Docket No. 17618CON5B (AP)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Acheampong, *et al.*	Examiner: TBA
Serial No.: TBA	Group Art Unit: TBA
Filed: Herewith	Confirmation No. TBA
For: METHODS OF PROVIDING THERAPEUTIC EFFECTS USING CYCLOSPORIN COMPONENTS	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. 13/961,818 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 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.

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

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

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

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

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

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

44. (New) The method of Claim 37, wherein the emulsion comprises Pemulen in an amount of about 0.05% by weight.

45. (New) The method of Claim 37, wherein the emulsion further comprises glycerine in an amount of about 2.2% by weight and a buffer.

46. (New) The method of Claim 45, wherein the buffer is sodium hydroxide.

47. (New) The method of Claim 37, wherein, when the emulsion 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 cyclosporin A.

48. (New) The method of Claim 42, wherein the emulsion has a pH in the range of about 7.2 to about 7.6.

49. (New) The method of Claim 37, wherein the 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 method of Claim 37, wherein the 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 method of Claim 37, 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 compared to an emulsion that contains only 50% as much castor oil.

52. (New) The method of Claim 37, wherein the 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 method of Claim 52, wherein the adverse events include side effects.

54. (New) A method of reducing side effects in a human suffering from dry eye syndrome, the method comprising the step of 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;

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 method of Claim 54, wherein the buffer is sodium hydroxide.

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

57. (New) The method of Claim 54, wherein, when the emulsion is administered to the 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 A.

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

59. (New) The method of Claim 54, wherein the emulsion is effective in treating dry eye disease.

60. (New) A method of treating dry eye disease, the method comprising the step of topically administering to an eye of a human an emulsion, the 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 effective in treating dry eye disease.

61. (New) The method of Claim 60, wherein the 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 37-61. Support for the limitations recited in the new claims may be found throughout the specification, and at least at page 4, line 25 – page 5, line 14, page 10, lines 1-7, 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/

Date: August 14, 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

Doc Code: TRACK1.REQ
Document Description: TrackOne Request

PTO/AIA/424 (03-13)

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.
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 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:	17618CON5B (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	5	80	400
Independent claims in excess of 3	1201	1	420	420

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Miscellaneous-Filing:				
Publ. Fee- Early, Voluntary, or Normal	1504	1	300	300
OTHER PUBLICATION PROCESSING FEE	1808	1	130	130
Petition:				
Patent-Appeals-and-Interference:				
Post-Allowance-and-Post-Issuance:				
Extension-of-Time:				
Miscellaneous:				
		Total in USD ($)		**6850**

Electronic Acknowledgement Receipt

EFS ID:	16593100
Application Number:	13967179
International Application Number:	
Confirmation Number:	8654
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:	17618CON5B (AP)
Receipt Date:	14-AUG-2013
Filing Date:	
Time Stamp:	18:49:39
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	Deposit Account
Payment was successfully received in RAM	$6850
RAM confirmation Number	6223
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	17618CON5B_ADS.pdf	1509913 f4175733ae4deae0cc2419f6f51cf83740f4f3c5	no	8
Warnings:					
Information:					
3	Oath or Declaration filed	17618CON5B_DECS.pdf	645090 1cc2bbfb0fbf9a783362f088e6b132ea37de5ba3	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	17618CON5B_POA.pdf	1931210 0bcb7a2e471e5bfbe0f5c1769aa60a43fbca1109	no	2
Warnings:					
Information:					
5		17618CON5B_PRELIM_AMENDMENTS.pdf	106465 c04b4e0a11bc2314b05581c0329afa77487cbaed	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	17618CON5B_PRIORITIZED_EXAM.pdf	153243 e3999ce6355f3b02c50e19c9b45dd819e5901b53	no	2
Warnings:					
Information:					
7	Fee Worksheet (SB06)	fee-info.pdf	43444 c1a3bc365ea64539580c43dc2cc0c53849d5ec9a	no	2
Warnings:					
Information:					
		Total Files Size (in bytes):	8749815		

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.

D-3111CON

METHODS OF PROVIDING THERAPEUTIC EFFECTS USING CYCLOSPORIN COMPONENTS

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 entirety herein by reference.

Background of the Invention

The present invention relates to methods of providing desired therapeutic effects to humans or animals using 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 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. 6,350,442, this disclosure of each of which is incorporated in its entirely 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 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, 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;* "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, *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 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 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 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 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 cyclosporin-containing emulsions.

Summary of the Invention

New methods of treating a human or animal using cyclosporin component-containing emulsions have been 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 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 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 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.

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 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 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 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 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 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.

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 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.

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.

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.

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 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.

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

Detailed Description

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. 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 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 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 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, 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 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 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 below or less than 0.1 ng/ml are therefore considered substantially undetectable.

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

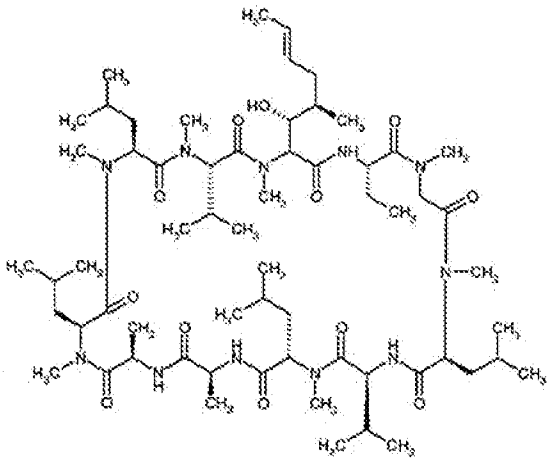
One ml of blood is acidified with 0.2 ml of 0.1 N HCl solution, then extracted with 5 ml of methyl t-butyl ether. After separation from the acidified aqueous layer, the organic phase is neutralized with 2 ml of 0.1 N NaOH, evaporated, reconstituted in a water/acetonitrile-based mobil phase, and injected onto a 2.1 x 50 mm, 3μm pore size C-8 reverse phase high pressure liquid chromatography (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

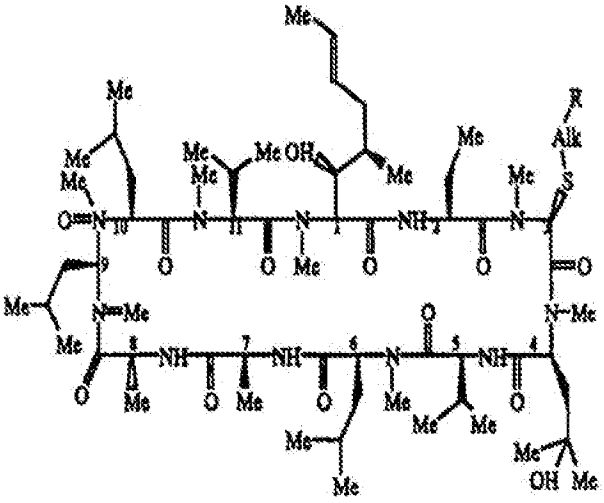


As used herein the term "derivatives" of a cyclosporin refer to compounds having structures sufficiently similar to the cyclosporin so as to function in a manner substantially similar to or substantially identical to the cyclosporin, for example, cyclosporin A, in the present methods. Included, without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

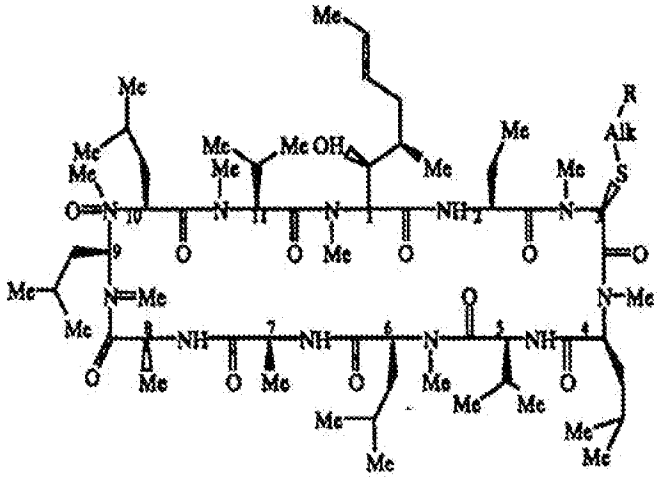
Formula II

(II)



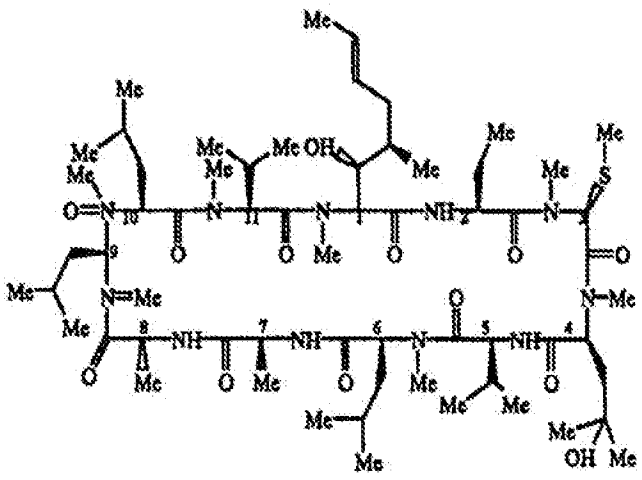
Formula III

(III)



Formula IV

(I)



wherein Me is methyl; Alk is 2-6C alkylene or 3-6C cycloalkylene; R is OH, COOH, alkoxycarbonyl, $-NR_1R_2$ or $N(R_3)-(CH_2)-NR_1R_2$; wherein R_1, R_2 is H, alkyl, 3-6C cycloalkyl, phenyl (optionally substituted by halo, alkoxy, alkoxycarbonyl, 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.

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 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 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 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.

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 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 amphorteric 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.

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 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 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 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-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:

metal carboxy methylcelluloses
metal carboxy methylhydroxyethylcelluloses

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

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 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 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 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 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.

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 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 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.

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 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 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. 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®.

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 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 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); 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. 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 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 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 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 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 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 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 thermodynamicaly 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:

	Composition I	Composition II
	wt%	wt%
Cyclosporin A	0.1	0.05
Castor Oil	1.25	1.25
Polysorbate 80	1.00	1.00
Premulen®	0.05	0.05
Glycerine	2.20	2.20
Sodium hydroxide	qs	qs
Purified Water	qs	qs
pH	7.2-7.6	7.2-7.6
Weight Ratio of Cyclosporin A to Castor Oil	0.08	0.04

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

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.

PTO/AIA/14 (03-13)
Approved for use through 01/31/2014. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Application Data Sheet 37 CFR 1.76	Attorney Docket Number	17618CON5B (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

☐ 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.)

