Pemulen, water, and castor oil in an amount of about 1.25% by weight; and wherein the topical ophthalmic emulsion is effective in treating dry eye disease. Thus, it inherently discloses a topical ophthalmic emulsion for treating an eye of a human, wherein the topical ophthalmic emulsion comprises cyclosporin A in an amount of about 0.05% by weight, polysorbate 80, Pemulen, water, and castor oil in an amount of about 1.25% by weight; and wherein the topical ophthalmic emulsion is therapeutically effective in treating dry eye disease (claim 37 of the instant application). The other claims in US '818 are also drawn to the corresponding use of the claimed compositions. Moreover, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical [see MPEP 2144.05 (II)]. Furthermore, to establish **unexpected results** over a claimed range, applicants should compare a sufficient number of tests both inside and outside the claimed range to show the criticality of the claimed range (MPEP 716.02).

This is a provisional nonstatutory double patenting rejection because the patentably indistinct claims have not in fact been patented.

11. Claims 37-60 are provisionally rejected on the ground of nonstatutory double patenting as being unpatentable over claims 37-61 of copending Application No. 13/961,835. Although the claims at issue are not identical, they are not patentably distinct from each other because US '835 is drawn to a method of increasing tear production in the eye of a human, the method comprising topically administering to the eye of the human an emulsion at a frequency of twice a day, wherein the emulsion comprises cyclosporin A in an amount of about 0.05% by weight, polysorbate 80, Pemulen, water, and castor oil in an amount of about 1.25% by weight; and wherein the topical ophthalmic emulsion is effective in increasing tear production.

Thus, it inherently discloses a topical ophthalmic emulsion for treating an eye of a human, wherein the topical ophthalmic emulsion comprises cyclosporin A in an amount of about 0.05% by weight, polysorbate 80, Pemulen, water, and castor oil in an amount of about 1.25% by weight; and wherein the topical ophthalmic emulsion is therapeutically effective in treating dry eye disease (claim 37 of the instant application). The other claims in US '179 are also drawn to the corresponding use of the claimed compositions. Moreover, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical [see MPEP 2144.05 (II)]. Furthermore, to establish **unexpected results** over a claimed range, applicants should compare a sufficient number of tests both inside and outside the claimed range to show the criticality of the claimed range (MPEP 716.02).

This is a provisional nonstatutory double patenting rejection because the patentably indistinct claims have not in fact been patented.

Statutory double patenting

12. A rejection based on double patenting of the “same invention” type finds its support in the language of 35 U.S.C. 101 which states that “whoever invents or discovers any new and useful process... may obtain a patent therefor...” (Emphasis added). Thus, the term “same invention,” in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the claims that are directed to the same invention so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

13. Claims 37-60 are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 37-60 of copending Application No. 13/961,808. This is a provisional statutory double patenting rejection since the claims directed to the same invention have not in fact been patented.

The claims are identical to each other, i.e., claim 37 in both applications is drawn to a topical ophthalmic emulsion for treating an eye of a human, wherein the topical ophthalmic emulsion comprises cyclosporin A in an amount of about 0.05% by weight, polysorbate 80, Pemulen, water, and castor oil in an amount of about 1.25% by

weight; and wherein the topical ophthalmic emulsion is therapeutically effective in treating dry eye disease.

The other claims (38-56, 58-61 in the instant application and 38-60 in US '808) are also identical.

14. Claims 37-60 are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 37-56, 58-61 of copending Application No. 13/967,163. This is a provisional statutory double patenting rejection since the claims directed to the same invention have not in fact been patented.

The claims are identical too each other, i.e., claim 37 in both applications is drawn to a topical ophthalmic emulsion for treating an eye of a human, wherein the topical ophthalmic emulsion comprises cyclosporin A in an amount of about 0.05% by weight, polysorbate 80, Pemulen, water, and castor oil in an amount of about 1.25% by weight; and wherein the topical ophthalmic emulsion is therapeutically effective in treating dry eye disease.

The other claims (38-56, 58-61 in the instant application and 38-60 in US '808) are also identical.

15. Claims 37-60 are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 37-56, 58-61 of copending Application No. 13/961,828. This is a provisional statutory double patenting rejection since the claims directed to the same invention have not in fact been patented.

The claims are identical too each other, i.e., claim 37 in both applications is drawn to a topical ophthalmic emulsion for treating an eye of a human, wherein the

topical ophthalmic emulsion comprises cyclosporin A in an amount of about 0.05% by weight, polysorbate 80, Pemulen, water, and castor oil in an amount of about 1.25% by weight; and wherein the topical ophthalmic emulsion is therapeutically effective in treating dry eye disease.

The other claims (38-61 in the instant application and 38-61 in US '828) are also identical.

Conclusion

16. No claim is currently allowed.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to MARCELA M. CORDERO GARCIA whose telephone number is (571)272-2939. The examiner can normally be reached on M-F 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Karlheinz R. Skowronek can be reached on (571)-272-9047. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should

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you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/MARCELA M CORDERO GARCIA/
Primary Examiner, Art Unit 1658

MMCG 10/2013

<i>Applicant-Initiated Interview Summary</i>	Application No. 13/967,189	Applicant(s) ACHEAMPONG ET AL.	
	Examiner MARCELA M. CORDERO GARCIA	Art Unit 1658	

All participants (applicant, applicant's representative, PTO personnel):

(1) MARCELA M. CORDERO GARCIA. (3)_____.

(2) LAURA WINE. (4)_____.

Date of Interview: 27 September 2013.

Type: Telephonic Video Conference
 Personal [copy given to: applicant applicant's representative]

Exhibit shown or demonstration conducted: Yes No.
If Yes, brief description: _____.

Issues Discussed 101 112 102 103 Others
(For each of the checked box(es) above, please describe below the issue and detailed description of the discussion)

Claim(s) discussed: 37 and 59.

Identification of prior art discussed: Ding et al. (US 5,474,979).

Substance of Interview

(For each issue discussed, provide a detailed description and indicate if agreement was reached. Some topics may include: identification or clarification of a reference or a portion thereof, claim interpretation, proposed amendments, arguments of any applied references etc...)

See Continuation Sheet.

Applicant recordation instructions: The formal written reply to the last Office action must include the substance of the interview. (See MPEP section 713.04). If a reply to the last Office action has already been filed, applicant is given a non-extendable period of the longer of one month or thirty days from this interview date, or the mailing date of this interview summary form, whichever is later, to file a statement of the substance of the interview

Examiner recordation instructions: Examiners must summarize the substance of any interview of record. A complete and proper recordation of the substance of an interview should include the items listed in MPEP 713.04 for complete and proper recordation including the identification of the general thrust of each argument or issue discussed, a general indication of any other pertinent matters discussed regarding patentability and the general results or outcome of the interview, to include an indication as to whether or not agreement was reached on the issues raised.

Attachment

Summary of Record of Interview Requirements

Manual of Patent Examining Procedure (MPEP), Section 713.04, Substance of Interview Must be Made of Record

A complete written statement as to the substance of any face-to-face, video conference, or telephone interview with regard to an application must be made of record in the application whether or not an agreement with the examiner was reached at the interview.

Title 37 Code of Federal Regulations (CFR) § 1.133 Interviews

Paragraph (b)

In every instance where reconsideration is requested in view of an interview with an examiner, a complete written statement of the reasons presented at the interview as warranting favorable action must be filed by the applicant. An interview does not remove the necessity for reply to Office action as specified in §§ 1.111, 1.135. (35 U.S.C. 132)

37 CFR §1.2 Business to be transacted in writing.

All business with the Patent or Trademark Office should be transacted in writing. The personal attendance of applicants or their attorneys or agents at the Patent and Trademark Office is unnecessary. The action of the Patent and Trademark Office will be based exclusively on the written record in the Office. No attention will be paid to any alleged oral promise, stipulation, or understanding in relation to which there is disagreement or doubt.

The action of the Patent and Trademark Office cannot be based exclusively on the written record in the Office if that record is itself incomplete through the failure to record the substance of interviews.

It is the responsibility of the applicant or the attorney or agent to make the substance of an interview of record in the application file, unless the examiner indicates he or she will do so. It is the examiner's responsibility to see that such a record is made and to correct material inaccuracies which bear directly on the question of patentability.

Examiners must complete an Interview Summary Form for each interview held where a matter of substance has been discussed during the interview by checking the appropriate boxes and filling in the blanks. Discussions regarding only procedural matters, directed solely to restriction requirements for which interview recordation is otherwise provided for in Section 812.01 of the Manual of Patent Examining Procedure, or pointing out typographical errors or unreadable script in Office actions or the like, are excluded from the interview recordation procedures below. Where the substance of an interview is completely recorded in an Examiners Amendment, no separate Interview Summary Record is required.

The Interview Summary Form shall be given an appropriate Paper No., placed in the right hand portion of the file, and listed on the "Contents" section of the file wrapper. In a personal interview, a duplicate of the Form is given to the applicant (or attorney or agent) at the conclusion of the interview. In the case of a telephone or video-conference interview, the copy is mailed to the applicant's correspondence address either with or prior to the next official communication. If additional correspondence from the examiner is not likely before an allowance or if other circumstances dictate, the Form should be mailed promptly after the interview rather than with the next official communication.

The Form provides for recordation of the following information:

- Application Number (Series Code and Serial Number)
- Name of applicant
- Name of examiner
- Date of interview
- Type of interview (telephonic, video-conference, or personal)
- Name of participant(s) (applicant, attorney or agent, examiner, other PTO personnel, etc.)
- An indication whether or not an exhibit was shown or a demonstration conducted
- An identification of the specific prior art discussed
- An indication whether an agreement was reached and if so, a description of the general nature of the agreement (may be by attachment of a copy of amendments or claims agreed as being allowable). Note: Agreement as to allowability is tentative and does not restrict further action by the examiner to the contrary.
- The signature of the examiner who conducted the interview (if Form is not an attachment to a signed Office action)

It is desirable that the examiner orally remind the applicant of his or her obligation to record the substance of the interview of each case. It should be noted, however, that the Interview Summary Form will not normally be considered a complete and proper recordation of the interview unless it includes, or is supplemented by the applicant or the examiner to include, all of the applicable items required below concerning the substance of the interview.

A complete and proper recordation of the substance of any interview should include at least the following applicable items:

- 1) A brief description of the nature of any exhibit shown or any demonstration conducted,
- 2) an identification of the claims discussed,
- 3) an identification of the specific prior art discussed,
- 4) an identification of the principal proposed amendments of a substantive nature discussed, unless these are already described on the Interview Summary Form completed by the Examiner,
- 5) a brief identification of the general thrust of the principal arguments presented to the examiner,
(The identification of arguments need not be lengthy or elaborate. A verbatim or highly detailed description of the arguments is not required. The identification of the arguments is sufficient if the general nature or thrust of the principal arguments made to the examiner can be understood in the context of the application file. Of course, the applicant may desire to emphasize and fully describe those arguments which he or she feels were or might be persuasive to the examiner.)
- 6) a general indication of any other pertinent matters discussed, and
- 7) if appropriate, the general results or outcome of the interview unless already described in the Interview Summary Form completed by the examiner.

Examiners are expected to carefully review the applicant's record of the substance of an interview. If the record is not complete and accurate, the examiner will give the applicant an extendable one month time period to correct the record.