Inventor Information:

Inventor 1 Remove

Legal Name

Prefix	Given Name	Middle Name	Family Name	Suffix
	Andrew		Acheampong	

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

City	Irvine	State/Province	CA	Country of Residence i	US

Mailing Address of Inventor:

Address 1	16 Wintergreen		
Address 2			
City	Irvine	State/Province	CA
Postal Code	92604	Country i	US

Inventor 2 Remove

Legal Name

Prefix	Given Name	Middle Name	Family Name	Suffix
	Diane	D.	Tang-Liu	

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

City	Las Vegas	State/Province	NV	Country of Residence i	US

Mailing Address of Inventor:

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 Remove

Legal Name

Prefix	Given Name	Middle Name	Family Name	Suffix
	James	N.	Chang	

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

Application Data Sheet 37 CFR 1.76	Attorney Docket Number	17618CON5B (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 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. Add

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	Add Email	Remove Email

Application Information:

Title of the Invention	METHODS OF PROVIDING THERAPEUTIC EFFECTS USING CYCLOSPORIN COMPONENTS		
Attorney Docket Number	17618CON5B (AP)	Small Entity Status Claimed	☐
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	17618CON5B (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:	◉ Customer Number	○ US Patent Practitioner	○ 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	13961818	2013-08-07
Prior Application Status	Pending		Remove
Application Number	Continuity Type	Prior Application Number	Filing Date (YYYY-MM-DD)
13961818	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:

Application Data Sheet 37 CFR 1.76	Attorney Docket Number	17618CON5B (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) [i] 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 [i] (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

Application Data Sheet 37 CFR 1.76	Attorney Docket Number	17618CON5B (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 Remove

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.

Clear

(•) Assignee	( ) Legal Representative under 35 U.S.C. 117	( ) Joint Inventor
( ) Person to whom the inventor is obligated to assign.	( ) 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. [X]

Organization Name	Allergan, Inc.		
Mailing Address Information:			
Address 1	2525 Dupont Drive		
Address 2			
City	Irvine	**State/Province**	CA
Country [i]	US	Postal Code	92612
Phone Number		Fax Number	

PTO/AIA/14 (03-13)
Approved for use through 01/31/2014. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Application Data Sheet 37 CFR 1.76	Attorney Docket Number	17618CON5B (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. Add

Non-Applicant Assignee Information:

Providing assignment information in this section does not subsitute 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).

Remove

If the Assignee is an Organization check here. ☐

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. Add

Signature:

Remove

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. Add

PTO/AIA/14 (03-13)
Approved for use through 01/31/2014. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Application Data Sheet 37 CFR 1.76	Attorney Docket Number	17618CON5B (AP)
	Application Number	
Title of Invention	METHODS OF PROVIDING THERAPEUTIC EFFECTS USING CYCLOSPORIN COMPONENTS	

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.

PTO/AIA/01 (06-12)
Approved for use through 01/31/2014. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

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.: 17618CON5(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 13/961,818

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: A Acheampong

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.

PTO/AIA/01 (06-12)
Approved for use through 01/31/2014. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

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.: 17618CON5(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 13/961,818

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 TANG-LIU Date (Optional): _____

Signature: Diane Tang-Liu

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.

PTO/AIA/01 (06-12)
Approved for use through 01/31/2014. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

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.: 17618CON5(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 13/961,818 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: David F. Power

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.

Doc code: Oath
Document Description: Oath or declaration filed

PTO/AIA/02 (08-12)
Approved for use through 01/31/2014. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

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.: 17618CON5(AP)

This statement is directed to:

☐ The attached application,

OR

☒ United States application or PCT international application number 13/961,818 filed on 8-7-13.

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	State	Country
Newport Beach	CA	US

Mailing Address (except for a deceased or legally incapacitated inventor):

36 Cervantes

City	State	Zip	Country
Newport Beach	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:

- ☐ Legal Representative (for deceased or legally incapacitated inventor only),
- ☒ Assignee,
- ☐ Person to whom the inventor is under an obligation to assign,
- ☐ Person who otherwise shows a sufficient proprietary interest in the matter (petition under 37 CFR 1.46 is required), or
- ☐ Joint inventor.

PTO/SB/AIA02 (06-12)
Approved for use through 01/31/2014. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

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 (ASSIGNEE) COMPANY: ALLERGAN, INC. | Date (Optional):

Signature: /Debra D. Condino/

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

City	State	Country
Irvine	CA	US

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

2525 Dupont Drive-T2-7H

City	State	Zip	Country
Irvine	CA	92612	US

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.
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 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.

PTO/AIA/82A (07-12)
Approved for use through 11/30/2014. OMB 0651-0035
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

TRANSMITTAL FOR POWER OF ATTORNEY TO ONE OR MORE REGISTERED PRACTITIONERS

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	17618CON5B (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.**

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

PTO/AIA/82B(07-12)
Approved for use through 11/30/2014. OMB 0651-0035
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

POWER OF ATTORNEY BY APPLICANT

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

[X] 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:

[X] The address associated with the above-mentioned Customer Number.

OR

[ ] The address associated with Customer Number:

OR

[ ] Firm or Individual Name					
Address					
City		State		Zip	
Country					
Telephone		Email			

I am the Applicant:

[ ] Inventor or Joint Inventor

[ ] Legal Representative of a Deceased or Legally Incapacitated Inventor

[X] 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	/D Condino/	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.

Document code: WFEE

United States Patent and Trademark Office
Sales Receipt for Accounting Date: 09/04/2013

ABALINAN SALE #00000009 Mailroom Dt: 08/14/2013 010885 13967179
01 FC : 1830 140.00 DA

Document code: WFEE

United States Patent and Trademark Office
Sales Receipt for Accounting Date: 09/04/2013

ABALINAN ADJ #00000010 Mailroom Dt: 08/14/2013
Seq No: 6223 Sales Acctg Dt: 08/15/2013 010885 13967179
06 FC : 1201 420.00 CR

Document code: WFEE

United States Patent and Trademark Office
Sales Receipt for Accounting Date: 09/04/2013

ABALINAN ADJ #00000011 Mailroom Dt: 08/14/2013
Seq No: 6223 Sales Acctg Dt: 08/15/2013 010885 13967179
08 FC : 1808 130.00 CR

PTO/SB/06 (09-11)
Approved for use through 1/31/2014. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
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.

PATENT APPLICATION FEE DETERMINATION RECORD Substitute for Form PTO-875	Application or Docket Number 13/967,179	Filing Date 08/14/2013	☐ To be Mailed

ENTITY: ☒ LARGE ☐ SMALL ☐ MICRO

APPLICATION AS FILED – PART I

FOR	(Column 1) NUMBER FILED	(Column 2) NUMBER EXTRA	RATE ($)	FEE ($)
☐ BASIC FEE (37 CFR 1.16(a), (b), or (c))	N/A	N/A	N/A	
☐ SEARCH FEE (37 CFR 1.16(k), (i), or (m))	N/A	N/A	N/A	
☐ EXAMINATION FEE (37 CFR 1.16(o), (p), or (q))	N/A	N/A	N/A	
TOTAL CLAIMS (37 CFR 1.16(i))	minus 20 =	*	X $ =	
INDEPENDENT CLAIMS (37 CFR 1.16(h))	minus 3 =	*	X $ =	
☐ APPLICATION SIZE FEE (37 CFR 1.16(s))	If the specification and drawings exceed 100 sheets of paper, the application size fee due is $310 ($155 for small entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(s).			
☐ MULTIPLE DEPENDENT CLAIM PRESENT (37 CFR 1.16(j))				
* If the difference in column 1 is less than zero, enter "0" in column 2.			TOTAL	

APPLICATION AS AMENDED – PART II

AMENDMENT 08/14/2013

	(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA	RATE ($)	ADDITIONAL FEE ($)
Total (37 CFR 1.16(i))	* 25	Minus	** 25	= 0	X $80 =	0
Independent (37 CFR 1.16(h))	* 3	Minus	***3	= 0	X $420 =	0
☐ Application Size Fee (37 CFR 1.16(s))						
☐ FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))						
					TOTAL ADD'L FEE	0

AMENDMENT

	(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA	RATE ($)	ADDITIONAL FEE ($)
Total (37 CFR 1.16(i))	*	Minus	**	=	X $ =	
Independent (37 CFR 1.16(h))	*	Minus	***	=	X $ =	
☐ Application Size Fee (37 CFR 1.16(s))						
☐ FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))						
					TOTAL ADD'L FEE	

* If the entry in column 1 is less than the entry in column 2, write "0" in column 3.
** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 20, enter "20".
*** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 3, enter "3".
The "Highest Number Previously Paid For" (Total or Independent) is the highest number found in the appropriate box in column 1.

LIE
/RAMONA WILSON/

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	GRP ART UNIT	FIL FEE REC'D	ATTY.DOCKET.NO	TOT CLAIMS	IND CLAIMS
13/967,179	08/14/2013	1653	2300	17618CON5B (AP)	25	3

CONFIRMATION NO. 8654

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

FILING RECEIPT

OC000000063591965

Date Mailed: 09/09/2013

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)

Andrew Acheampong, Irvine, CA;
Diane D. Tang-Liu, Las Vegas, NV;
James N. Chang, Newport Beach, CA;
David F. Power, Hubert, NC;

Applicant(s)

Allergan, Inc., Irvine, CA

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 13/961,818 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.

Permission to Access - A proper **Authorization to Permit Access to Application by Participating Offices** (PTO/SB/39 or its equivalent) has been received by the USPTO.

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 13/967,179**

Projected Publication Date: 12/19/2013

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

PROTECTING YOUR INVENTION OUTSIDE THE UNITED STATES

Since the rights granted by a U.S. patent extend only throughout the territory of the United States and have no effect in a foreign country, an inventor who wishes patent protection in another country must apply for a patent in a specific country or in regional patent offices. Applicants may wish to consider the filing of an international application under the Patent Cooperation Treaty (PCT). An international (PCT) application generally has the same effect as a regular national patent application in each PCT-member country. The PCT process **simplifies** the filing of patent applications on the same invention in member countries, but **does not result** in a grant of "an international patent" and does not eliminate the need of applicants to file additional documents and fees in countries where patent protection is desired.

Almost every country has its own patent law, and a person desiring a patent in a particular country must make an application for patent in that country in accordance with its particular laws. Since the laws of many countries differ in various respects from the patent law of the United States, applicants are advised to seek guidance from specific foreign countries to ensure that patent rights are not lost prematurely.

Applicants also are advised that in the case of inventions made in the United States, the Director of the USPTO must issue a license before applicants can apply for a patent in a foreign country. The filing of a U.S. patent application serves as a request for a foreign filing license. The application's filing receipt contains further information and guidance as to the status of applicant's license for foreign filing.

Applicants may wish to consult the USPTO booklet, "General Information Concerning Patents" (specifically, the section entitled "Treaties and Foreign Patents") for more information on timeframes and deadlines for filing foreign patent applications. The guide is available either by contacting the USPTO Contact Center at 800-786-9199, or it can be viewed on the USPTO website at http://www.uspto.gov/web/offices/pac/doc/general/index.html.

For information on preventing theft of your intellectual property (patents, trademarks and copyrights), you may wish to consult the U.S. Government website, http://www.stopfakes.gov. Part of a Department of Commerce initiative, this website includes self-help "toolkits" giving innovators guidance on how to protect intellectual property in specific countries such as China, Korea and Mexico. For questions regarding patent enforcement issues, applicants may call the U.S. Government hotline at 1-866-999-HALT (1-866-999-4258).

LICENSE FOR FOREIGN FILING UNDER

Title 35, United States Code, Section 184

Title 37, Code of Federal Regulations, 5.11 & 5.15

GRANTED

The applicant has been granted a license under 35 U.S.C. 184, if the phrase "IF REQUIRED, FOREIGN FILING LICENSE GRANTED" followed by a date appears on this form. Such licenses are issued in all applications where the conditions for issuance of a license have been met, regardless of whether or not a license may be required as set forth in 37 CFR 5.15. The scope and limitations of this license are set forth in 37 CFR 5.15(a) unless an earlier license has been issued under 37 CFR 5.15(b). The license is subject to revocation upon written notification. The date indicated is the effective date of the license, unless an earlier license of similar scope has been granted under 37 CFR 5.13 or 5.14.

This license is to be retained by the licensee and may be used at any time on or after the effective date thereof unless it is revoked. This license is automatically transferred to any related applications(s) filed under 37 CFR 1.53(d). This license is not retroactive.

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 AssetsControl, 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).

PATENT APPLICATION FEE DETERMINATION RECORD

Substitute for Form PTO-875

Application or Docket Number: 13/967,179

APPLICATION AS FILED - PART I

FOR	(Column 1) NUMBER FILED	(Column 2) NUMBER EXTRA	SMALL ENTITY RATE($)	SMALL ENTITY FEE($)	OR	OTHER THAN SMALL ENTITY RATE($)	OTHER THAN SMALL ENTITY FEE($)
BASIC FEE (37 CFR 1.16(a), (b), or (c))	N/A	N/A	N/A			N/A	280
SEARCH FEE (37 CFR 1.16(k), (i), or (m))	N/A	N/A	N/A			N/A	600
EXAMINATION FEE (37 CFR 1.16(o), (p), or (q))	N/A	N/A	N/A			N/A	720
TOTAL CLAIMS (37 CFR 1.16(i))	25 minus 20 =	* 5			OR	x 80 =	400
INDEPENDENT CLAIMS (37 CFR 1.16(h))	3 minus 3 =	*				x 420 =	0.00
APPLICATION SIZE FEE (37 CFR 1.16(s))	If the specification and drawings exceed 100 sheets of paper, the application size fee due is $310 ($155 for small entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(s).						0.00
MULTIPLE DEPENDENT CLAIM PRESENT (37 CFR 1.16(j))							0.00
* If the difference in column 1 is less than zero, enter "0" in column 2.			TOTAL			TOTAL	2000

APPLICATION AS AMENDED - PART II

		(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA	SMALL ENTITY RATE($)	SMALL ENTITY ADDITIONAL FEE($)	OR	OTHER THAN SMALL ENTITY RATE($)	OTHER THAN SMALL ENTITY ADDITIONAL FEE($)
AMENDMENT A	Total (37 CFR 1.16(i))	*	Minus	**	=	x =		OR	x =	
	Independent (37 CFR 1.16(h))	*	Minus	***	=	x =		OR	x =	
	Application Size Fee (37 CFR 1.16(s))									
	FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))							OR		
						TOTAL ADD'L FEE		OR	TOTAL ADD'L FEE	

		(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA	SMALL ENTITY RATE($)	SMALL ENTITY ADDITIONAL FEE($)	OR	OTHER THAN SMALL ENTITY RATE($)	OTHER THAN SMALL ENTITY ADDITIONAL FEE($)
AMENDMENT B	Total (37 CFR 1.16(i))	*	Minus	**	=	x =		OR	x =	
	Independent (37 CFR 1.16(h))	*	Minus	***	=	x =		OR	x =	
	Application Size Fee (37 CFR 1.16(s))									
	FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))							OR		
						TOTAL ADD'L FEE		OR	TOTAL ADD'L FEE	

* If the entry in column 1 is less than the entry in column 2, write "0" in column 3.

** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 20, enter "20".

*** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 3, enter "3".

The "Highest Number Previously Paid For" (Total or Independent) is the highest found in the appropriate box in column 1.

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
13/967,179	08/14/2013	Andrew Acheampong	17618CON5B (AP)

CONFIRMATION NO. 8654

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

POA ACCEPTANCE LETTER

OC000000063515649

Date Mailed: 09/09/2013

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.

/dberios/

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

Doc code: IDS
Doc description: Information Disclosure Statement (IDS) Filed

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (**Not for submission under 37 CFR 1.99)**		
	Application Number	13967179
	Filing Date	2013-08-14
	First Named Inventor	ACHEAMPONG, ANDREW
	Art Unit	1653
	Examiner Name	TBD
	Attorney Docket Number	17618-US-BCON5-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	Delevallee 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 STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	13967179
	Filing Date	2013-08-14
	First Named Inventor	ACHEAMPONG, ANDREW
	Art Unit	1653
	Examiner Name	TBD
	Attorney Docket Number	17618-US-BCON5-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	

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	13967179
	Filing Date	2013-08-14
	First Named Inventor	ACHEAMPONG, ANDREW
	Art Unit	1653
	Examiner Name	TBD
	Attorney Docket Number	17618-US-BCON5-AP

	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	

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	13967179
	Filing Date	2013-08-14
	First Named Inventor	ACHEAMPONG, ANDREW
	Art Unit	1653
	Examiner Name	TBD
	Attorney Docket Number	17618-US-BCON5-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	

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	13967179
	Filing Date	2013-08-14
	First Named Inventor	ACHEAMPONG, ANDREW
	Art Unit	1653
	Examiner Name	TBD
	Attorney Docket Number	17618-US-BCON5-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	

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	13967179
	Filing Date	2013-08-14
	First Named Inventor	ACHEAMPONG, ANDREW
	Art Unit	1653
	Examiner Name	TBD
	Attorney Docket Number	17618-US-BCON5-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	

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	13967179
	Filing Date	2013-08-14
	First Named Inventor	ACHEAMPONG, ANDREW
	Art Unit	1653
	Examiner Name	TBD
	Attorney Docket Number	17618-US-BCON5-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	

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	13967179
	Filing Date	2013-08-14
	First Named Inventor	ACHEAMPONG, ANDREW
	Art Unit	1653
	Examiner Name	TBD
	Attorney Docket Number	17618-US-BCON5-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	Olejnik et al	
	84	6569463		2003-03-27	Patel et al	
	85	6582718		2003-06-24	Yoichi Kawashima	

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	13967179
	Filing Date	2013-08-14
	First Named Inventor	ACHEAMPONG, ANDREW
	Art Unit	1653
	Examiner Name	TBD
	Attorney Docket Number	17618-US-BCON5-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

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	13967179
	Filing Date	2013-08-14
	First Named Inventor	ACHEAMPONG, ANDREW
	Art Unit	1653
	Examiner Name	TBD
	Attorney Docket Number	17618-US-BCON5-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 STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	13967179
	Filing Date	2013-08-14
	First Named Inventor	ACHEAMPONG, ANDREW
	Art Unit	1653
	Examiner Name	TBD
	Attorney Docket Number	17618-US-BCON5-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)		
	Application Number	13967179
	Filing Date	2013-08-14
	First Named Inventor	ACHEAMPONG, ANDREW
	Art Unit	1653
	Examiner Name	TBD
	Attorney Docket Number	17618-US-BCON5-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**

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	13967179
	Filing Date	2013-08-14
	First Named Inventor	ACHEAMPONG, ANDREW
	Art Unit	1653
	Examiner Name	TBD
	Attorney Docket Number	17618-US-BCON5-AP

	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**
	43	20130059796		2013-03-07	Chang et al	U.S. Application No. 13/649,287 and its entire prosecution history**

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

FOREIGN PATENT DOCUMENTS

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(**Not for submission under 37 CFR 1.99)**

Application Number	13967179
Filing Date	2013-08-14
First Named Inventor	ACHEAMPONG, ANDREW
Art Unit	1653
Examiner Name	TBD
Attorney Docket Number	17618-US-BCON5-AP

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		☐
	2	0471293	EP		1992-02-19	ABBOTT LABORATORIES		☐
	3	0547229	EP		1993-01-07	LLT Institute Co., Ltd.		☐
	4	0760237	EP		1997-03-05	Cipla Limited		☐
	5	1995-031211	WO		1995-11-23	Allergan Inc.		☐
	6	2000-000179	WO		2000-01-06	Won Jin Biopharma Co., Ltd		☐
	7	2001-032142	WO		2001-05-10	Cipla Limited		☐
	8	2001-041671	WO		2001-06-14	Transneuronix, Inc.		☐
	9	2002-009667	WO		2002-02-07	Pharmasol GMBH		☐
	10	2002-049603	WO		2002-06-27	LG Household & Health Care Ltd.		☐

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	13967179
	Filing Date	2013-08-14
	First Named Inventor	ACHEAMPONG, ANDREW
	Art Unit	1653
	Examiner Name	TBD
	Attorney Docket Number	17618-US-BCON5-AP

	11	2003-030834	WO		2003-04-17	Enanta Pharmaceuticals, Inc.		☐
	12	2003-053405	WO		2003-07-03	Yissum Research Development Company of the Hebrew		☐

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]
	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)	☐
	2	ACHEAMPONG, ANDREW ET AL, Cyclosporine Distribution into the Conjunctiva, Cornea, Lacrimal Gland and Systemic Blood Following Topical Dosing of Cyclosporine to Rabbit, Dog and Human eyes, 1996, 179	☐
	3	ACHEAMPONG, ANDREW ET AL, Cyclosporine Distribution Into The Conjunctiva, Cornea, Lacrimal Gland, and Systemic Blood Following Topical Dosing of Cyclosporine to Rabbit, Dog, and Human Eyes, Adv. Exp. Med. Biol., 1998, 1001-1004, 438	☐
	4	ACHEAMPONG, ANDREW ET AL, Distribution of Cyclosporin A in Ocular Tissues After Topical Administration to Albino Rabbits and Beagle Dogs, Current Eye Research, 1999, 91-103, 18(2)	☐
	5	AKPEK, ESEN KARAMURSEL ET AL, A Randomized Trial of Topical Cyclosporin 0.05% in Topical Steroid-Resistant Atopic Keratoconjunctivitis, Ophthalmology, 2004, 476-482, 111	☐
	6	ANGELOV, O. ET AL, Preclinical Safety Studies of Cyclosporine Ophthalmic Emulsion, Adv Exp Med Biol, 1998, 991-995, 438	☐
	7	ANGELOV, O. ET AL, Safety Assessment of Cyclosporine Ophthalmic Emulsion in Rabbits and Dogs, XIth Congress of the European Society of Ophthalmology, 1997, 25-28, 1-5, Soc. Ophthalmol Eur., HU	☐

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	13967179
	Filing Date	2013-08-14
	First Named Inventor	ACHEAMPONG, ANDREW
	Art Unit	1653
	Examiner Name	TBD
	Attorney Docket Number	17618-US-BCON5-AP