Examiner to Check for Accuracy

If the claims are allowable for other reasons of record, the examiner should send a letter setting forth the examiner's version of the statement attributed to him or her. If the record is complete and accurate, the examiner should place the indication, "Interview Record OK" on the paper recording the substance of the interview along with the date and the examiner's initials.

Continuation of Substance of Interview including description of the general nature of what was agreed to if an agreement was reached, or any other comments: Applicants' representative contacted Examiner to request an in-person interview to discuss the case and also indicated that Applicants would be willing to amend the trademark Pemulen in the claims for acrylate/C10-30 alkyl acrylate cross-polymer (see attachment). This potential amendment was not deemed sufficient to make the claims allowable. During the in-person interview on 10/3/2013 the following attendees were present: Laura Wine, Debra Condino, Dr. Rhett Schiffman, Dr. Maysa Attar and Examiner Cordero Garcia. Applicant's representatives described the backround of dry eye disease, the process of arriving at the claimed invention and discussed: a) unexpected results, b) commercial success and c) long felt need. Further, the Ding et al. patent (US 5,474,979) was discussed with regards to its contents and relation to the claimed invention. With regards to the presented unexpected results, Examiner indicated that it would be necessary to include in a 37 CFR 1.32 declaration all the experimental conditions for the various clinical trials used in the 'unexpected results' evidence, in order to determine whether these clinical trials can be effectively used in the comparison of therapeutic effects of the cyclosporin compositions of Ding et al. with the claimed invention. Examiner also indicated that a first Office Action on the merits would be provided shortly after the interview since the proposed amendment would not obviate all rejections deemed necessary (see attached Office Action) and also briefly discussed potential statutory and non-statutory double patenting issues for the instant application. A courtesy draft of the Office Action was provided to Applicants' representatives.

EAST Search History

EAST Search History (Prior Art)

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	12	cyclosporin same castor same polysorbate same pemulen	US-PGPUB; USPAT; EPO; JPO; DERWENT	ADJ	ON	2013/10/05 09:54
L2	19	cyclosporin same "0.05" same castor same "1.25"	US-PGPUB; USPAT; EPO; JPO; DERWENT	ADJ	ON	2013/10/05 09:59
L3	89	cyclosporin same castor same polysorbate	US-PGPUB; USPAT; EPO; JPO; DERWENT	ADJ	ON	2013/10/05 10:21
L4	4	cyclosporin same castor same polysorbate same pemulen same hydroxide	US-PGPUB; USPAT; EPO; JPO; DERWENT	ADJ	ON	2013/10/05 10:21

10/ 5/ 2013 10:22:28 AM

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)	Application Number		13967189
	Filing Date		2013-08-14
	First Named Inventor	ACHEAMPONG, ANDREW	
	Art Unit	1653	
	Examiner Name	TBD	
	Attorney Docket Number	17618-US-BCON2-AP	

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /M.M.C.G./

U.S.PATENTS						
Examiner Initial*	Cite No	Patent Number	Kind Code ¹	Issue Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1	3278447		1966-10-11	Thomas McNicholas	
	2	4388229		1983-06-14	Cherng-Chyi Fu	
	3	4388307		1983-06-14	Thomas Cavanak	
	4	4614736		1986-09-30	Devallee et al	
	5	4649047		1987-03-10	Renee Kaswan	
	6	4764503		1988-08-16	Roland Wenger	
	7	4814323		1989-03-21	Andrieu et al	
	8	4839342		1989-06-13	Renee Kaswan	

Receipt date: 09/04/2013 INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)	Application Number		13967189	13967189 - GAU: 1658	
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	Examiner Name	TBD			
	Attorney Docket Number		17618-US-BCON2-AP		

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	9	4970076		1990-11-13	David Horrobin	
	10	4990337		1991-02-05	Kurihara et al	
	11	4996193		1991-02-26	Hewitt et al	
	12	5047396		1991-09-10	Orban et al	
	13	5051402		1991-09-24	Kurihara et al	
	14	5053000		1991-10-01	Booth et al	
	15	5286730		1994-02-15	Caufield et al	
	16	5286731		1994-02-15	Caufield et al	
	17	5294604		1994-03-15	Nussenblatt et al	
	18	5296158		1994-03-22	MacGilp et al	
	19	5342625		1994-08-30	Hauer et al	

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	Attorney Docket Number		17618-US-BCON2-AP		

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	20	5368854		1994-11-29	Donna Rennick	
	21	5411952		1995-05-02	Renee Kaswan	
	22	5424078		1995-06-13	Anthony Dziabo	
	23	5474919		1995-12-12	Chartrain et al	
	24	5474979		1995-12-12	Ding et al	U.S. Application No. 08/243,279 and its entire prosecution history**
	25	5504068		1996-04-02	Komiya et al	
	26	5540931		1996-07-30	Hewitt et al	
	27	5543393		1996-08-06	Kim et al	
	28	5589455		1996-12-31	Jong Woo	
	29	5591971		1997-01-07	Shahar et al	
	30	5614491		1997-03-25	Walch et al	

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	Attorney Docket Number	17618-US-BCON2-AP	

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /M.M.C.G./

	31	5639724		1997-06-17	Thomas Cavanak	
	32	5652212		1997-07-29	Cavanak et al	
	33	5719123		1998-02-17	Morley et al	
	34	5739105		1998-04-14	Kim et al	
	35	5753166		1998-05-19	Dalton et al	
	36	5766629		1998-06-16	Cho et al	
	37	5798333		1998-08-25	Bernard Sherman	
	38	5807820		1998-09-15	Elias et al	
	39	5827822		1998-10-27	Floch'h et al	
	40	5827862		1998-10-27	Yoshitaka Yamamura	
	41	5834017		1998-11-10	Cho et al	

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	42	5843452		1998-12-01	Wiedmann et al	
	43	5843891		1998-12-01	Bernard Sherman	
	44	5858401		1999-01-12	Bhalani et al	
	45	5866159		1999-02-02	Hauer et al	
	46	5891846		1999-04-06	Ishida et al	
	47	5916589		1999-06-29	Hauer et al	
	48	5929030		1999-07-27	Hamied et al	
	49	5951971		1999-09-14	Kawashima et al	
	50	5962014		1999-10-05	Hauer et al	
	51	5962017		1999-10-05	Hauer et al	
	52	5962019		1999-10-05	Cho et al	

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ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /M.M.C.G./

	53	5977066		1999-11-02	Thomas Cavanak	
	54	5981479		1999-11-09	Ko et al	
	55	5981607		1999-11-09	Ding et al	U.S. Application No. 09/008,924 and its entire prosecution history**
	56	5998365		1999-12-07	Bernard Sherman	
	57	6004566		1999-12-21	Friedman et al	
	58	6007840		1999-12-28	Hauer et al	
	59	6008191		1999-12-28	Amarjit Singh	
	60	6008192		1999-12-28	Al-Razzak et al	
	61	6022852		2000-02-08	Klokkers et al	
	62	6024978		2000-02-15	Hauer et al	
	63	6046163		2000-04-04	Stuchlik et al	

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	Examiner Name	TBD		
	Attorney Docket Number		17618-US-BCON2-AP	

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /M.M.C.G./

	64	6057289		2000-05-02	Nirmal Mulye	
	65	6159933		2000-12-12	Bernard Sherman	
	66	6197335		2001-03-06	Bernard Sherman	
	67	6254860		2001-07-03	Michael Garst	
	68	6254885		2001-07-03	Cho et al	
	69	6267985		2001-07-31	Chen et al	
	70	6284268		2001-09-04	Mishra et al	
	71	6294192		2001-09-25	Patel et al	
	72	6306825		2001-10-23	Thomas Cavanak	
	73	6323204		2001-11-27	James Burke	
	74	6346511		2002-02-12	Singh et al	

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	Examiner Name	TBD	
	Attorney Docket Number	17618-US-BCON2-AP	

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	76	6413547		2002-07-02	Bennett et al	
	77	6420355		2002-07-16	Richter et al	
	78	6468968		2002-10-22	Cavanak et al	
	79	6475519		2002-11-05	Meinzer et al	
	80	6486124		2002-11-26	Olbrich et al	
	81	6544953		2003-04-08	Tsuzuki et al	
	82	6555526		2003-04-29	Toshihiko Matsuo	
	83	6562873		2003-05-13	Olejniak et al	
	84	6569463		2003-03-27	Patel et al	
	85	6582718		2003-06-24	Yoichi Kawashima	

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68	U.S. Pending Application: 13/961,835 Filed on August 07, 2013	<input type="checkbox"/>
69	U.S. Pending Application: 13/967,179 Filed on August 14, 2013	<input type="checkbox"/>
70	U.S. Pending Application: 13/967,163 Filed on August 14, 2013	<input type="checkbox"/>
71	U.S. Pending Application: 13/967,168 Filed on August 14, 2013	<input type="checkbox"/>

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EXAMINER SIGNATURE

Examiner Signature	/Marcela Cordero Garcia/	Date Considered	10/04/2013
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*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through a citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Receipt date: 09/04/2013 INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)	Application Number	13967189	13967189 - GAU: 1658
	Filing Date	2013-08-14	
	First Named Inventor	ACHEAMPONG, ANDREW	
	Art Unit	1653	
	Examiner Name	TBD	
	Attorney Docket Number	17618-US-BCON2-AP	

¹ See Kind Codes of USPTO Patent Documents at www.USPTO.GOV or MPEP 901.04. ² Enter office that issued the document, by the two-letter code (WIPO Standard ST.3). ³ For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁴ Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. ⁵ Applicant is to place a check mark here if English language translation is attached.

Receipt date: 09/04/2013 INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)	Application Number	13967189	13967189 - GAU: 1658
	Filing Date	2013-08-14	
	First Named Inventor	ACHEAMPONG, ANDREW	
	Art Unit	1653	
	Examiner Name	TBD	
	Attorney Docket Number	17618-US-BCON2-AP	

CERTIFICATION STATEMENT

Please see 37 CFR 1.97 and 1.98 to make the appropriate selection(s):

That each item of information contained in the information disclosure statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(1).

OR

That no item of information contained in the information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application, and, to the knowledge of the person signing the certification after making reasonable inquiry, no item of information contained in the information disclosure statement was known to any individual designated in 37 CFR 1.56(c) more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(2).

** Signature indicates consideration of publication and file history. The Examiner has access to these materials through the PTO computer systems. If additional copies are desired, please notify the Applicants through their attorneys.

- See attached certification statement.
- Fee set forth in 37 CFR 1.17 (p) has been submitted herewith.
- None

SIGNATURE

A signature of the applicant or representative is required in accordance with CFR 1.33, 10.18. Please see CFR 1.4(d) for the form of the signature.