	8	ARDIZZONE, SANDRO ET AL, A Practical Guide to the Management of Distal Ulcerative Colitis, Drugs, 1998, 519-542, 55(4)	☐
	9	BANIC, MARKO ET AL, Effect of Cyclosporine in a Murine Model of Experimental Colitis, Digestive Diseases and Sciences, June 2002, 1362-1368, 47(6)	☐
	10	BONINI, S. ET AL, Vernal Keratoconjunctivitis, Eye, 2004, 345-351, 18	☐
	11	BREWSTER, MARCUS ET AL, Enhanced Delivery of Ganciclovir to the Brain Through the Use of Redox Targeting, Antimicrobial Agents and Chemotherapy, Apr 1994, 817-823, 38(4)	☐
	12	BREWSTER, MARCUS ET AL, Intravenous and Oral Pharmacokinetic Evaluation of a 2-Hydroxypropyl-ß-cyclodextrin-Based Formulation of Carbamazepine in the Dog: Comparison with Commercially Available Tablets and Suspensions, Journal of Pharmaceutical Sciences, March 1997, 335-339, 86(3)	☐
	13	BREWSTER, MARCUS ET AL, Preparation, Characterization, and Anesthetic Properties of 2-Hydroxypropyl-ß-cyclodextrin Complexes of Pregnanolone and Pregnenolone in Rat and Mouse, Journal of Pharmaceutical Sciences, October 1995, 1154-1159, 84(10)	☐
	14	BRINKMEIER, THOMAS ET AL, Pyodermatitis-Pyostomatitis Vegetans: A Clinical Course of Two Decades with Response to Cyclosporine and Low-Dose Prednisolone, Acta Derm Venereol, 2001, 134-136, 81	☐
	15	CASTILLO, JOSE M. BENITEZ DEL ET AL, Influence of Topical Cyclosporine A and Dissolvent on Corneal Epithelium Permeability of Fluorescein, Documenta Ophthalmologica, 1995, 49-55, 91	☐
	16	CHEEKS, LISA ET AL, Influence of Vehicle and Anterior Chamber Protein Concentration on Cyclosporine Penetration Through the Isolated Rabbit Cornea, Current Eye Research, 1992, 641-649, 11(7)	☐
	17	Database WPI Week 200044, Derwent Pub. Ltd., London, GB; An 2000-492678 & JP2000/143542, 2000, 2 Pages	☐
	18	DING, SHULIN ET AL, Cyclosporine Ophthalmic O/W emulsion: Formulation and Emulsion Characterization, Pharm Res, 1997, 1 page, 14 (11)	☐

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	13967179
	Filing Date	2013-08-14
	First Named Inventor	ACHEAMPONG, ANDREW
	Art Unit	1653
	Examiner Name	TBD
	Attorney Docket Number	17618-US-BCON5-AP

	19	DONNENFELD, ERIC D., The Economics Of Using Restasis, Ophthalmology Management, 10/2003, 3 pages, US	☐
	20	DROSOS, A. A. ET AL, Efficacy and Safety of Cyclosporine-A Therapy for Primary Sjogren's Syndrome, Ter. Arkh., 1998, 77-80, 60(4)	☐
	21	DROSOS, A.A. ET AL, Cyclosporin A Therapy in Patients with Primary Sjogren's Syndrome: Results at One Year, Scand J Rheumatology, 1986, 246-249, 61	☐
	22	EISEN, DRORE ET AL, Topical Cyclosporine for Oral Mucosal Disorders, J Am Acad Dermatol, Dec. 1990, 1259-1264, 23	☐
	23	EPSTEIN, JOEL ET AL, Topical Cyclosporine in a Bioadhesive for Treatment of Oral Lichenoid Muscosal Reactions, Oral Surg Oral Med Oral Pathol Oral, 1996, 532-536, 82	☐
	24	ERDMANN, S. ET AL, Pemphigus Vulgaris Der Mund- Und Kehlkopfschleimhaut Pemphigus Vulgaris of the Oral Mucosa and the Larynx, H+G Zeitschrift Fuer Hautkrankheiten, 1997, 283-286, 72(4)	☐
	25	FDA Concludes Restasis (Cyclosporine) Not Effective for Dry Eye (6/18/1999). Accessed online at http://www.dryeyeinfo.org/Restasis_Cyclosporine.htm on 8/14/09. 1 Page	☐
	26	GAETA, G.M. ET AL, Cyclosporin Bioadhesive Gel in the Topical Treatment of Erosive Oral Lichen Planus, International Journal of Immunopathology and Pharmacology, 1994, 125-132, 7(2)	☐
	27	GIPSON, ILENE ET AL, Character of Ocular Surface Mucins and Their Alteration in Dry Eye Disease, The Ocular Surface, April 2004, 131-148, 2(2)	☐
	28	GREMSE, DAVID ET AL, Ulcerative Colitis in Children, Pediatr Drugs, 2002, 807-815, 4(12)	☐
	29	GUNDUZ, KAAN ET AL, Topical Cyclosporin Treatment of Keratoconjunctivitis Sicca in Secondary Sjogren's Syndrome, Acta Ophthalmologica, 1994, 438-442, 72	☐

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	13967179
	Filing Date	2013-08-14
	First Named Inventor	ACHEAMPONG, ANDREW
	Art Unit	1653
	Examiner Name	TBD
	Attorney Docket Number	17618-US-BCON5-AP

	30	http://web.archive.org/web/2001030625323/http://www.surfactant.co.kr/surfactants/pegester.html, 2001, 6 Pages, retrieved on 7/05/2008	☐
	31	HUNTER, P.A. ET AL, Cyclosporin A Applied Topically to the Recipient Eye Inhibits Corneal Graft Rejection, Clin Exp Immunol, 1981, 173-177, 45	☐
	32	JUMAA, MUHANNAD ET AL, Physicochemical Properties and Hemolytic Effect of Different Lipid Emulsion Formulations Using a Mixture of Emulsifiers, Pharmaceutica Acta Helvetiae, 1999, 293-301, 73	☐
	33	KANAI, A. ET AL, The Effect on the Cornea of Alpha Cyclodextrin Vehicle for Eye Drops, Transplantation Proceedings, Febraury 1989, 3150-3152, Vol. 21	☐
	34	KANPOLAT, AYFER ET AL, Penetration of Cyclosporin A into the Rabbit Cornea and Aqueous Humor after Topical Drop and Collagen Shield Administration, Cornea/External Disease, April 1994, 119-122, 20(2)	☐
	35	KAUR, RABINDER ET AL, Solid Dispersions of Drugs in Polyocyethylene 40 Stearate: Dissolution Rates and Physico-Chemical Interactions, Journal of Pharmacy and Pharmacology, December 1979, 48P	☐
	36	KUWANO, MITSUAKI ET AL, Cyclosporine A Formulation Affects Its Ocular Distribution in Rabbits, Pharmaceutical Research, January 2002, 108-111, 19(1)	☐
	37	Lambert Technologies Corp. Material Safety Data Sheet for LUMULSE ™ POE-40 MS KP, last revision 8/22/2003. 3 pages	☐
	38	LEIBOVITZ, Z. ET AL., Our Experience In Processing Maize (Corn) Germ Oil, Journal Of The American Oil Chemists Society, 02/1983, 395-399, 80 (2), US	☐
	39	LIXIN, XIE ET AL, Effect Of Cyclosporine A Delivery System in Corneal Transplantation, Chinese Medical Journal, 2002, 110-113, 115 (1), US	☐
	40	LOPATIN, D.E., Chemical Compositions and Functions of Saliva, 8/24/2001, 31 Pages	☐

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	13967179
	Filing Date	2013-08-14
	First Named Inventor	ACHEAMPONG, ANDREW
	Art Unit	1653
	Examiner Name	TBD
	Attorney Docket Number	17618-US-BCON5-AP

	41	LYONS, R.T. ET AL, Influence of Three Emulsion Formulation Parameters on the Ocular Bioavailability of Cyclosporine A in Albino Rabbits, Am Assoc Pharm Sci, 2000, 1 Page, 2(4)	☐
	42	PEDERSEN, ANNE MARIE ET AL, Primary Sjogren's Syndrome: Oral Aspects on Pathogenesis, Diagnostic Criteria, Clinical Features and Approaches for Therapy, Expert Opin Pharma, 2001, 1415-1436, 2(9)	☐
	43	PHILLIPS, THOMAS ET AL, Cyclosporine Has a Direct Effect on the Differentiation of a Mucin-Secreting Cell Line, Journal of Cellular Physiology, 2000, 400-408, 184	☐
	44	PRESENT, D.H. ET AL, Cyclosporine and Other Immunosuppressive Agents: Current and Future Role in the Treatment of Inflammatory Bowel Disease, American Journal of Gastroenterology, 1993, 627-630, 88(5)	☐
	45	Restasis ® Product Information Sheet, Allergan, Inc., 2009, 5 Pages	☐
	46	Restasis® Increasing Tear Production, Retrieved on 08/14/2009, http://www.restasisprofessional.com/_clinical/clinical_increasing.htm 3 pages	☐
	47	ROBINSON, N.A. ET AL, Desquamative Gingivitis: A Sign of Mucocutaneous Disorders - a Review, Australian Dental Journal, 2003, 205-211, 48(4)	☐
	48	RUDINGER, J., Characteristics of the Amino Acids as Components of a Peptide Hormone Sequence, Peptide Hormones, 1976, 1-7	☐
	49	SALL, KENNETH ET AL, Two Multicenter, Randomized Studies of the Efficacy and Safety of Cyclosporine Ophthalmic Emulsion in Moderate to Severe Dry Eye Disease, Ophthalmology, 2000, 631-639, 107	☐
	50	SANDBORN, WILLIAM ET AL, A Placebo-Controlled Trial of Cyclosporine Enemas for Mildly to Moderately Active Left-Sided Ulcerative Colitis, Gastroenterology, 1994, 1429-1435, 106	☐
	51	SANDBORN, WILLIAM ET AL, Cyclosporine Enemas for Treatment-Resistant, Mildly to Moderately Active, Left-Sided Ulcerative Colitis, American Journal of Gastroenterology, 1993, 640-645, 88(5)	☐

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	13967179
	Filing Date	2013-08-14
	First Named Inventor	ACHEAMPONG, ANDREW
	Art Unit	1653
	Examiner Name	TBD
	Attorney Docket Number	17618-US-BCON5-AP