Signature	/Laura L. Wine/	Date (YYYY-MM-DD)	2013-09-04
Name/Print	Laura L. Wine	Registration Number	68,681

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 1 hour to complete, including gathering, preparing and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. **DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

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5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.
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7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.
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NEWS	11	FEB	22	2013 MARPAT Backfile Expansion Update
NEWS	12	MAR	06	Derwent World Patents Index (DWPI) New Coverage - Indonesia
NEWS	13	MAR	11	JAPIO Will No Longer Be Updated from March 2013 Onwards
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NEWS	17	APR	30	Derwent WPI: The New Cooperative Patent Classification Is Now Available
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NEWS	19	MAY	24	CABA Has Been Reloaded on May 24, 2013
NEWS	20	MAY	28	STN Adds Indian Patent Full Text File - INFULL
NEWS	21	JUL	09	TULSA and TULSA2 were reloaded on July 8, 2013
NEWS	22	JUL	15	New IFIALL Database on STN Increases US Patent Retrieval Capabilities
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NEWS	26	AUG	15	PCTFULL documents with Chinese, Japanese, or Korean as filing language have English machine translations
NEWS	27	AUG	16	The 2013 Inventory of Existing Chemical Substances in China is Now Available on STN
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NEWS	30	SEP	24	Emtree Thesaurus Updated in Embase
NEWS	31	SEP	27	Application Numbers for U.S. Patents in CA/CAPLUS and USPATFUL/USPAT2 Enhanced with U.S. Series Code Information

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=> (cyclosporin or cyclosporine) (10A) (castor (3a) oil)

L1 261 (CYCLOSPORIN OR CYCLOSPORINE) (10A) (CASTOR (3A) OIL)

=> (cyclosporin or cyclosporine) (10A) (castor (3a) oil) (10a) ((0.05) and (1.25))

PROXIMITY OPERATION NOT ALLOWED

Certain operators may not be nested in combination with other operators. A nested operator is valid only when it occurs at the same level or above the operator outside the nested phrase as determined by the following precedence list:

1. Numeric
2. (W), (NOTW), (A), (NOTA)
3. (S), (NOTS)
4. (P), (NOTP)
5. (L), (NOTL)
6. AND, NOT
7. OR

For example, '(MONOCLONAL(W)ANTIBOD?)(L)ANTIGEN?' is valid since (W) is above (L) on the precedence list. However, '((THIN(W)LAYER)(L)PHOSPHOLIPID#)(A)LACTONE#' is not valid since (L)

is below (A) on the precedence list. The only exception is the 'OR' operator. This operator may be used in combination with any other operator. For example, '(ATOMIC OR NUCLEAR)(W)REACTOR' is valid.

=> (cyclosporin or cyclosporine) (10A) (castor (3a) oil) (10a) (pemulen and polysorbate)

PROXIMITY OPERATION NOT ALLOWED

Certain operators may not be nested in combination with other operators. A nested operator is valid only when it occurs at the same level or above the operator outside the nested phrase as determined by the following precedence list:

1. Numeric
2. (W), (NOTW), (A), (NOTA)
3. (S), (NOTS)
4. (P), (NOTP)
5. (L), (NOTL)
6. AND, NOT
7. OR

For example, '(MONOCLONAL(W)ANTIBOD?)(L)ANTIGEN?' is valid since (W) is above (L) on the precedence list. However, '((THIN(W)LAYER)(L)PHOSPHOLIPID#)(A)LACTONE#' is not valid since (L) is below (A) on the precedence list. The only exception is the 'OR' operator. This operator may be used in combination with any other operator. For example, '(ATOMIC OR NUCLEAR)(W)REACTOR' is valid.

=> (cyclosporin or cyclosporine) (10A) (castor oil) (10a) (pemulen and polysorbate)
PROXIMITY OPERATION NOT ALLOWED

Certain operators may not be nested in combination with other operators. A nested operator is valid only when it occurs at the same level or above the operator outside the nested phrase as determined by the following precedence list:

1. Numeric
2. (W), (NOTW), (A), (NOTA)
3. (S), (NOTS)
4. (P), (NOTP)
5. (L), (NOTL)
6. AND, NOT
7. OR

For example, '(MONOCLONAL(W)ANTIBOD?)(L)ANTIGEN?' is valid since (W) is above (L) on the precedence list. However, '((THIN(W)LAYER)(L)PHOSPHOLIPID#)(A)LACTONE#' is not valid since (L) is below (A) on the precedence list. The only exception is the 'OR' operator. This operator may be used in combination with any other operator. For example, '(ATOMIC OR NUCLEAR)(W)REACTOR' is valid.

=> (cyclosporin or cyclosporine) (10A) (castor oil) (10a) (pemulen) 10a polysorbate
MISSING OPERATOR PEMULEN) 10A

The search profile that was entered contains terms or nested terms that are not separated by a logical operator.

=> (cyclosporin or cyclosporine) (10A) (castor oil) (10A) (pemulen) (10a)
(polysorbate)

L2 1 (CYCLOSPORIN OR CYCLOSPORINE) (10A) (CASTOR OIL) (10A) (PEMULEN)
(10A) (POLYSORBATE)

=> d ibib abs total

L2 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2013 ACS on STN

ACCESSION NUMBER: 1996:38846 CAPLUS
 DOCUMENT NUMBER: 124:66660
 ORIGINAL REFERENCE NO.: 124:12317a,12320a
 TITLE: Lacrimal gland-specific emulsions for topical application to ocular tissue
 INVENTOR(S): Ding, Shulin; Tien, Walter L.; Olejnik, Orest
 PATENT ASSIGNEE(S): Allergan, Inc., USA
 SOURCE: PCT Int. Appl., 27 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9531211	A1	19951123	WO 1995-US6302	19950517
W:			AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US, UZ	
RW:			KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG	
US 5474979	A	19951212	US 1994-243279	19940517
CA 2190485	A1	19951123	CA 1995-2190485	19950517
CA 2190485	C	20030415		
CA 2309033	A1	19951123	CA 1995-2309033	19950517
CA 2309033	C	20030826		
AU 9526409	A	19951205	AU 1995-26409	19950517
AU 693213	B2	19980625		
EP 759773	A1	19970305	EP 1995-921294	19950517
EP 759773	B1	20010808		
R:			AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE	
CN 1152876	A	19970625	CN 1995-194078	19950517
CN 1229136	C	20051130		
BR 9507664	A	19971007	BR 1995-7664	19950517
JP 10500414	T	19980113	JP 1995-529895	19950517
JP 3441462	B2	20030902		
EP 1044678	A1	20001018	EP 2000-202069	19950517
EP 1044678	B1	20030312		
R:			AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE	
AT 203911	T	20010815	AT 1995-921294	19950517
ES 2161895	T3	20011216	ES 1995-921294	19950517
PT 759773	E	20020228	PT 1995-921294	19950517
AT 234076	T	20030315	AT 2000-202069	19950517
PT 1044678	E	20030829	PT 2000-202069	19950517
ES 2194670	T3	20031201	ES 2000-202069	19950517
MX 2002000724	A	20030425	MX 2002-724	19961115
CN 1288722	A	20010328	CN 2000-120126	20000714
CN 1198587	C	20050427		
HK 1034190	A1	20051209	HK 2001-104710	20010709
GR 3036945	T3	20020131	GR 2001-401814	20011018
KR 450703	B1	20041001	KR 2001-88637	20011229
JP 2003231646	A	20030819	JP 2003-63234	20030310
JP 4119284	B2	20080716		
PRIORITY APPLN. INFO.:			US 1994-243279	A 19940517
			CA 1995-2190485	A3 19950517
			EP 1995-921294	A3 19950517
			JP 1995-529895	A3 19950517
			WO 1995-US6302	W 19950517
			KR 1996-706523	A3 19961118

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB A pharmaceutical composition is disclosed in the form of a nonirritating emulsion which includes at least one cyclosporin in admixt. with a higher fatty acid glyceride and polysorbate 80. More particularly, the cyclosporin may be cyclosporine A and the higher fatty acid glyceride may be castor oil. The composition allows a high comfort level and low irritation potential suitable for delivery of medications to sensitive areas such as ocular tissues with enhanced absorption in the lacrimal gland. In addition, the composition has stability for up to 9 mo without crystallization of cyclosporin.

For example, an ophthalmic emulsion containing cyclosporin A 0.2, castor oil 2.5, Polysorbate-80 1.0, Pemulen 0.05, glycerol 2.2, NaOH q.s., and purified water to 100% was formulated to treat keratoconjunctivitis sicca.

OS.CITING REF COUNT: 36 THERE ARE 36 CAPLUS RECORDS THAT CITE THIS RECORD (38 CITINGS)
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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Interview Agenda

U.S. Patent Application Nos. 13/967,189; 13/967,179; 13/967,163; and 13/967,168 – METHODS OF PROVIDING THERAPEUTIC EFFECTS USING CYCLOSPORIN COMPONENTS

Examiner Marcela Cordero Garcia – (410) 262-3037

- **Introduction**
- **Discussion of Claimed Subject Matter**
 - **Background on Dry Eye Disease**
 - **The Development and Innovation of the Claimed Formulation**
- **Presentation of Objective Evidence of Non-Obviousness**
 - **Unexpected Results**
 - **Commercial Success**
 - **Long Felt Need/Failure of Others**
- **Brief Discussion of Prior Art**
 - **Ding (U.S. Patent No. 5,474,979)**
- **Discussion of Clarifying Amendments**


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BIB DATA SHEET
CONFIRMATION NO. 4818

SERIAL NUMBER	FILING or 371(c) DATE RULE	CLASS	GROUP ART UNIT	ATTORNEY DOCKET NO.		
13/967,189	08/14/2013	514	1658	17618CON2B (AP)		
APPLICANTS						
Allergan, Inc., Irvine, CA, Assignee (with 37 CFR 1.172 Interest); Andrew Acheampong, Irvine, CA; Diane D. Tang-Liu, Las Vegas, NV; James N. Chang, Newport Beach, CA; David F. Power, Hubert, NC;						
** CONTINUING DATA *****						
This application is a CON of 13/961,808 08/07/2013 which is a CON of 11/897,177 08/28/2007 which is a CON of 10/927,857 08/27/2004 ABN which claims benefit of 60/503,137 09/15/2003						
** FOREIGN APPLICATIONS *****						
** IF REQUIRED, FOREIGN FILING LICENSE GRANTED ** 08/29/2013						
Foreign Priority claimed <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No	35 USC 119(a-d) conditions met <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No	<input type="checkbox"/> Met after Allowance	STATE OR COUNTRY	SHEETS DRAWINGS	TOTAL CLAIMS	INDEPENDENT CLAIMS
Verified and Acknowledged	/MARCELA M CORDERO GARCIA/ Examiner's Signature	_____ Initials	CA	0	24	3
ADDRESS						
ALLERGAN, INC. 2525 DUPONT DRIVE, T2-7H IRVINE, CA 92612-1599 UNITED STATES						
TITLE						
METHODS OF PROVIDING THERAPEUTIC EFFECTS USING CYCLOSPORIN COMPONENTS						
FILING FEE RECEIVED 2220	FEES: Authority has been given in Paper No. _____ to charge/credit DEPOSIT ACCOUNT No. _____ for following:			<input type="checkbox"/> All Fees <input type="checkbox"/> 1.16 Fees (Filing) <input type="checkbox"/> 1.17 Fees (Processing Ext. of time) <input type="checkbox"/> 1.18 Fees (Issue) <input type="checkbox"/> Other _____ <input type="checkbox"/> Credit		

DRAFT CLAIM AMENDMENT
U.S. Patent Application No. 13/967,189
Attorney Ref: 17618CON2B (AP)
FOR DISCUSSION PURPOSES ONLY

37. (**Currently Amended**) A topical ophthalmic emulsion for treating an eye of a human, wherein the topical ophthalmic emulsion comprises cyclosporin A in an amount of about 0.05% by weight, polysorbate 80, ~~Pemulen-acrylate/C10-30 alkyl acrylate cross-polymer~~, water, and castor oil in an amount of about 1.25% by weight; and

wherein the topical ophthalmic emulsion is therapeutically effective in treating dry eye disease.