	52	SCHWAB, MATTHIAS ET AL, Pharmacokinetic Considerations in the Treatment of Inflammatory Bowel Disease, Clin Pharm, 2001, 723-751, 60(10)	☐
	53	SECCHI, ANTONIO ET AL, Topical Use of Cyclosporine in the Treatment of Vernal Keratoconjunctivitis, American Journal of Ophthalmology, December 1990, 641-645, 110	☐
	54	SMALL, DAVE ET AL, The Ocular Pharmacokinetics of Cyclosporine in Albino Rabbits and Beagle Dogs, Ocular Drug Delivery and Metabolism, 1999, 54	☐
	55	SMALL, DAVID ET AL, Blood Concentrations of Cyclosporin A During Long-Term Treatment With Cyclosporin A ophthalmic Emulsions in Patients with Moderate to Severe Dry Eye Disease, Journal of Ocular Pharmacology and Therapeutics, 2002, 411-418, 18(5)	☐
	56	SMILEK, DAWN ET AL, A Single Amino Acid Change in a Myelin Basic Protein Peptide Confers the Capacity to Prevent Rather Than Induce Experimental Autoimmune Encephalomyelitis, Proc. Natl. Acad. Sci., Nov 1991, 9633-9637, 88	☐
	57	STEPHENSON, MICHELLE, The Latest Uses Of Restasis, Review Of Ophthalmology, 12/30/2005, 7 Pages, US	☐
	58	STEVENSON, DARA ET AL, Efficacy and Safety of Cyclosporin A ophthalmic Emulsion in the Treatment of Moderate-to-Severe Dry Eye Disease, Ophthalmology, 2000, 967-974, 107	☐
	59	TESAVIBUL, N. ET AL, Topical Cyclosporine A (CsA) for Ocular Surface Abnormalities in Graft Versus Host Disease Patients, Invest Ophthalmol Vis Sci, Feb 1996, S1026, 37(3)	☐
	60	The Online Medical Dictionary, Derivative, Analog, Analogue, Xerostomia, accessed 7/7/2005 and 7/13/2005, 6 Pages	☐
	61	TIBELL, A. ET AL., Cyclosporin A In Fat Emulsion Carriers: Experimental Studies On Pharmacokinetics And Tissue Distribution, Pharmacology & Toxicology, 1995, 115-121, 76, US	☐
	62	TSUBOTA, KAZUO ET AL, Use of Topical Cyclosporin A in a Primary Sjogren's Syndrome Mouse Model, Invest Ophthalmol Vis Sci, Aug. 1998, 1551-1559, 39(9)	☐

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	13967179
	Filing Date	2013-08-14
	First Named Inventor	ACHEAMPONG, ANDREW
	Art Unit	1653
	Examiner Name	TBD
	Attorney Docket Number	17618-US-BCON5-AP

	63	VAN DER REIJDEN, WILLY ET AL, Treatment of Oral Dryness Related Complaints (Xerostomia) in Sjogren's Syndrome, Ann Rheum Dis, 1999, 465-473, 58	☐
	64	WINTER, T.A. ET AL, Cyclosporin A Retention Enemas in Refractory Distal Ulcerative Colitis and 'Pouchitis', Scand J Gastroenterol, 1993, 701-704, 28	☐
	65	U.S. Pending Application: 13/967,189 Filed on August 14, 2013	☐
	66	U.S. Pending Application: 13/961,818 Filed on August 07, 2013	☐
	67	U.S. Pending Application: 13/961,828 Filed on August 07, 2013	☐
	68	U.S. Pending Application: 13/961,835 Filed on August 07, 2013	☐
	69	U.S. Pending Application: 13/961,808 Filed on August 07, 2013	☐
	70	U.S. Pending Application: 13/967,163 Filed on August 14, 2013	☐
	71	U.S. Pending Application: 13/967,168 Filed on August 14, 2013	☐
	72	U.S. Re-Examination Application: 90/009,944 Filed on August, 27, 2011	☐

If you wish to add additional non-patent literature document citation information please click the Add button

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (**Not for submission under 37 CFR 1.99)**		
	Application Number	13967179
	Filing Date	2013-08-14
	First Named Inventor	ACHEAMPONG, ANDREW
	Art Unit	1653
	Examiner Name	TBD
	Attorney Docket Number	17618-US-BCON5-AP

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	13967179
Filing Date	2013-08-14
First Named Inventor	ACHEAMPONG, ANDREW
Art Unit	1653
Examiner Name	TBD
Attorney Docket Number	17618-US-BCON5-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)	2013-09-11
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 record s.

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:	16830205
Application Number:	13967179
International Application Number:	
Confirmation Number:	8654
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:	17618CON5B (AP)
Receipt Date:	11-SEP-2013
Filing Date:	14-AUG-2013
Time Stamp:	21:04:32
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	no

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)	17618CON5B-IDS_09_11_2013.pdf	541587 b802daf71f3dacee0e7d8f97db3023f9a6e5b875	no	24

Warnings:	
Information:	

This is not an USPTO supplied IDS fillable form					
2	Foreign Reference	DE19810655A1.pdf	642493 a134d524e4c7505c5732a8cab9f7ff85e484f7b9	no	6
Warnings:					
Information:					
3	Foreign Reference	EP-0471293.pdf	1658633 f4204d9aae9add3360e71d625b87af99e5fcbb41	no	7
Warnings:					
Information:					
4	Foreign Reference	EP-0547229.pdf	8161789 81ccdbb5d595b1c2a663b402f22b952405b3ade6	no	17
Warnings:					
Information:					
5	Foreign Reference	EP-0760237.PDF	364223 11ca6edfbedb8a6c1f617c247c539021b6d7c292	no	11
Warnings:					
Information:					
6	Foreign Reference	WO-1995-031211.pdf	609318 785816ee787dd5564887887c172789c0434e5316	no	28
Warnings:					
Information:					
7	Foreign Reference	WO2000-000179.pdf	1156948 9ccd79b7e6bf89086a66181561ecf369d4c6df5a	no	67
Warnings:					
Information:					
8	Foreign Reference	WO-2001-032142.pdf	393715 2363e2b822d3076474c793023490c20efaf9c7fa	no	19
Warnings:					
Information:					
9	Foreign Reference	WO2001-041671.pdf	477723 a384ff47dd523974818c54030a51b37a8918ffbf	no	21
Warnings:					
Information:					
10	Foreign Reference	WO2002-009667.pdf	2610140 f18e7844afe73b52f294b3cde2c525461d8f6da8	no	47

Warnings:					
Information:					
11	Foreign Reference	WO2002-049603.pdf	540840 206d73970083fdb8f2793db01373453fd9928caf	no	25
Warnings:					
Information:					
12	Foreign Reference	WO2003-030834.pdf	884924 73f73deb9297abb6844121ece2cf99d1170cce48	no	36
Warnings:					
Information:					
13	Foreign Reference	WO2003-053405.pdf	495859 0d8699e29563ce29b3373ac58605c6958ccbbfb1	no	22
Warnings:					
Information:					
14	Non Patent Literature	Abdulrazik-2001.pdf	2020446 b968c117d8bcaecd650fd6654bae4ba3db2b0fef	no	6
Warnings:					
Information:					
15	Non Patent Literature	Acheampong-1996.pdf	77280 fdcc9ecdd28fa37ec7a80c28fe04a96b186308e3	no	1
Warnings:					
Information:					
16	Non Patent Literature	Acheampong-1998.pdf	143254 66c7df564002661f5af66d6c394f16f314f024f4	no	4
Warnings:					
Information:					
17	Non Patent Literature	Acheampong_1999.pdf	3760656 56867109cd7e843043e532d47d09b7e2ef238663	no	13
Warnings:					
Information:					
18	Non Patent Literature	AkpekOph111_3_476_482_2004.pdf	667675 749fbcc7440650cffe44ba25d09130c7ca7ffd2f	no	8
Warnings:					
Information:					
19	Non Patent Literature	Angelov-1998.pdf	747092 3babe85b48f13e0b436934e2fb66a6f224c2cb44	no	5

Warnings:					
Information:					
20	Non Patent Literature	AngelovSafetyAssessmentAN98071079_1997.pdf	214241 ae47dd3e3dccda539cebee3d5766073e8171482a	no	4
Warnings:					
Information:					
21	Non Patent Literature	ArdizzoneGBPoroDrugs519_542_1998.pdf	3937988 ddc7128be23a94fb204d5a5f13047aa0133a9a11	no	26
Warnings:					
Information:					
22	Non Patent Literature	BanicDigDisSci1362_1638_2002.pdf	848297 bd631465aef4a7f1f3f1660872a340421d06bd24	no	8
Warnings:					
Information:					
23	Non Patent Literature	Bonini_2004.pdf	2094249 9295f1e169d3ca4f4a97007838344654f73a0ab4	no	9
Warnings:					
Information:					
24	Non Patent Literature	Brewster_1994.pdf	2611645 f8dd875c527914d4d072c7d0b00c7c10c30e04b0	no	7
Warnings:					
Information:					
25	Non Patent Literature	Brewster_1997.pdf	2034358 c8c310235391b73a2515b79e5b7e69614cc154a1	no	5
Warnings:					
Information:					
26	Non Patent Literature	Brewster_1995.pdf	2435845 a87c613e9945ed2cb3e12ca36fc33523b6a62f2d	no	6
Warnings:					
Information:					
27	Non Patent Literature	Brinkmeier_PyodermatitisActa Derm_4_2001.pdf	462833 060bc24a76f2e8db058262428845c9fb8b9f914b	no	4
Warnings:					
Information:					
28	Non Patent Literature	Castillo_1995.pdf	2056885 f717067b8ac69bd61564f4dd29c6d1b10f5005d6	no	8

Warnings:					
Information:					
29	Non Patent Literature	CheeksInfluenceofVehicle1992.pdf	2450001 42b02fe1b3a1aac46ca35d929021b4907a8823ca	no	9
Warnings:					
Information:					
30	Non Patent Literature	Database_200044.pdf	76280 a1aa73b3e4580a5dbf752ca3d23b9aa23e0f0fb3	no	2
Warnings:					
Information:					
31	Non Patent Literature	DingPharmacAn98040585_1997.pdf	48725 0b046fb716cb7285c9f07c53e6595d8370eaaa2e	no	1
Warnings:					
Information:					
32	Non Patent Literature	Donnenfeld_2003.pdf	1514822 7a86cc202c471cce379f185113a1353747c98e63	no	3
Warnings:					
Information:					
33	Non Patent Literature	Drosos_1998.pdf	1638443 0e40d7b9b2ae76200baa9068530b5f21eefeaefb	no	5
Warnings:					
Information:					
34	Non Patent Literature	Drosos_1986.pdf	1032892 820c8e084c1b12333b1f635ec09c8afefd19579e	no	5
Warnings:					
Information:					
35	Non Patent Literature	EisenTopicalcyclosporine6_1990.pdf	752102 32ad87759ef79c77880006a594495cd6b992032d	no	6
Warnings:					
Information:					
36	Non Patent Literature	Epstein_1996.pdf	1582082 f316d19218cefdc0cca0e9be34264fe6f7503daa	no	5
Warnings:					
Information:					
37	Non Patent Literature	ErdmannMeetingattheDeptofDerm4_1997.pdf	462543 9f3fbb7197e803def6b46260fd835c5aaa5eef07	no	4