59. (**Currently Amended**) A topical ophthalmic emulsion for treating an eye of a human, the topical ophthalmic emulsion comprising:

cyclosporin A in an amount of about 0.05% by weight;

castor oil in an amount of about 1.25% by weight;

polysorbate 80 in an amount of about 1.0% by weight;

~~Pemulen-acrylate/C10-30 alkyl acrylate cross-polymer~~ in an amount of about 0.05% by weight;

glycerine in an amount of about 2.2% by weight;

sodium hydroxide; and

water;

wherein the emulsion is therapeutically effective in treating dry eye disease.

Search Notes 	Application/Control No. 13967189	Applicant(s)/Patent Under Reexamination ACHEAMPONG ET AL.
	Examiner MARCELA M CORDERO GARCIA	Art Unit 1658

CPC- SEARCHED		
Symbol	Date	Examiner

CPC COMBINATION SETS - SEARCHED		
Symbol	Date	Examiner

US CLASSIFICATION SEARCHED			
Class	Subclass	Date	Examiner
none	none	10/4/2013	MMCG

SEARCH NOTES		
Search Notes	Date	Examiner
EAST search (attached)	10/5/2013	MMCG
STN search (attached)	10/5/2013	MMCG
also ran PALM inventor search	10/5/2013	MMCG

INTERFERENCE SEARCH			
US Class/ CPC Symbol	US Subclass / CPC Group	Date	Examiner

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)	Application Number		13967189	
	Filing Date		2013-08-14	
	First Named Inventor	ACHEAMPONG, ANDREW		
	Art Unit	1653		
	Examiner Name	TBD		
	Attorney Docket Number	17618-US-BCON2-AP		

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /M.M.C.G./

U.S.PATENTS						
Examiner Initial*	Cite No	Patent Number	Kind Code ¹	Issue Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
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Examiner Initial*	Cite No	Publication Number	Kind Code ¹	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1					

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Receipt date: 09/25/2013 INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)	Application Number		13967189	13967189 - GAU: 1658
	Filing Date		2013-08-14	
	First Named Inventor	ACHEAMPONG, ANDREW		
	Art Unit	1653		
	Examiner Name	TBD		
	Attorney Docket Number	17618-US-BCON2-AP		

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /M.M.C.G./

	1	U.S. Re-Examination Application: 90/009,944 and its entire prosecution history, Filed on August, 27, 2011 **	<input type="checkbox"/>
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If you wish to add additional non-patent literature document citation information please click the Add button

EXAMINER SIGNATURE

Examiner Signature	<i>/Marcela Cordero Garcia/</i>	Date Considered	10/04/2013
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*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through a citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ See Kind Codes of USPTO Patent Documents at www.USPTO.GOV or MPEP 901.04. ² Enter office that issued the document, by the two-letter code (WIPO Standard ST.3). ³ For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁴ Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. ⁵ Applicant is to place a check mark here if English language translation is attached.

Receipt date: 09/25/2013 INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)	Application Number	13967189	13967189 - GAU: 1658
	Filing Date	2013-08-14	
	First Named Inventor	ACHEAMPONG, ANDREW	
	Art Unit	1653	
	Examiner Name	TBD	
	Attorney Docket Number	17618-US-BCON2-AP	

CERTIFICATION STATEMENT

Please see 37 CFR 1.97 and 1.98 to make the appropriate selection(s):

That each item of information contained in the information disclosure statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(1).

OR

That no item of information contained in the information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application, and, to the knowledge of the person signing the certification after making reasonable inquiry, no item of information contained in the information disclosure statement was known to any individual designated in 37 CFR 1.56(c) more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(2).

** Signature indicates consideration of publication and file history. The Examiner has access to these materials through the PTO computer systems. If additional copies are desired, please notify the Applicants through their attorneys.

- See attached certification statement.
- Fee set forth in 37 CFR 1.17 (p) has been submitted herewith.
- None

SIGNATURE

A signature of the applicant or representative is required in accordance with CFR 1.33, 10.18. Please see CFR 1.4(d) for the form of the signature.

Signature	/Laura L. Wine/	Date (YYYY-MM-DD)	2013-09-24
Name/Print	Laura L. Wine	Registration Number	68,681

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 1 hour to complete, including gathering, preparing and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. **DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

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7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.
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9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Acheampong, *et al.*

Examiner: Marcela M Cordero Garcia

Serial No.: 13/967,189

Group Art Unit: 1658

Filed: August 14, 2013

Confirmation No. 4818

For: METHODS OF PROVIDING
THERAPEUTIC EFFECTS USING
CYCLOSPORIN COMPONENTS

Customer No.: 51957

RESPONSE TO NON FINAL OFFICE ACTION DATED OCTOBER 10, 2013

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

These papers are filed in reply to the Office Action mailed October 10, 2013.

Amendments to the claims begin at page 2;

Summary of the Interview begins at page 6;

Remarks follow on page 7.

AMENDMENTS TO THE CLAIMS

The following claims replace all prior versions of claims submitted in this application. Only those claims being amended herein show their changes in highlighted form, where insertions appear as underlined text (e.g., insertions) while deletions appear as strikethrough or surrounded by double brackets (e.g. deletions or [[deletions]]).

1. – 36. (Canceled)

37. **(Currently Amended)** A first topical ophthalmic emulsion for treating an eye of a human, wherein the first topical ophthalmic emulsion comprises cyclosporin A in an amount of about 0.05% by weight, polysorbate 80, ~~Permulen~~ acrylate/C10-30 alkyl acrylate cross-polymer, water, and castor oil in an amount of about 1.25% by weight; and

wherein the first topical ophthalmic emulsion is therapeutically effective in treating dry eye disease; and

wherein the first topical ophthalmic emulsion provides overall efficacy substantially equal to a second topical ophthalmic emulsion comprising cyclosporin A in an amount of about 0.1% by weight and castor oil in an amount of about 1.25% by weight.

38. **(Currently Amended)** The first topical ophthalmic emulsion of Claim 37, wherein the first topical ophthalmic emulsion further comprises a tonicity agent or a demulcent component.

39. **(Currently Amended)** The first topical ophthalmic emulsion of Claim 38, wherein the tonicity agent or the demulcent component is glycerine.

40. **(Currently Amended)** The first topical ophthalmic emulsion of Claim 37, wherein the first topical ophthalmic emulsion further comprises a buffer.

41. **(Currently Amended)** The first topical ophthalmic emulsion of Claim 40, wherein the buffer is sodium hydroxide.

42. **(Currently Amended)** The first topical ophthalmic emulsion of Claim 37, wherein the first topical ophthalmic emulsion further comprises glycerine and a buffer.

43. **(Currently Amended)** The first topical ophthalmic emulsion of Claim 37, wherein the first topical ophthalmic emulsion comprises polysorbate 80 in an amount of about 1.0% by weight.

44. **(Currently Amended)** The first topical ophthalmic emulsion of Claim 37, wherein the first topical ophthalmic emulsion comprises ~~Penulen~~ acrylate/C10-30 alkyl acrylate cross-polymer in an amount of about 0.05% by weight.

45. **(Currently Amended)** The first topical ophthalmic emulsion of Claim 37, wherein the first topical ophthalmic emulsion further comprises glycerine in an amount of about 2.2% by weight and a buffer.

46. **(Currently Amended)** The first topical ophthalmic emulsion of Claim 45, wherein the buffer is sodium hydroxide.

47. **(Currently Amended)** The first topical ophthalmic emulsion of Claim 37, wherein, when the first topical ophthalmic emulsion is administered to an eye of a human in an effective amount in treating dry eye disease, the blood of the human has substantially no detectable concentration of cyclosporin A.

48. **(Currently Amended)** The first topical ophthalmic emulsion of Claim 42, wherein the first topical ophthalmic emulsion has a pH in the range of about 7.2 to about 7.6.

49. – 60. (Canceled)

61. **(New)** A first topical ophthalmic emulsion for treating an eye of a human, wherein the first topical ophthalmic emulsion comprises 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; and

wherein the first topical ophthalmic emulsion is therapeutically effective in treating dry eye disease and wherein the first topical ophthalmic emulsion achieves at least as much therapeutic effectiveness as a second topical ophthalmic emulsion comprising cyclosporin A in an amount of about 0.1% by weight and castor oil in an amount of about 1.25% by weight.

62. **(New)** A first topical ophthalmic emulsion for treating an eye of a human, wherein the first topical ophthalmic emulsion comprises 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; and

wherein the first topical ophthalmic emulsion breaks down more quickly in the eye of a human, once administered to the eye of the human, thereby reducing vision distortion in the eye of the human as compared to a second topical ophthalmic emulsion that contains only about 50% as much castor oil as the first topical ophthalmic emulsion.

63. **(New)** A first topical ophthalmic emulsion for treating an eye of a human, wherein the first topical ophthalmic emulsion comprises 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; and

wherein the first topical ophthalmic emulsion, when administered to the eye of a human, demonstrates a reduction in adverse events in the human, relative to a second topical ophthalmic emulsion comprising cyclosporin A in an amount of about 0.1% by weight and castor oil in an amount of about 1.25% by weight.

64. **(New)** The first topical ophthalmic emulsion of Claim 63, wherein the adverse events are side effects.

65. **(New)** The first topical ophthalmic emulsion of Claim 64, wherein the side effects are selected from the group consisting of visual distortion and eye irritation.

66. **(New)** The first topical ophthalmic emulsion of Claim 61, wherein, when the first topical ophthalmic emulsion is administered to an eye of a human, the blood of the human has substantially no detectable concentration of cyclosporin A.

67. **(New)** The first topical ophthalmic emulsion of Claim 62, wherein, when the first topical ophthalmic emulsion is administered to an eye of a human, the blood of the human has substantially no detectable concentration of cyclosporin A.

68. **(New)** The first topical ophthalmic emulsion of Claim 63, wherein, when the first topical ophthalmic emulsion is administered to an eye of a human, the blood of the human has substantially no detectable concentration of cyclosporin A.

SUMMARY OF INTERVIEW

Attendees, Date and Type of Interview

An in-person interview was conducted on October 3, 2013 at the USPTO and was attended by Examiner Cordero Garcia, Laura L. Wine, Dr. Rhett Schiffman, Dr. Mayssa Attar, and Debra Condino.

Exhibits and/or Demonstrations

Data demonstrating unexpected results and commercial success of the claimed formulation were presented. Data and information regarding the claimed formulation's satisfaction of a long felt need were also presented.

Identification of Claims Discussed

The Claims were discussed, focusing on Claims 37 and 54.

Identification of Prior Art Discussed

The prior art of record was discussed, focusing on Ding (U.S. Patent No. 5,474,979).

Principal Arguments and Other Matters

The Applicants presented data demonstrating unexpected results, commercial success, and satisfaction of a long felt need of the claimed formulation. While the Applicants do not acquiesce to any *prima facie* case of obviousness, the evidence of non-obviousness presented at the interview overcomes the *prima facie* obviousness rejection.

Results of Interview

It was agreed that the evidence of non-obviousness presented rendered the claims allowable and overcame the prior art of record. It was agreed that the Applicants would file a response, presenting arguments discussed at the interview.

REMARKS

This Reply responds to the Office Action sent October 10, 2013, in which the Office Action rejected Claims 37-60. Claims 49-60 are newly cancelled. Claims 37-48 have been amended. Claims 61-68 are new. Thus, Claims 37-48 and 61-68 are currently pending. No new matter has been added by this amendment, and all amendments to the claims are fully supported by the originally filed application. The Applicants respectfully submit that the claims are in condition for allowance.

Claim Rejections

35 U.S.C. § 112, second paragraph

Claims 37-60 were rejected under 35 U.S.C. § 112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. The Applicants submit that the amendments to the claims submitted herewith render the rejection under 35 U.S.C. § 112, second paragraph moot. Thus, the Applicants respectfully request that the claim rejections under 35 U.S.C. § 112, second paragraph be withdrawn.

35 U.S.C. 103(a)

The Office Action rejected Claims 37-60 under 35 U.S.C. 103(a) as being unpatentable as obvious in view of U.S. Patent No. 5,474,979 to Ding et al. (“Ding”).

The Applicants submit that the *prima facie* case of obviousness has not been properly established against the pending claims. However, the Applicants submit that the unexpected results, commercial success, and satisfaction of long felt need obtained with the claimed formulations and failure of others overcome the *prima facie* obviousness rejection asserted in the Office Action.

The Federal Circuit has held that objective evidence of nonobviousness must always be taken into account before a conclusion on obviousness is reached. Similarly, M.P.E.P. 716.01(a) states that “[a]ffidavits or declarations, when timely presented, containing evidence of criticality or unexpected results, commercial success, long-left but unsolved needs, failure of others, skepticism of experts, etc., must be considered by the

Patent Office in determining the issue of obviousness of claims for patentability under 35 U.S.C. 103.” Thus, the *Graham* factors, including the use of objective evidence of secondary considerations to rebut a *prima facie* case of obviousness, remains the framework to be followed for a determination of obviousness. The Federal Circuit has even stated that “evidence of secondary considerations may often be the most probative and cogent evidence in the record. It may often establish that an invention appearing to have been obvious in light of the prior art was not.” *See, Stratoflex Inc. v. Aeroquip Corp.*, 713 F.2d 1530, 1538 (Fed. Cir. 1983).

The Claimed Formulations Provide Surprising and Unexpected Results

As discussed in the interview with the Examiner, the claimed formulations provide surprising and unexpected results in view of the prior art (e.g. Ding). According to MPEP § 2144.05 (III), the Applicants can rebut a presumption of obviousness based on a claimed invention that falls within a prior art range by showing “(1) [t]hat the prior art taught away from the claimed invention...or (2) **that there are new and unexpected results relative to the prior art.**” *Iron Grip Barbell Co., Inc. v. USA Sports, Inc.*, 392 F.3d 1317, 1322, 73 USPQ2d 1225, 1228 (Fed. Cir. 2004).

In support of this position, the Applicants submit herewith as Exhibit 1 a Declaration of Dr. Rhett M. Schiffman under 37 C.F.R. § 1.132 (hereinafter, “Schiffman Declaration 1”), Chief Medical Officer at Neurotech, with over 12 years of experience as a clinician in the eye care field. The Applicants also submit herewith as Exhibit 2, a Declaration of Dr. Mayssa Attar under 37 C.F.R. § 1.132 (hereinafter, “Attar Declaration”), Research Investigator at Allergan, Inc., the assignee of record of the present application, with about 15 years of experience in the pharmacokinetics field.

As described by Dr. Schiffman and Dr. Attar in their respective declarations, supported by examples and experiments, the claimed formulations provided unexpected results compared to the prior art with regards to two key objective testing parameters for dry eye or keratoconjunctivis sicca: Schirmer Tear Testing and decrease in corneal staining, and with regards to reduction in blurred vision and decreased use of artificial tears. Specifically, the claimed formulations provided unexpected results compared to

formulations 1E and 1D disclosed in Ding, which included 0.05% by weight cyclosporin A and 0.625% by weight castor oil and 0.10% by weight cyclosporin A and 1.25% by weight castor oil, respectively. See Ding, col. 4, lines 34-43.

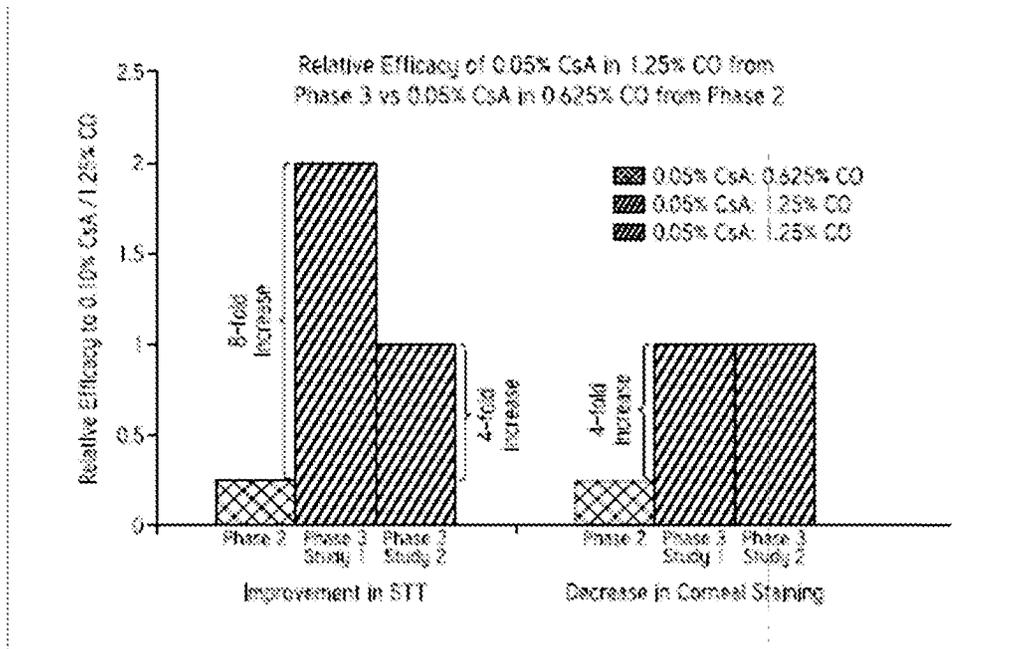
As described by Dr. Schiffman in paragraphs 17-20 of Schiffman Declaration 1 and as seen in Exhibits E and F to Schiffman Declaration 1, surprisingly, the claimed formulation demonstrated an 8-fold increase in relative efficacy for the Schirmer Tear Test score in the first study of Allergan’s Phase 3 trials compared to the relative efficacy for the 0.05% by weight cyclosporin A/0.625% by weight castor oil formulation disclosed in Example 1E of Ding, tested in Phase 2 trials. The data presented herewith represents the subpopulation of Phase 2 patients with the same reductions in tear production (≤ 5 mm/5 min) as those enrolled in the Phase 3 studies. Schiffman Declaration 1 at ¶ 8. Exhibits E and F also illustrate that the claimed formulations also demonstrated a 4-fold improvement in the relative efficacy for the Schirmer Tear Test score for the second study of Phase 3 and a 4-fold increase in relative efficacy for decrease in corneal staining score in both of the Phase 3 studies compared to the 0.05% by weight cyclosporin A/0.625% by weight castor oil formulation tested in Phase 2 and disclosed in Ding (Ding 1E). This was clearly a very surprising and unexpected result.

Exhibit E of Schiffman Declaration 1

	Phase 2 001	Phase 3 (1 st study)	Phase 3 (2 nd study)
	0.05% CsA in 0.625% CO	0.05% CsA in 1.25% CO	0.05% CsA in 1.25% CO
	Compared with 0.1% CsA in 1.25% CO		
Improvement in STT	0.25	2 (8-Fold Improvement*)	1 (4-Fold Improvement*)
Decrease in Corneal Staining	0.25	1 (4-Fold Improvement*)	1 (4-Fold Improvement*)

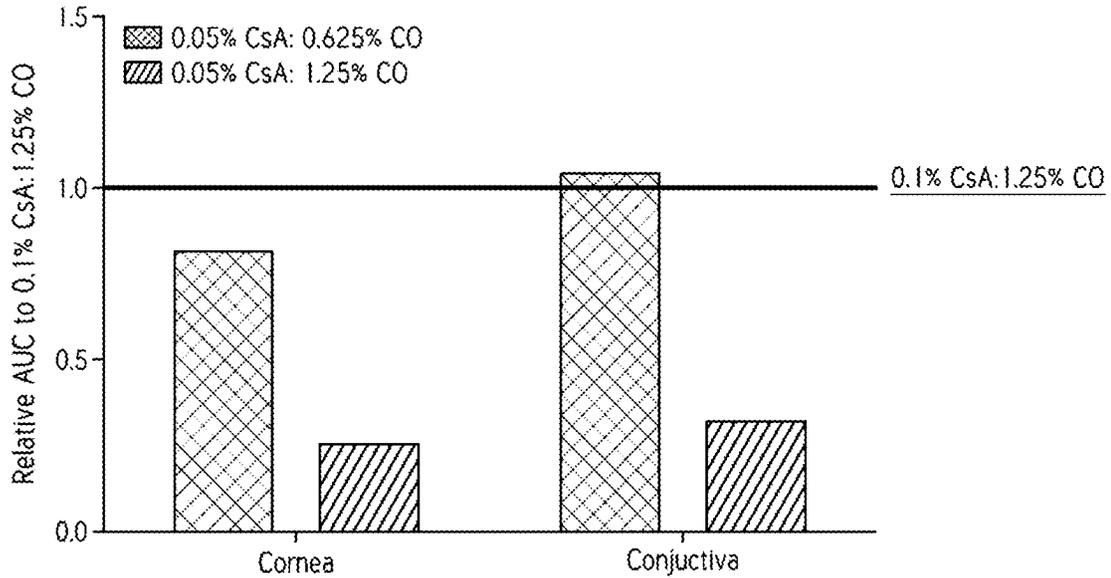
*Compared to the 0.05% CsA/0.625% CO Phase 2 formulation (disclosed in Ding)

Exhibit F of Schiffman Declaration 1



This dramatic increase in relative efficacy between the claimed formulation and the formulation disclosed in Examples 1E and 1D of Ding was especially unexpected in view of pharmacokinetic data. As described by Dr. Attar in paragraph 7 of the Attar Declaration, pharmacokinetic studies were performed on animal eyes, which compared the pharmacokinetic properties of several cyclosporin A-containing formulations, including formulations containing 0.05% by weight cyclosporin A and 0.625% by weight castor oil, formulations containing 0.05% by weight cyclosporin A and 1.25% by weight castor oil, and formulations containing 0.1% by weight cyclosporin A and 1.25% by weight castor oil. This data was compiled and organized in Exhibit B to the Attar Declaration, reproduced below:

Exhibit B to Attar Declaration



As described in paragraph 7 of the Attar Declaration, this chart shows that the amount of cyclosporin A that reaches the cornea and conjunctiva, ocular tissues that are highly relevant for the treatment of dry eye or keratoconjunctivitis sicca, is higher for the formulation containing 0.05% by weight cyclosporin A and 0.625% by weight castor oil (Ding 1E) than the formulation containing 0.05% by weight cyclosporin A and 1.25% by weight castor oil (the claimed formulation) relative to the formulation containing 0.1% by weight cyclosporin A and 1.25% by weight castor oil (Ding 1D). According to Dr. Attar, this data teaches that the formulation containing 0.05% by weight cyclosporin A and 1.25% by weight castor oil would be less therapeutically effective than the formulation containing 0.05% by weight cyclosporin A and 0.625% by weight castor oil or the formulation containing 0.10% by weight cyclosporin A and 1.25% by weight castor oil. Attar Declaration at ¶ 8. Similarly, according to Dr. Schiffman, this data shows that, since lower levels of cyclosporin A were reaching the ocular tissues relevant for the treatment of dry eye, one of skill in the art would have expected patients receiving the claimed formulation to exhibit a lesser decrease from baseline in corneal staining score

and a lesser increase from baseline in Schirmer Score relative to the corneal staining scores and Schirmer Scores of the patients receiving the 0.05% by weight cyclosporin A / 0.625% by weight castor oil formulation (Ding 1E) in the Phase 2 trials, as illustrated in Schiffman Declaration 1, Exhibit B. *See* Schiffman Declaration 1 at ¶ 13.