Warnings:					
Information:					
38	Non Patent Literature	FDA_Concludes_Restasis_1999.pdf	93984 63cff26925570cb091fa44ee5b19b28a3ff6ab6b	no	1
Warnings:					
Information:					
39	Non Patent Literature	Gaeta_1994.pdf	1817635 70f11e97d1851a46d0c18bb53f489f7f7ac5a37e	no	9
Warnings:					
Information:					
40	Non Patent Literature	Gipson_vol2no2_18_2004.pdf	2242587 0dc513ea67454195d9aef8bd3a8703267cb04156	no	18
Warnings:					
Information:					
41	Non Patent Literature	Gremse_UlcerativeColitis_in_Children10.pdf	1041954 091237aaaaa18ec3e0d7b0639e55086a00c290a2	no	10
Warnings:					
Information:					
42	Non Patent Literature	Gunduz_TopicalcyclosporinActaOphth6_1994.pdf	618144 4e3e7164d3de6e5be5691d0d7c6e8bc52a76e871	no	6
Warnings:					
Information:					
43	Non Patent Literature	Polyethylene_Glycol_Ester_2001.pdf	459916 86544da882fd05b2012425cb171c42eb144c32ab	no	6
Warnings:					
Information:					
44	Non Patent Literature	Hunter_1981.pdf	3004241 774fdd0660b54d79c4de0be05f7a3f8afdd571da	no	5
Warnings:					
Information:					
45	Non Patent Literature	Jumaa_1999.pdf	1946168 f50e943dc61513d9fed6651eee99968f6d36a553	no	9
Warnings:					
Information:					
46	Non Patent Literature	KanaiEffectontheCornea1989.pdf	868139 f60019d56376bcecff6bb85e0eb3238f954590b4	no	3

Warnings:					
Information:					
47	Non Patent Literature	KanpolatPenetrationofCyclosporin1994.pdf	359650 43be2c9cd6ba4e612554d7dd526b1e2b4f343b4e	no	4
Warnings:					
Information:					
48	Non Patent Literature	Kaur_1979.pdf	906300 496c705d93f0d7baa2424db48fbbf424512f96e6	no	2
Warnings:					
Information:					
49	Non Patent Literature	KuwanoCyclosporineA_Pharma19_1_108_111_2002.pdf	1878659 4e9a19149a7164165e1106060b80c8485b150be7	no	4
Warnings:					
Information:					
50	Non Patent Literature	Lambert_2003.pdf	460126 a4c43396f9847fb7308e6c0741e187941cd8aca8	no	3
Warnings:					
Information:					
51	Non Patent Literature	Leibovitz_1983.pdf	1024735 2c50222cc641655f84228b313ee6df845bcb2761	no	5
Warnings:					
Information:					
52	Non Patent Literature	Lixin_2002.pdf	1887719 6552422b21a2e5430452221f662f614d7560ede7	no	4
Warnings:					
Information:					
53	Non Patent Literature	LopatinChemicalcompositions31pgs2001.pdf	13079081 55c1ea8f4cfcf4343e8d36c01dadadf7516e0c55	no	31
Warnings:					
Information:					
54	Non Patent Literature	LyonsInfluenceofThreeEmulsion2000.pdf	59547 ea3c95c367170b2d95ca78b32f69875baf2a4c35	no	1
Warnings:					
Information:					
55	Non Patent Literature	PedersenExpertOpin1415_1436_2001.pdf	4262912 0ffbacdd587d316724d2c00a7e64fcdbc6ed49e4	no	22

Warnings:					
Information:					
56	Non Patent Literature	Phillips_CyclosporineJOCP1_2000.pdf	1385594 63acdf4c243d41621f7001e9c76dbf167d4ec51d	no	10
Warnings:					
Information:					
57	Non Patent Literature	Present_1993.pdf	1624134 baefc9d58e2e27ac5b6a99bd9151eb6a41e80d81	no	4
Warnings:					
Information:					
58	Non Patent Literature	RestasisProductInfoSheets.pdf	56377 844b6588f9ea989c6c37ffe4c0b220c950ffadea	no	5
Warnings:					
Information:					
59	Non Patent Literature	Restasis_Increasing_tear_Production_2009.pdf	332259 0a1285bcf642f927562ba180ba3ba5446eb2afe4	no	3
Warnings:					
Information:					
60	Non Patent Literature	Robinsonaustraliandentaljournal206_211_2003.pdf	768117 798558b0fd44a086f71fe1076b47333898b7e976	no	6
Warnings:					
Information:					
		Total Files Size (in bytes):	92386804		

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.

Electronic Acknowledgement Receipt

EFS ID:	16830268
Application Number:	13967179
International Application Number:	
Confirmation Number:	8654
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:	17618CON5B (AP)
Receipt Date:	11-SEP-2013
Filing Date:	14-AUG-2013
Time Stamp:	21:27:33
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	no

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Non Patent Literature	RudingerPeptideHormones1_7_1976.pdf	2488192 b6fc18b6ad98c34de41f2d461a1f5736500be985	no	11

Warnings:	
Information:	

2	Non Patent Literature	Sall_2000.pdf	208829 065c18613831a6d2cf5a88066e70ae03daae1b29	no	9
Warnings:					
Information:					
3	Non Patent Literature	SandbornGastroenterology1429_1435_1994.pdf	872000 730e8bcd0c58076ab6f0163f4551eff0f507e5c6	no	7
Warnings:					
Information:					
4	Non Patent Literature	Sandborn_1993.pdf	1969241 10802f861668ec206f085b7aa854a3b76526cf59	no	6
Warnings:					
Information:					
5	Non Patent Literature	SchwabPharmacokinet723_751_2001.pdf	4260474 decfedf8ccd3394e49e7e8a02f40d13d5023683f	no	30
Warnings:					
Information:					
6	Non Patent Literature	Secchi_1990.pdf	3200224 8a65624bb284fb7ad8fc4cc8ba5ee1a92ffe4b94	no	5
Warnings:					
Information:					
7	Non Patent Literature	Small_1999.pdf	166579 a6352b5109a02b19264b6b81164b62c48168e92f	no	1
Warnings:					
Information:					
8	Non Patent Literature	Small_2002.pdf	70523 777a603fb0b19562a66c525571b8108210c829a2	no	8
Warnings:					
Information:					
9	Non Patent Literature	Smilek_1991.pdf	1645292 a604ec7f03b90bf8fd3c8882dedce3c7b3fc802d	no	5
Warnings:					
Information:					
10	Non Patent Literature	Stephenson_The_latest_uses_of_Restasis.pdf	2875746 c5d5cdd66d2f333c39c173e5e665d5bacd00edad	no	7
Warnings:					
Information:					

11	Non Patent Literature	Stevenson_2000.pdf	255058 2f70a01929808bc46f5e822eb9cfcc28fcea7ab4	no	8
Warnings:					
Information:					
12	Non Patent Literature	TesavibulTopicalCyclosporine1996.pdf	56707 fc4bba0a0ffd0194e2146e1e1dbb52551410edeb	no	1
Warnings:					
Information:					
13	Non Patent Literature	Medical_Dictionary_2005.pdf	670357 2816eb8d1deb894d8911bacd15ed728364426c81	no	6
Warnings:					
Information:					
14	Non Patent Literature	Tibell_Cyclosporin_A_in_Fat_Emulsion_115_121_76.pdf	697241 5c1942bd49b4119100efa0409c42cda5c7182d19	no	7
Warnings:					
Information:					
15	Non Patent Literature	Tsubota_1998.pdf	2353818 f0929e8a59cf1006529e4db58b285eec963b5c0e	no	10
Warnings:					
Information:					
16	Non Patent Literature	Van_der_Reijden_1999.pdf	2709253 daff1e358e3501bdaae2d9ea3dbc422c6cdda1af	no	9
Warnings:					
Information:					
17	Non Patent Literature	Winter_1993.pdf	1231303 441701043d7f2a34aab980c3e2a2b0db53eb3d7f	no	4
Warnings:					
Information:					
18	Non Patent Literature	13967189.pdf	2596695 cc36a1673580aa9caaa9d65aa78f8267278ec4e3	no	34
Warnings:					
Information:					
19	Non Patent Literature	13961818.pdf	2596695 2646cb6a43b286789cda2d11e5189ca4a1ef6e93	no	34
Warnings:					
Information:					

20	Non Patent Literature	13961828.pdf	2596695 660e95b406b8f6ac91600605af4712d74c8677bb	no	34
Warnings:					
Information:					
21	Non Patent Literature	13961835.pdf	2596695 b413c7b00aa4d49d4ac9b55502711b44656b4027	no	34
Warnings:					
Information:					
22	Non Patent Literature	13961808.pdf	2596695 b8da58d00b60f65ec787da63f914356d1a9e5412	no	34
Warnings:					
Information:					
23	Non Patent Literature	13967163.pdf	2596695 597b1bba8cf47cb818eb51c45eca2e943c4b4463	no	34
Warnings:					
Information:					
24	Non Patent Literature	13967168.pdf	2596695 2244ea61fc0c84bfa743e5a148d34b2d6ba9564e	no	34
Warnings:					
Information:					
25	Non Patent Literature	90009944.pdf	1904560 4b5aa1ab68a1940d5930d4265e9053cf67203dc9	no	39
Warnings:					
Information:					
			Total Files Size (in bytes):	45812262	

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.

UNITED STATES PATENT AND TRADEMARK OFFICE

Commissioner for Patents
United States Patent and Trademark Office
P.O. Box 1450
Alexandria, VA 22313-1450
www.uspto.gov

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

MAILED
SEP 13 2013
OFFICE OF PETITIONS

Doc Code: TRACK1.GRANT

Decision Granting Request for Prioritized Examination (Track I or After RCE)	Application No.: 13/967,179

1. THE REQUEST FILED 8/14/13 IS **GRANTED**.

The above-identified application has met the requirements for prioritized examination

A. ☒ for an original nonprovisional application (Track I).
B. ☐ for an application undergoing continued examination (RCE).

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:

A. filing a **petition for extension of time** to extend the time period for filing a reply;
B. filing an **amendment to amend the application to contain more than four independent claims, more than thirty total claims**, or a multiple dependent claim;
C. filing a **request for continued examination**;
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.

Telephone inquiries with regard to this decision should be directed to Cheryl Gibson-Baylor at (571)272-3213, Office of Petitions. In his/her absence, calls may be directed to Brian W. Brown, (571)272-5338.

Cheryl Gibson-Baylor
/Cheryl Gibson-Baylor/
[*Signature*]

Petitions Paralegal Specialist
(Title)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Acheampong, *et al.*	Examiner: Marcela M. Cordero Garcia
Serial No.: 13/967,179	Group Art Unit: 1658
Filed: August 14, 2013	Confirmation No. 8654
For: METHODS OF PROVIDING THERAPEUTIC EFFECTS USING CYCLOSPORIN COMPONENTS	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:	17013211
Application Number:	13967179
International Application Number:	
Confirmation Number:	8654
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:	17618CON5B (AP)
Receipt Date:	01-OCT-2013
Filing Date:	14-AUG-2013
Time Stamp:	19:16:20
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	no

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Miscellaneous Incoming Letter	17618CON5B-Comm-Under-502.pdf	104507 27fabc7494c99d9559b63782512d870f9b2bc149	no	1

Warnings:	
Information:	

Total Files Size (in bytes):	104507

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.