As described by Dr. Schiffman in paragraphs 14-15 of Schiffman Declaration 1, surprisingly, the claimed formulation was equally or more therapeutically effective for the treatment of dry eye or keratoconjunctivitis sicca than the formulation containing 0.10% by weight cyclosporin A and 1.25% by weight castor oil (Ding 1D) according to corneal staining score, Schirmer Score, an improvement in the common dry eye/keratoconjunctivitis sicca symptom of blurred vision and a greater decrease in the number of artificial tears used by patients.

Taking the results of the studies and data presented in the Attar and Schiffman 1 Declarations together, it is clear 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 or keratoconjunctivitis sicca.

Accordingly, the Applicants submit that the Declarations of Drs. Rhett M. Schiffman (Schiffman Declaration 1) and Attar, together with the data presented in those declarations, provide clear and convincing objective evidence that establishes that the claimed formulations, including 0.05% by weight cyclosporin A and 1.25% by weight castor oil, demonstrate surprising and unexpected results, including improved Schirmer Tear Test scores and corneal staining scores (key objective measures of efficacy for dry eye or keratoconjunctivitis sicca) and improved visual blurring and reduced artificial tear use as compared to the prior art, for example, emulsion formulations disclosed in Ding, including formulations with 0.05% by weight cyclosporin A and 0.625% by weight castor oil (Ding 1E) and formulations with 0.10% by weight cyclosporin A and 1.25% by weight castor oil (Ding 1D).

The Claimed Formulations are Commercially Successful

As discussed during the Examiner interview, in addition to having surprising and unexpected results, the claimed formulations have demonstrated commercial success. In

support of this position, the Applicants submit herewith as Exhibit 3, a Declaration of Aziz Mottiwala under 37 C.F.R. § 1.132 (hereinafter, “Mottiwala Declaration”), Vice President of Marketing at Allergan for Allergan’s Dry Eye Product Franchise.

As explained by Mr. Mottiwala, RESTASIS®, which is a commercial embodiment of the claimed formulation, has been sold since 2003. *See* Mottiwala Declaration at ¶ 2. Since the launch of RESTASIS® in 2003, worldwide sales of the drug have increased steadily. *See* Mottiwala Declaration at ¶ 3 and Exhibit B to Mottiwala Declaration. Currently, annual world-wide net sales for RESTASIS® are over \$200 million per quarter, and nearing \$800 million annually. *See* Mottiwala Declaration at ¶ 4. This is strong evidence of commercial success. *See Id.* As there is no other FDA-Approved therapeutic treatment for dry eye available on the US market, RESTASIS® owns 100% of the market share. *Id.*

Accordingly, the Applicants assert that the Declaration of Aziz Mottiwala provides objective evidence that unequivocally establishes that the present invention as embodied in RESTASIS® has been met with commercial success.

The Claimed Formulations Satisfied a Long-Felt Need

As discussed during the Interview, the claimed formulations also resolve a long-felt need. In support of this position, the Applicants submit herewith as Exhibit 4, a Declaration of Dr. Rhett M. Schiffman under 37 C.F.R. § 1.132 (hereinafter, “Schiffman Declaration 2”).

According to the MPEP, establishing long-felt need requires objective evidence that an art recognized problem existed in the art for a long period of time without solution. *See* MPEP § 716.04.

First, the need must have been a persistent one that was recognized by those of ordinary skill in the art. *Id.* As explained by Dr. Schiffman, dry eye/keratoconjunctivis sicca has been a known, persistent ocular disorder for many years. Publications on dry eye date back to at least the 1970’s, and interest and publication on the subject has increased substantially since. *See* Schiffman Declaration 2 at ¶¶ 2-4.

Second, the long-felt need must not have been satisfied by another before the invention by applicant. MPEP 716.04. As explained by Dr. Schiffman, no other therapeutic dry-eye drug has been approved by the FDA before or since RESTASIS®. *See Schiffman Declaration 2 at ¶ 8.* Other treatments for dry eye, such as artificial tears, have been commercially available, but they only exhibit a palliative effect, and do not work to increase tear production or otherwise treat the disease. *See Schiffman Declaration 2 at ¶ 4.*

Third, the invention must in fact satisfy the long-felt need. MPEP 716.04. As shown by the FDA's approval of RESTASIS®, and the praise in the industry discussed by Dr. Schiffman at paragraph 8 of Schiffman Declaration 2, the claimed methods have satisfied the long felt need. As explained above, RESTASIS® has been met with great commercial success, which further shows the satisfaction of the long felt need.

Several other companies have tried to develop therapeutic drugs for FDA approval, but many have failed. *See Schiffman Declaration 2 at ¶ 9 and Exhibit N.* The Federal Circuit has implicitly accepted that failure to obtain FDA approval is relevant evidence of failure of others. *Knoll Pharm. Co. v Teva Pharms. USA, Inc.*, 367 F.3d 1381, 1385 (Fed. Cir. 2004).

Accordingly, the Applicants assert that the second Declaration of Dr. Rhett M. Schiffman provides objective evidence that unequivocally establishes that the present invention as embodied in RESTASIS® has satisfied a long felt need and that others have failed to meet such a long felt need.

Hence, in view of the evidence presented above and presented in the attached declarations, the Applicants submit that the unexpected results, commercial success, and satisfaction of long felt need obtained from the claimed formulations successfully rebut the *prima facie* case of obviousness presented in the Office Action. Thus, the Applicants respectfully request that the Examiner withdraw the outstanding rejections under 35 U.S.C. § 103.

Obviousness-Type Double Patenting Rejections

Claims 37-60 were rejected for non-statutory obvious-type double patenting in view of claims 1-8 of the Ding reference.

The Applicants submit that the pending claims are patentably distinct from claims 1-8 of Ding for at least the same reasons argued above. The Applicants respectfully request, therefore, that the Office withdraw the double patenting rejection of Claims 37-60 in view of claims 1-8 of Ding.

Provisional Obviousness-Type Double Patenting Rejection

Claims 37-60 were rejected for provisional non-statutory obvious-type double patenting in view of claims 37-61 of copending U.S. Patent Application No. 13/967,179, claims 37-60 of copending U.S. Patent Application No. 13/961,835, claims 37-61 of copending U.S. Patent Application No. 13/961,818, and claims 37-60 of copending U.S. Patent Application No. 13/967,168.

While the Applicants do not necessarily agree with the provisional non-statutory obviousness-type double patenting rejections recited above, in order to expedite prosecution, terminal disclaimers in the aforementioned applications were filed on October 7, 2013. Thus, the Applicants submit that the provisional obviousness-type double patenting rejection has been rendered moot and request that this provisional obviousness-type double patenting rejection be withdrawn.

Statutory Double Patenting Rejection

Claims 37-60 were provisionally rejected for statutory double patenting in view of claims 37-56, 58-61 of copending U.S. Patent Application No. 13/967,163 and claims 37-56, 58-61 of copending U.S. Patent Application No. 13/961,828. Claims 37-60 were also provisionally rejected for statutory double patenting in view of claims 37-60 of copending U.S. Patent Application No. 13/961,808. The Applicants submit that the amendments to the claims filed herewith render the provisional statutory double patenting rejection over claims 37-56, 58-61 of copending U.S. Patent Application No. 13/967,163 and claims 37-56, 58-61 of copending U.S. Patent Application No. 13/961,828 moot.

Since this is a provisional statutory double patenting rejection, the Applicants request that the Examiner allow the present case to proceed to allowance over copending U.S. Patent Application No. 13/961,808. *See* MPEP § 804(2). Applicants respectfully request, therefore, that the Office withdraw the provisional statutory double patenting rejections.

Conclusion

In view of the foregoing, the Applicants believe all claims now pending in the present application are in condition for allowance.

The Commissioner is hereby authorized to charge any fees required or necessary for the filing, processing or entering of this paper or any of the enclosed papers, and to refund any overpayment, to deposit account 01-0885.

If the Examiner believes a telephone conference would expedite prosecution of this application, please contact the undersigned at (714) 246-6996.

Respectfully submitted,

/Laura L. Wine/

Date: October 23, 2013

Laura L. Wine
Attorney of Record
Registration Number 68,681

Please direct all inquiries and correspondence to:
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Electronic Patent Application Fee Transmittal

Application Number:	13967189			
Filing Date:	14-Aug-2013			
Title of Invention:	METHODS OF PROVIDING THERAPEUTIC EFFECTS USING CYCLOSPORIN COMPONENTS			
First Named Inventor/Applicant Name:	Andrew Acheampong			
Filer:	Laura Lee Wine			
Attorney Docket Number:	17618CON2B (AP)			
Filed as Large Entity				
Utility under 35 USC 111(a) Filing Fees				
Description	Fee Code	Quantity	Amount	Sub-Total in USD(\$)
Basic Filing:				
Pages:				
Claims:				
Independent claims in excess of 3	1201	1	420	420
Miscellaneous-Filing:				
Petition:				
Patent-Appeals-and-Interference:				
Post-Allowance-and-Post-Issuance:				
Extension-of-Time:				

Description	Fee Code	Quantity	Amount	Sub-Total in USD(\$)
Miscellaneous:				
Total in USD (\$)				420

Electronic Acknowledgement Receipt

EFS ID:	17210168
Application Number:	13967189
International Application Number:	
Confirmation Number:	4818
Title of Invention:	METHODS OF PROVIDING THERAPEUTIC EFFECTS USING CYCLOSPORIN COMPONENTS
First Named Inventor/Applicant Name:	Andrew Acheampong
Customer Number:	51957
Filer:	Laura Lee Wine
Filer Authorized By:	
Attorney Docket Number:	17618CON2B (AP)
Receipt Date:	23-OCT-2013
Filing Date:	14-AUG-2013
Time Stamp:	17:23:23
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	Deposit Account
Payment was successfully received in RAM	\$420
RAM confirmation Number	4890
Deposit Account	010885
Authorized User	

The Director of the USPTO is hereby authorized to charge indicated fees and credit any overpayment as follows:

Charge any Additional Fees required under 37 C.F.R. Section 1.16 (National application filing, search, and examination fees)

Charge any Additional Fees required under 37 C.F.R. Section 1.17 (Patent application and reexamination processing fees)

Charge any Additional Fees required under 37 C.F.R. Section 1.19 (Document supply fees)

Charge any Additional Fees required under 37 C.F.R. Section 1.20 (Post Issuance fees)

Charge any Additional Fees required under 37 C.F.R. Section 1.21 (Miscellaneous fees and charges)

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Affidavit-traversing rejectns or objectns rule 132	17618CON2B-Exhibit-1.pdf	670148	no	26
			d43c6d440b6bac54805bd50936ee9689001a8f9d		

Warnings:

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Information:

2	Affidavit-traversing rejectns or objectns rule 132	17618CON2B-Exhibit-2.pdf	452124	no	19
			312fb156acf1ee5b36c77f3d5c9608e9d365b4ac		

Warnings:

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Information:

3	Affidavit-traversing rejectns or objectns rule 132	17618CON2B-Exhibit-3.pdf	269817	no	10
			60467d2777513aa6b96972fa56ad6d929b9e4f6c		

Warnings:

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Information:

4	Affidavit-traversing rejectns or objectns rule 132	17618CON2B-Exhibit-4.pdf	7072016	no	115
			e9b31287d9350c7259b0d288ff61512da926e736		

Warnings:

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Information:

5		17618CON2B_Response_NFOA .pdf	1512843	yes	16
			a394fc7e91e22e29842271951aae21efed928f73		

Multipart Description/PDF files in .zip description

Document Description	Start	End
Amendment/Req. Reconsideration-After Non-Final Reject	1	1
Claims	2	5

	Applicant summary of interview with examiner	6	6
	Applicant Arguments/Remarks Made in an Amendment	7	16

Warnings:

Information:

6	Fee Worksheet (SB06)	fee-info.pdf	30754	no	2
			5457404800ecb2db02ad2375ff5d929aed23f221		

Warnings:

Information:

Total Files Size (in bytes):		10007702
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This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

EXHIBIT 1

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

DECLARATION UNDER 37 C.F.R. 1.132

of Dr. Rhett M. Schiffman,

I, Rhett M. Schiffman, M.D., declare as follows:

1. I am currently a Vice President and Chief Medical Officer at Neurotech. I have an M.D, Masters Degrees in Clinical Research Design and Statistical Analysis and in Health Services Administration, a Bachelor's degree in Bioengineering, and over 12 years of experience in the pharmaceutical industry at Allergan, Inc. ("Allergan"). I was also a clinical investigator in the Phase 3 studies for Restasis®. I am a co-inventor on several issued patents and pending applications related to treatment methods using ophthalmic products. My *curriculum vita*, which contains a list of my publications to which I contributed, is attached to this declaration as Exhibit A.
2. I have been informed of the general nature of the rejections made by the Patent Office with respect to the previously presented claims of the above-referenced patent application and I am familiar with the references that the Patent Office has relied on in making these rejections. For example, I am aware of U.S. Patent No. 5,474,979 to Ding et al. ("Ding").
3. Restasis® is an FDA approved product that is a commercial embodiment of the invention. Specifically, Restasis® is approved as a 0.05% by weight cyclosporin ophthalmic emulsion useful for the treatment of ophthalmic conditions, such as dry eye. Specifically, Restasis® ophthalmic emulsion is indicated to increase tear production in patients whose tear production is presumed to be suppressed due to ocular inflammation associated with keratoconjunctivitis sicca.
4. I have reviewed the pending claims in the present application, and the pending claims cover the specific formulation of Restasis® and/or the approved methods of treatment of dry eye or keratoconjunctivitis sicca for Restasis®.
5. In creating and testing the claimed methods and compositions, several unexpected benefits were discovered using the claimed compositions and/or claimed methods.
6. During development of a drug for the treatment of dry eye disease or keratoconjunctivitis sicca, Allergan performed a randomized, multicenter, double-masked, parallel-group, dose-response controlled Phase 2 trial on several cyclosporin-A and castor oil-containing formulations. In this Phase 2 study of moderate to severe KCS, the safety and efficacy of

four cyclosporin A-containing emulsion compositions were compared to one another: 0.05% by weight cyclosporin A with 0.625% by weight castor oil, 0.10% by weight cyclosporin A with 1.25% by weight castor oil, 0.20% by weight cyclosporin A with 2.5% by weight castor oil, and 0.40% by weight cyclosporin A with 5.0% by weight castor oil. A vehicle containing 2.5% by weight castor oil was also tested and compared to these formulations. In this study, patients with moderate to severe dry eye disease were treated twice daily with one of the aforementioned cyclosporin A-containing formulations or a vehicle. All of the cyclosporin A-containing formulations as well as the vehicle also included 2.2% by weight glycerine, 1.0% by weight polysorbate 80, 0.05% by weight Pemulen, sodium hydroxide, and water. To the best of my knowledge, the specific cyclosporin-A containing formulations tested in humans in this Phase 2 study are disclosed in the Ding reference. Results from this study illustrating the change from baseline in corneal staining and change from baseline in Schirmer Score, key objective testing measures for dry eye or KCS, are shown in Exhibit B, Figures 1 and 2, respectively.

7. As shown in Exhibit B, Figure 1, the 0.1% by weight cyclosporin A/ 1.25% by weight castor oil formulation demonstrated a greater decrease in corneal staining than the 0.05% by weight cyclosporin A/0.625% by weight castor oil formulation. As shown in Exhibit B, Figure 2 the 0.1% by weight cyclosporin A/ 1.25% by weight castor oil formulation demonstrated a greater increase in Schirmer Score (tear production) at week 12 than any other formulation tested, including the 0.05% by weight cyclosporin A/0.625% by weight castor oil formulation. Corneal staining and Schirmer score are key objective measures for determining dry eye or keratoconjunctivitis sicca disease severity.

8. After Allergan's Phase 2 study, Allergan initiated a Phase 3 study. In Allergan's multicenter, randomized, double-masked Phase 3 trials, Allergan compared the efficacy and safety of the formulation containing 0.10% by weight cyclosporin A and 1.25% by weight castor oil to a the claimed formulation (containing 0.05% by weight cyclosporin A and 1.25% by weight castor oil), and to a vehicle containing 1.25% by weight castor oil. The data presented in Exhibit B represents the subpopulation of moderate to severe Phase 2 patients with the same reductions in tear production (≤ 5 mm/5 min) as those enrolled in the Phase 3 studies. In this study, patients with moderate to severe dry eye disease were treated twice daily with either a formulation containing 0.10% by weight cyclosporin A and 1.25% by weight castor oil, a formulation containing 0.05% by weight cyclosporin and 1.25% by weight castor oil, or the vehicle. Both cyclosporin A-containing formulations and the vehicle also included 2.2% by weight glycerine, 1.0% by weight polysorbate 80, 0.05% by weight Pemulen, sodium hydroxide, and water.

9. I have reviewed the Declaration of Dr. Mayssa Attar (“Attar Declaration”), and I agree with her statements made in paragraphs 6-8, reproduced here. I have attached Exhibit B to the Attar Declaration to this Declaration as Exhibit C:

10. “It was known in the art at the time this application was filed that cyclosporin could be administered topically locally to the eye to target and treat dry eye by using cyclosporin A’s immunomodulatory properties to inhibit T cell activation which would lead to an increase in tear production and potentially other therapeutic effects related cyclosporine’s anti-inflammatory and anti-apoptotic effects and thus limit chronic inflammation in the pathology of dry eye. To elicit it’s therapeutic effect, cyclosporine must be effectively delivered to multiple target tissues of the ocular surface such as the cornea, conjunctiva, and lacrimal gland. The rate and extent at which cyclosporine is differentially delivered to the putative sites of action is critical to achieving therapeutic success in treating dry eye. Generally speaking, it was understood that pharmacokinetic/pharmacodynamic relationship would indicate that as more cyclosporin A reaches the target tissues of the ocular surface, such as the cornea and conjunctiva, the more immunomodulatory and more anti-inflammatory activity can take place and the more therapeutically effective a drug can be in treating dry eye.

11. Pharmacokinetic studies were performed on animal eyes, which compared the pharmacokinetic properties of several cyclosporin A-containing formulations. Those results are attached to this declaration in Exhibit B. As shown in Exhibit B, the relative extent at cyclosporin was absorbed increased in the relevant ocular tissues, here, the cornea and the conjunctiva, where the amount of oil present in the formulation was decreased. Specifically, the amount of cyclosporin A that reached the relevant ocular tissue was higher for the formulation containing 0.05% by weight cyclosporin A and 0.625% by weight castor oil than the formulation containing 0.05% by weight cyclosporin A and 1.25% by weight castor oil relative to the formulation containing 0.1% by weight cyclosporin A and 1.25% by weight castor oil.

12. One of skill in the art would have understood such a result to mean that since there was more cyclosporin A present in the relevant ocular tissues in the formulation containing 0.05% by weight cyclosporin A and 0.625% by weight castor oil and the formulation containing 0.1% by weight cyclosporine A and 1.25% by weight castor oil than the claimed formulation, that those formulations would have been more therapeutically effective than the claimed formulation. Specifically, this data suggests that the formulation containing 0.05% by weight cyclosporin A and 0.625% by weight castor oil would have been more therapeutically effective than the claimed formulation.”

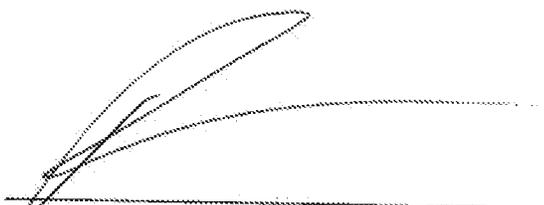
13. Specifically, one of skill in the art would have expected patients receiving the claimed formulations and methods to exhibit a lesser decrease from baseline in corneal staining score and a lesser increase from baseline in Schirmer Score, relative to the patient corneal staining scores and Schirmer Scores demonstrated by the patients receiving the 0.05% by weight cyclosporin A / 0.625% by weight castor oil formulation (Ding 1E) in the Phase 2 trials illustrated in Exhibit B.
14. Surprisingly, the claimed formulation and method was equally or more therapeutically effective for the treatment of dry eye/keratoconjunctivitis sicca than the formulation containing 0.10% by weight cyclosporin A and 1.25% by weight castor oil according to at least four testing parameters. This result was surprising and completely unexpected. These results are attached to this declaration in Exhibit D.
15. As shown in the results in Exhibit D, the claimed formulation and method was unexpectedly superior to the 0.10% by weight cyclosporin A / 1.25% by weight castor oil formulation with respect to several properties. For example, the claimed formulations and methods surprisingly exhibited a comparable or greater decrease in corneal staining score (see Exhibit D, Figure 1), a greater increase in Schirmer Score (see Exhibit D, Figure 2), an improvement in the common dry eye/keratoconjunctivitis sicca symptom of blurred vision (see Exhibit D, Figure 3) and a greater decrease in the number of artificial tears used by patients (see Exhibit D, Figure 4) compared to the formulation containing 0.10% by weight cyclosporin A and 1.25% by weight castor oil.
16. This result was even more surprising, given earlier testing from the Phase 2 study that illustrated that compositions containing 0.10% by weight cyclosporin A and 1.25% by weight castor oil provided more improvement in objective measures (such as corneal staining and increase in Schirmer Score – as illustrated in Exhibit B) in dry eye patients than compositions containing 0.05% by weight cyclosporin A and 0.625% castor oil.
17. I have compared the objective results showing the surprising therapeutic efficacy of the claimed formulation and method relative to the 0.10% by weight cyclosporin A and 1.25% by weight castor oil formulation tested in Phase 3 to the 0.05% by weight cyclosporin A and 0.625% by weight castor oil formulation relative to the 0.10% by weight cyclosporin A and 1.25% by weight castor oil formulation tested in Phase 2. This comparison is attached to this declaration as Exhibit E.
18. As seen in Exhibit E, in the Phase 2 study, the 0.05% by weight cyclosporin A/0.625% by weight castor oil formulation (Ding 1E) only achieved 0.25 times the improvement in Schirmer Tear Test score as the 0.1 % by weight cyclosporin A/1.25% by weight castor

oil formulation and only achieved 0.25 times the decrease in corneal staining as the 0.1 % by weight cyclosporin A/1.25% by weight castor oil formulation. However, in the Phase 3 studies, the claimed formulation and method achieved twice the improvement in Schirmer Tear Test score as the 0.1 % by weight cyclosporin A/1.25% by weight castor oil formulation in the first study and substantially the same improvement in Schirmer Tear Test score as the 0.1 % by weight cyclosporin A/1.25% by weight castor oil formulation in the second Phase 3 study. Also, the claimed formulation achieved substantially the same decrease in corneal staining score compared to the 0.1 % by weight cyclosporin A/1.25% by weight castor oil formulation.