Doc Code: DIST.E.FILE **Document Description: Electronic Terminal Disclaimer - Filed**	PTO/SB/25 U.S. Patent and Trademark Office Department of Commerce

Electronic Petition Request	**TERMINAL DISCLAIMER TO OBVIATE A PROVISIONAL DOUBLE PATENTING REJECTION OVER A PENDING "REFERENCE" APPLICATION**
Application Number	13967179
Filing Date	14-Aug-2013
First Named Inventor	Andrew Acheampong
Attorney Docket Number	17618CON5B (AP)
Title of Invention	METHODS OF PROVIDING THERAPEUTIC EFFECTS USING CYCLOSPORIN COMPONENTS

☒ Filing of terminal disclaimer does not obviate requirement for response under 37 CFR 1.111 to outstanding Office Action

☒ 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)

13967168 filed on 08/14/2013

13967163 filed on 08/14/2013

13967189 filed on 08/14/2013

13961835 filed on 08/07/2013

13961828 filed on 08/07/2013

13961818 filed on 08/07/2013

13961808 filed on 08/07/2013

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:	13967179
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:	17618CON5B (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**

Doc Code: DISQ.E.FILE
Document Description: Electronic Terminal Disclaimer – Approved

Application No.: 13967179

Filing Date: 14-Aug-2013

Applicant/Patent under Reexamination: Acheampong et al.

Electronic Terminal Disclaimer filed on October 7, 2013

☒ APPROVED

This patent is subject to a terminal disclaimer

☐ DISAPPROVED

Approved/Disapproved by: Electronic Terminal Disclaimer automatically approved by EFS-Web

U.S. Patent and Trademark Office

Electronic Acknowledgement Receipt

EFS ID:	17062332
Application Number:	13967179
International Application Number:	
Confirmation Number:	8654
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:	17618CON5B (AP)
Receipt Date:	07-OCT-2013
Filing Date:	14-AUG-2013
Time Stamp:	19:31:16
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	Deposit Account
Payment was successfully received in RAM	$160
RAM confirmation Number	5957
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	Electronic Terminal Disclaimer-Filed	eTerminal-Disclaimer.pdf	39374 c2c983bcfd82da71713f9bb87ed4f1942d41aac5	no	3
Warnings:					
Information:					
2	Fee Worksheet (SB06)	fee-info.pdf	30824 adc23204cfc3d33fde7f4b4c9e488e66842454fe	no	2
Warnings:					
Information:					
		Total Files Size (in bytes):	70198		

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.

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 NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
13/967,179	08/14/2013	Andrew Acheampong	17618CON5B (AP)	8654

51957 7590 10/11/2013

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

EXAMINER	
CORDERO GARCIA, MARCELA M	
ART UNIT	PAPER NUMBER
1658	

NOTIFICATION DATE	DELIVERY MODE
10/11/2013	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

Examiner-Initiated Interview Summary	Application No.	Applicant(s)	
	13/967,179	ACHEAMPONG ET AL.	
	Examiner	Art Unit	
	MARCELA M. CORDERO GARCIA	1658	

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

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

(2) *LAURA WINE*. (4)_____.

Date of Interview: *9/27/2013*.

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 60*.

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: It is not necessary for applicant to provide a separate record of the substance of 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

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

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 backroung 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 for a related case was provided to Applicant's representatives. .

Office Action Summary	Application No. 13/967,179	Applicant(s) ACHEAMPONG ET AL.	
	Examiner MARCELA M. CORDERO GARCIA	Art Unit 1658	AIA (First Inventor to File) Status No

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *8/14/2013*.

☐ A declaration(s)/affidavit(s) under **37 CFR 1.130(b)** was/were filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

4)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

5)☒ Claim(s) *37-61* is/are pending in the application.

5a) Of the above claim(s) _____ is/are withdrawn from consideration.

6)☐ Claim(s) _____ is/are allowed.

7)☒ Claim(s) *37-61* is/are rejected.

8)☐ Claim(s) _____ is/are objected to.

9)☐ Claim(s) _____ are subject to restriction and/or election requirement.

* If any claims have been determined allowable, you may be eligible to benefit from the **Patent Prosecution Highway** program at a participating intellectual property office for the corresponding application. For more information, please see http://www.uspto.gov/patents/init_events/pph/index.jsp or send an inquiry to PPHfeedback@uspto.gov.

Application Papers

10)☐ The specification is objected to by the Examiner.

11)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

Certified copies:

a)☐ All b)☐ Some * c)☐ None of the:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)

2) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/11/2013*.

3) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. *20131007*.

4) ☐ Other: _____.

DETAILED ACTION

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

Status of the claims

2. Claims 37-61 are pending in the application. Claims 37-61 are presented for examination on the merits.

Claim Rejections - 35 USC § 112

> 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 60 (and dependent claims thereof, i.e., 38-53, 55-59 and 61) 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 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 negatived by the manner in which the invention was made.

5. Claims 37-61 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), and a method comprising topically administering to the eye the human emulsion (see next page):

	Example 1				
	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

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 (and method thereof) 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). Furthermore, one of ordinary skill in the art would have been motivated to determine adequate daily frequency of administration in order to find suitable administration

regimes (e.g., twice a day.), one of ordinary skill in the art at the time the invention was made would have had reasonable expectation of success given that the 0.1% containing cyclosporin emulsion was effective in treating KCS (see Examples).

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”, “wherein the adverse events include side effects” and “wherein the emulsion is effective in increasing tear production in the human having KCS”, it is noted that such functional effects would necessarily flow

from the compositions of Ding et al. and methods thereof which comprise administration of all the claimed components and amounts in the claimed method, 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 37-61 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. The specification of Ding et al. was used as dictionary and it was determined that the compositions were used to treat dry eye (KCS) and that the compositions encompassed Examples 1A-E, wherein 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). Furthermore, one of ordinary skill in the art would have been motivated to determine adequate daily frequency of administration (e.g., once, twice, thrice, etc.) in order to find suitable administration regimes, one of ordinary skill in the art at the time the invention was made would have had reasonable expectation of success given that the 0.1% containing cyclosporin emulsion was effective in treating KCS (see Examples).

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", "wherein the adverse events include side effects" and "wherein the emulsion is effective in increasing tear production in the human having KCS"; it is noted that such functional effects would necessarily flow from the compositions and methods claimed and exemplified by Ding et al. which comprise all the claimed components, amounts and methods 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 37-61 are provisionally rejected on the ground of nonstatutory double patenting as being unpatentable over claims 37-60 of copending Application No. 13/961,168. Although the claims at issue are not identical, they are not patentably distinct from each other because US '168 is drawn to a method which encompasses a method comprising topically administering to the eye of the human in need thereof 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, acrylate/C10-30 alkyl acrylate cross-polymer, water and castor oil in an amount of about 1.25% by weight.

The other claims in US '168 are also drawn to the corresponding methods.

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

9. Claims 37-61 are provisionally rejected on the ground of nonstatutory double patenting as being unpatentable over claims 37-60 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 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.

The other claims in US '835 are also drawn to the corresponding methods.

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

10. Claims 37-61 are provisionally rejected on the ground of nonstatutory double patenting as being unpatentable over claims 37-61 of copending Application No. 13/967,163. Although the claims at issue are not identical, they are not patentably distinct from each other because US' 163 is drawn to an emulsion comprising 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 method of treating dry eye disease/increasing tear production (claim 37 of the instant application). The other claims in US '163 are also inherently drawn to the corresponding claimed methods. 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 37-61 are provisionally rejected on the ground of nonstatutory double patenting as being unpatentable over claims 37-61 of copending Application No. 13/961,828. Although the claims at issue are not identical, they are not patentably distinct from each other because US' 828 is drawn to an emulsion comprising 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 method of treating dry eye disease/increasing tear production (claim 37 of the instant application). The other claims in US '828 are also inherently drawn to the corresponding claimed methods. 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.

12. Claims 37-61 are provisionally rejected on the ground of nonstatutory double patenting as being unpatentable over claims 37-60 of copending Application No. 13/967,189. Although the claims at issue are not identical, they are not patentably distinct from each other because US' 189 is drawn to an emulsion comprising 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/increasing tear production. Thus, it inherently discloses a method of treating dry eye disease (claim 37 of the instant application). The other claims in US '189 are also inherently drawn to the corresponding claimed methods. 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.

13. Claims 37-61 are provisionally rejected on the ground of nonstatutory double patenting as being unpatentable over claims 37-60 of copending Application No. 13/961,808. Although the claims at issue are not identical, they are not patentably distinct from each other because US' 808 is drawn to an emulsion comprising 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 method of treating dry eye disease/increasing tear production (claim 37 of the instant application). The other claims in US '808 are also inherently drawn to the corresponding claimed methods. 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

14. 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.

15. Claims 37-61 are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 37-61 of copending Application No. 13/961,818. The claims are identical too each other, i.e., claim 37 in both applications are drawn to method of increasing tear production in the eye of a human, the method comprising topically administering to the eye of the human in need thereof 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, 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 effective in increasing tear production. The other claims in US '818 are identical to the corresponding claims in the instant invention.

This is a provisional statutory double patenting rejection since the claims directed to the same invention have not in fact been patented.

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 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

Examiner-Initiated Interview Summary	Application No.	Applicant(s)	
	13/967,179	ACHEAMPONG ET AL.	
	Examiner	Art Unit	
	MARCELA M. CORDERO GARCIA	1658	

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

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

(2) *LAURA WINE*. (4)_____.

Date of Interview: *9/27/2013*.

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 60*.

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: It is not necessary for applicant to provide a separate record of the substance of 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

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

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 backroung 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 for a related case was provided to Applicant's representatives. .