19. As seen in Exhibit E, and further illustrated in Exhibit F, surprisingly, the claimed formulation and method demonstrated an 8-fold increase in relative efficacy for the Schirmer Tear Test Score in the first study of phase 3 compared to the 0.05% by weight cyclosporin A/0.625% by weight castor oil formulation (Ding Example 1E) in the Phase 2 study. Exhibits E and F also illustrate that the claimed formulations demonstrated a 4-fold improvement in the relative efficacy for the Schirmer Tear Test score for the second study of Phase 3 and a 4-fold increase in relative efficacy for decrease in corneal staining score in both of the Phase 3 studies compared to the 0.05% by weight cyclosporin A/0.625% by weight castor oil formulation in the Phase 2 study, the formulation disclosed in the Ding reference (Ding 1E). This was clearly a very surprising result.

20. Taking the results of these studies together, it is clear that the specific combination of 0.05% by weight cyclosporin A with 1.25% by weight castor oil is surprisingly and unexpectedly critical for therapeutic effectiveness in the treatment of dry eye/keratoconjunctivitis sicca.

I hereby declare that all statements made herein of my own knowledge and belief are true; and that all statements made on information and belief are believed to be true; and further that these statements are made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patents issued thereon.



Dr. Rhett M. Schiffman

Date: 10/11/13

EXHIBIT A

CURRICULUM VITAE FOR RHETT M. SCHIFFMAN, M.D., M.S., M.H.S.A.

Current Title: Vice President and Chief Medical Officer
Neurotech

Work Address: 900 Highland Corporate Drive
Building #1, Suite #101
Cumberland, RI 02864

Home Address: 1843 Temple Hills
Laguna Beach, CA 92651

Office Telephone: (401) 495-2395
Cell Telephone: (313) 516-6924
Email: r.schiffman@neurotechusa.com

EDUCATION:

Professional: University of Michigan, School of Public Health,
Ann Arbor, Michigan
2000 M.H.S.A. Health Services Administration

University of Michigan, Rackham Graduate School,
Ann Arbor, Michigan
1989 M.S. Clinical Research Design & Statistical Analysis

Universidad Autonoma de Ciudad Juarez
Instituto de Ciencias Biomedicas
Juarez, Mexico
1983 M.D. Medicine

Undergraduate: Columbia University
School of Engineering and Applied Science
New York, NY
1978 B.S. Bioengineering

POSTDOCTORAL TRAINING:

Fellow: Uveitis and Ocular Immunology, National Eye Institute,
National Institutes of Health, Bethesda, MD
1996-1997

Resident: Ophthalmology, Henry Ford Hospital, Detroit, Michigan
1993 - 1996

Resident: Internal Medicine, Henry Ford Hospital, Detroit, Michigan
1984 - 1986

Intern: Internal Medicine, Henry Ford Hospital, Detroit, Michigan
1983 - 1984

CERTIFICATION AND LICENSURE

Medical Licensure: California, 2002 – C50825

Michigan, 1983 - 4301046984

Board Certification: American Board of Ophthalmology, 1999; 93th percentile on Board examination

American Board of Internal Medicine, 1986; 99th percentile on Board examination

PROFESSIONAL SOCIETIES:

Member, Association for Research in Vision and Ophthalmology
American Academy of Ophthalmology
American Medical Association

PROFESSIONAL EXPERIENCE:

2013-Present Vice President and Chief Medical Officer, Neurotech

2010-2013 Board Member, Glaucoma Research Foundation

2009-2013 Ophthalmology Therapeutic Area Head

2008-2013 Head of Development for Emerging Markets

2007-2013 Head, Global Product Enhancement/Life Cycle Management

2005-2013 Vice President, Development for Ophthalmology and Botox, Allergan Pharmaceuticals

2003-Present Clinical Associate Professor and Attending Physician in Ophthalmology, University of California at Irvine.

2001-2005 Senior Director, Ophthalmology Clinical Research, Allergan Pharmaceuticals, Irvine, California

1999-2001 Member, Leadership Council, Eye Care Services, Henry Ford Health System, Detroit, MI

1999-2001 Director, Quality Improvement, Eye Care Services, Henry Ford Health System, Detroit, MI

1998-2001 Director of the African-American Initiative for Male Health Improvement (AIMHI). Eye Disease Screening Program in Southeast Michigan. Funded by the Michigan Department of Community Health.

1997-2001 Director of Uveitis Services, Eye Care Services, Henry Ford Health System, Detroit, MI
Director of Clinical Research, Eye Care Services, Henry Ford Health System, Detroit, MI
Staff Investigator, Center for Health Services Research, Henry Ford Health System, Detroit, MI

1996-2001 Reviewer to Special Study Section, National Eye Institute, National Institutes of Health, Bethesda, Maryland.

1999-2001 Director, Clinical Research, Eye Care Services, Henry Ford Hospital, Detroit, Michigan

- 1996-1997 Senior Staff Physician, Eye Care Services, Ophthalmology, Henry Ford Health System, Detroit, Michigan (on intergovernmental personnel act to National Eye Institute, National Institutes of Health, Bethesda, Maryland)
- 1994-1995 Associate Medical Director, Henry Ford Hospital Pharmacology Research Unit, Detroit, Michigan
- 1993-2001 Associate Research Director, Eye Care Services, Henry Ford Hospital, Detroit, Michigan
- 1989-2001 Staff, Center for Clinical Effectiveness, Henry Ford Hospital, Detroit, Michigan
- 1988-1994 Requirements Advisory Committee to the Medical Information Management System, Henry Ford Hospital, Detroit, Michigan
- 1989-1993 Coordinator, General Internal Medicine Research, Henry Ford Hospital, Detroit, Michigan
- 1990-1993 Chairman, General Internal Medicine Research Committee, Henry Ford Hospital, Detroit, Michigan
- Member, Research and Academic Affairs Committee, Department of Medicine, Henry Ford Hospital, Detroit, Michigan
- 1986-1993 Senior Staff Physician, General Internal Medicine, Henry Ford Hospital, Detroit, Michigan

TEACHING EXPERIENCE:

- 2003-Present Ophthalmology Residency Training Program, University of California at Irvine
- 1997-2001 Ophthalmology Residency Training Program, Henry Ford Hospital, Detroit, Michigan
- 1986-1993 Internal Medicine Residency Training Program, Henry Ford Hospital, Detroit, Michigan
- 1988-1993 Preceptor, University of Michigan Medical Schools, Ann Arbor, Michigan
- 1991-1993 Preceptor, General Internal Medicine Fellows
- Medical Staff Seminars, General Internal Medicine, Henry Ford Hospital, Detroit, MI: Introduction to Epidemiology, Introduction to Personal Computing, Medical Decision Analysis

BOOKS & MONOGRAPHS:

1. Ocular Therapy chapter in: Oréfice, Fernando: Uveíte: Clínica e Cirúrgica. Ed. Cultura Médica. Published June 2000.
2. New Concepts in the Pathogenesis, Diagnosis and Treatment of Dry Eye. Ocular Surgery News Monograph; Slack Incorporated. July 1, 1999

3. Schiffman RM: Glaucoma, Ophthalmology chapter in Noble, John: Textbook of Primary Care Medicine. 2nd Edition. 1996. Mosby-Year Book, Inc. 1471-9.

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2. Callanan DG, Gupta S, Boyer DS, Ciulla TA, Singer MA, Kuppermann BD, Liu CC, Li XY, Hollander DA, Schiffman RM, Whitcup SM; Ozurdex PLACID Study Group. Dexamethasone Intravitreal Implant in Combination with Laser Photocoagulation for the Treatment of Diffuse Diabetic Macular Edema. *Ophthalmology*. 2013 May 22. S0161-6420(13)00152-8.
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9. Spaeth G, Bernstein P, Caprioli J, Schiffman RM. Control of Intraocular Pressure and Intraocular Pressure Fluctuation with Fixed Combination Brimonidine-Timolol versus Brimonidine or Timolol Monotherapy. *Am J Ophthalmol*. 2011 January;151:93-99.
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JOURNAL REVIEWER

1. British Journal of Ophthalmology
2. Current Eye Research
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5. The Lancet

SELECTED PAST SCIENTIFIC ACTIVITIES:

HFHS Principal Investigator

1. Schiffman RM, Chew E, Ferris F, Ellwein L, Hays R, Mangione C: A Randomized Comparison of the Cost, Quality and Acceptability of Four Modes of Administration the National Eye Institute Visual Functioning Questionnaire-25. National Eye Institute.
2. Schiffman RM: National Eye Institute Refractive Error Correction Questionnaire (NEI-RECQ) Phase II Protocol. National Eye Institute through Emmes Corporation.
3. Schiffman RM, Lesser GL, Imami N, Trick GL: A 48-Month, Multi-Center, Randomized, Double-Masked, Placebo-Controlled, Clinical Study to Evaluate the Effectiveness and Safety of Oral Memantine in Daily Doses of 20 Mg and 10 Mg in Patients with Chronic Open-Angle Glaucoma at Risk for Glaucomatous Progression - Allergan Protocol 192944-005.
4. Schiffman RM: A Multicenter, Investigator-Masked, Randomized, Parallel-Group Study to Compare the Safety and Efficacy and Safety of Restasis™ (Cyclosporine 0.05% Ophthalmic Emulsion) vs. An Artificial Tear (Refresh®) Used Twice Daily for Three Months in Patients with Moderate to Severe Keratoconjunctivitis Sicca (Allergan Protocol 192371-008)
5. Schiffman RM, Patel S, Crosswell M and Shankle J: The Retinal Thickness Analyzer in the Management of Uveitic Cystoid Macular Edema.
6. Schiffman RM, Trick GL: Retinal Thickness Analyzer (RTA) - Clinical Validation Study. Talia Technology Ltd.
7. A Multicenter, Randomized, Double-Masked, Controlled Study to Evaluate the Safety and Efficacy of an Intravitreal Fluocinolone Acetonide Insert in Patients with Non-Infectious Uveitis Affecting the Posterior Segment of the Eye. Bausch and Lomb.

SCIENTIFIC ACTIVITIES:

HFHS Collaborative Investigator:

1. Lesser B, Darnley D, Schiffman R: Ocular Hypertension Treatment Study. National Eye Institute, 1993- 1999.
2. Nussenblatt RB, Whitcup SM, Schiffman RM, et. al: The Treatment of Non-infectious Intermediate and Posterior Uveitis with Humanized Anti-Tac Monoclonal Antibody Therapy: Phase I and Phase II. National Eye Institute, National Institutes of Health.

EXHIBIT B