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**

Search Notes	Application/Control No.	Applicant(s)/Patent Under Reexamination
	13967179	ACHEAMPONG ET AL.
	Examiner	Art Unit
	MARCELA M CORDERO GARCIA	1658

CPC- SEARCHED		
Symbol	Date	Examiner

CPC COMBINATION SETS - SEARCHED		
Symbol	Date	Examiner

US CLASSIFICATION SEARCHED			
Class	Subclass	Date	Examiner
none	none	10/7/2013	MMCG

SEARCH NOTES		
Search Notes	Date	Examiner
STN search (attached)	10/7/2013	MMCG
EAST search (attached)	10/7/2013	MMCG
also ran PALM Inventor searchh	10/7/2013	MMCG

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

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (**Not for submission under 37 CFR 1.99)**		
	Application Number	13967179
	Filing Date	2013-08-14
	First Named Inventor	ACHEAMPONG, ANDREW
	Art Unit	1653
	Examiner Name	TBD
	Attorney Docket Number	17618-US-BCON5-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	Delevallee 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: 09/11/2013	Application Number	13967179 13967179 - GAU: 1658
INFORMATION DISCLOSURE STATEMENT BY APPLICANT (**Not for submission under 37 CFR 1.99)**	Filing Date	2013-08-14
	First Named Inventor	ACHEAMPONG, ANDREW
	Art Unit	1653
	Examiner Name	TBD
	Attorney Docket Number	17618-US-BCON5-AP

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

	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	

Receipt date: 09/11/2013	Application Number	13967179 13967179 - GAU: 1658
INFORMATION DISCLOSURE STATEMENT BY APPLICANT (**Not for submission under 37 CFR 1.99)**	Filing Date	2013-08-14
	First Named Inventor	ACHEAMPONG, ANDREW
	Art Unit	1653
	Examiner Name	TBD
	Attorney Docket Number	17618-US-BCON5-AP

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

	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	

Receipt date: 09/11/2013	Application Number	13967179 13967179 - GAU: 1658
INFORMATION DISCLOSURE STATEMENT BY APPLICANT (**Not for submission under 37 CFR 1.99)**	Filing Date	2013-08-14
	First Named Inventor	ACHEAMPONG, ANDREW
	Art Unit	1653
	Examiner Name	TBD
	Attorney Docket Number	17618-US-BCON5-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	

Receipt date: 09/11/2013

INFORMATION DISCLOSURE STATEMENT BY APPLICANT
(**Not for submission under 37 CFR 1.99)**

Application Number	13967179 13967179 - GAU: 1658
Filing Date	2013-08-14
First Named Inventor	ACHEAMPONG, ANDREW
Art Unit	1653
Examiner Name	TBD
Attorney Docket Number	17618-US-BCON5-AP

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

	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	

Receipt date: 09/11/2013

INFORMATION DISCLOSURE STATEMENT BY APPLICANT
(Not for submission under 37 CFR 1.99)

Application Number	13967179 13967179 - GAU: 1658
Filing Date	2013-08-14
First Named Inventor	ACHEAMPONG, ANDREW
Art Unit	1653
Examiner Name	TBD
Attorney Docket Number	17618-US-BCON5-AP

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	

Receipt date: 09/11/2013	Application Number	13967179 13967179 - GAU: 1658
INFORMATION DISCLOSURE STATEMENT BY APPLICANT (**Not for submission under 37 CFR 1.99)**	Filing Date	2013-08-14
	First Named Inventor	ACHEAMPONG, ANDREW
	Art Unit	1653
	Examiner Name	TBD
	Attorney Docket Number	17618-US-BCON5-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	

Receipt date: 09/11/2013	Application Number	13967179 13967179 - GAU: 1658
INFORMATION DISCLOSURE STATEMENT BY APPLICANT (**Not for submission under 37 CFR 1.99)**	Filing Date	2013-08-14
	First Named Inventor	ACHEAMPONG, ANDREW
	Art Unit	1653
	Examiner Name	TBD
	Attorney Docket Number	17618-US-BCON5-AP

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

	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	Olejnik et al	
	84	6569463		2003-03-27	Patel et al	
	85	6582718		2003-06-24	Yoichi Kawashima	

Receipt date: 09/11/2013	Application Number	13967179	13967179 - GAU: 1658
INFORMATION DISCLOSURE STATEMENT BY APPLICANT (**Not for submission under 37 CFR 1.99)**	Filing Date	2013-08-14	
	First Named Inventor	ACHEAMPONG, ANDREW	
	Art Unit	1653	
	Examiner Name	TBD	
	Attorney Docket Number	17618-US-BCON5-AP	

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

	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

Receipt date: 09/11/2013	Application Number	13967179 13967179 - GAU: 1658
INFORMATION DISCLOSURE STATEMENT BY APPLICANT (**Not for submission under 37 CFR 1.99)**	Filing Date	2013-08-14
	First Named Inventor	ACHEAMPONG, ANDREW
	Art Unit	1653
	Examiner Name	TBD
	Attorney Docket Number	17618-US-BCON5-AP

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

	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	

Receipt date: 09/11/2013	Application Number	13967179 13967179 - GAU: 1658
INFORMATION DISCLOSURE STATEMENT BY APPLICANT (**Not for submission under 37 CFR 1.99)**	Filing Date	2013-08-14
	First Named Inventor	ACHEAMPONG, ANDREW
	Art Unit	1653
	Examiner Name	TBD
	Attorney Docket Number	17618-US-BCON5-AP

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

	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	

Receipt date: 09/11/2013	Application Number	13967179	13967179 - GAU: 1658
INFORMATION DISCLOSURE STATEMENT BY APPLICANT (**Not for submission under 37 CFR 1.99)**	Filing Date	2013-08-14	
	First Named Inventor	ACHEAMPONG, ANDREW	
	Art Unit	1653	
	Examiner Name	TBD	
	Attorney Docket Number	17618-US-BCON5-AP	

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

	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**

Receipt date: 09/11/2013

INFORMATION DISCLOSURE STATEMENT BY APPLICANT
(**Not for submission under 37 CFR 1.99)**

Application Number	13967179 13967179 - GAU: 1658
Filing Date	2013-08-14
First Named Inventor	ACHEAMPONG, ANDREW
Art Unit	1653
Examiner Name	TBD
Attorney Docket Number	17618-US-BCON5-AP

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

	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**
	43	20130059796		2013-03-07	Chang et al	U.S. Application No. 13/649,287 and its entire prosecution history**

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

FOREIGN PATENT DOCUMENTS

Receipt date: 09/11/2013

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Not for submission under 37 CFR 1.99)

Application Number	13967179 13967179 - GAU: 1658
Filing Date	2013-08-14
First Named Inventor	ACHEAMPONG, ANDREW
Art Unit	1653
Examiner Name	TBD
Attorney Docket Number	17618-US-BCON5-AP

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

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		☐
	2	0471293	EP		1992-02-19	ABBOTT LABORATORIES		☐
	3	0547229	EP		1993-01-07	LLT Institute Co., Ltd.		☐
	4	0760237	EP		1997-03-05	Cipla Limited		☐
	5	1995-031211	WO		1995-11-23	Allergan Inc.		☐
	6	2000-000179	WO		2000-01-06	Won Jin Biopharma Co., Ltd		☐
	7	2001-032142	WO		2001-05-10	Cipla Limited		☐
	8	2001-041671	WO		2001-06-14	Transneuronix, Inc.		☐
	9	2002-009667	WO		2002-02-07	Pharmasol GMBH		☐
	10	2002-049603	WO		2002-06-27	LG Household & Health Care Ltd.		☐

Receipt date: 09/11/2013	Application Number	13967179 13967179 - GAU: 1658
INFORMATION DISCLOSURE STATEMENT BY APPLICANT (**Not for submission under 37 CFR 1.99)**	Filing Date	2013-08-14
	First Named Inventor	ACHEAMPONG, ANDREW
	Art Unit	1653
	Examiner Name	TBD
	Attorney Docket Number	17618-US-BCON5-AP

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

	11	2003-030834	WO		2003-04-17	Enanta Pharmaceuticals, Inc.		☐
	12	2003-053405	WO		2003-07-03	Yissum Research Development Company of the Hebrew		☐

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]
	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)	☐
	2	ACHEAMPONG, ANDREW ET AL, Cyclosporine Distribution into the Conjunctiva, Cornea, Lacrimal Gland and Systemic Blood Following Topical Dosing of Cyclosporine to Rabbit, Dog and Human eyes, 1996, 179	☐
	3	ACHEAMPONG, ANDREW ET AL, Cyclosporine Distribution Into The Conjunctiva, Cornea, Lacrimal Gland, and Systemic Blood Following Topical Dosing of Cyclosporine to Rabbit, Dog, and Human Eyes, Adv. Exp. Med. Biol., 1998, 1001-1004, 438	☐
	4	ACHEAMPONG, ANDREW ET AL, Distribution of Cyclosporin A in Ocular Tissues After Topical Administration to Albino Rabbits and Beagle Dogs, Current Eye Research, 1999, 91-103, 18(2)	☐
	5	AKPEK, ESEN KARAMURSEL ET AL, A Randomized Trial of Topical Cyclosporin 0.05% in Topical Steroid-Resistant Atopic Keratoconjunctivitis, Ophthalmology, 2004, 476-482, 111	☐
	6	ANGELOV, O. ET AL, Preclinical Safety Studies of Cyclosporine Ophthalmic Emulsion, Adv Exp Med Biol, 1998, 991-995, 438	☐
	7	ANGELOV, O. ET AL, Safety Assessment of Cyclosporine Ophthalmic Emulsion in Rabbits and Dogs, XIth Congress of the European Society of Ophthalmology, 1997, 25-28, 1-5, Soc. Ophthalmol Eur., HU	☐

Receipt date: 09/11/2013	Application Number	13967179 13967179 - GAU: 1658
INFORMATION DISCLOSURE STATEMENT BY APPLICANT (**Not for submission under 37 CFR 1.99)**	Filing Date	2013-08-14
	First Named Inventor	ACHEAMPONG, ANDREW
	Art Unit	1653
	Examiner Name	TBD
	Attorney Docket Number	17618-US-BCON5-AP

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

	8	ARDIZZONE, SANDRO ET AL, A Practical Guide to the Management of Distal Ulcerative Colitis, Drugs, 1998, 519-542, 55(4)	☐
	9	BANIC, MARKO ET AL, Effect of Cyclosporine in a Murine Model of Experimental Colitis, Digestive Diseases and Sciences, June 2002, 1362-1368, 47(6)	☐
	10	BONINI, S. ET AL, Vernal Keratoconjunctivitis, Eye, 2004, 345-351, 18	☐
	11	BREWSTER, MARCUS ET AL, Enhanced Delivery of Ganciclovir to the Brain Through the Use of Redox Targeting, Antimicrobial Agents and Chemotherapy, Apr 1994, 817-823, 38(4)	☐
	12	BREWSTER, MARCUS ET AL, Intravenous and Oral Pharmacokinetic Evaluation of a 2-Hydroxypropyl-ß-cyclodextrin-Based Formulation of Carbamazepine in the Dog: Comparison with Commercially Available Tablets and Suspensions, Journal of Pharmaceutical Sciences, March 1997, 335-339, 86(3)	☐
	13	BREWSTER, MARCUS ET AL, Preparation, Characterization, and Anesthetic Properties of 2-Hydroxypropyl-ß-cyclodextrin Complexes of Pregnanolone and Pregnenolone in Rat and Mouse, Journal of Pharmaceutical Sciences, October 1995, 1154-1159, 84(10)	☐
	14	BRINKMEIER, THOMAS ET AL, Pyodermatitis-Pyostomatitis Vegetans: A Clinical Course of Two Decades with Response to Cyclosporine and Low-Dose Prednisolone, Acta Derm Venereol, 2001, 134-136, 81	☐
	15	CASTILLO, JOSE M. BENITEZ DEL ET AL, Influence of Topical Cyclosporine A and Dissolvent on Corneal Epithelium Permeability of Fluorescein, Documenta Ophthalmologica, 1995, 49-55, 91	☐
	16	CHEEKS, LISA ET AL, Influence of Vehicle and Anterior Chamber Protein Concentration on Cyclosporine Penetration Through the Isolated Rabbit Cornea, Current Eye Research, 1992, 641-649, 11(7)	☐
	17	Database WPI Week 200044, Derwent Pub. Ltd., London, GB; An 2000-492678 & JP2000/143542, 2000, 2 Pages	☐
	18	DING, SHULIN ET AL, Cyclosporine Ophthalmic O/W emulsion: Formulation and Emulsion Characterization, Pharm Res, 1997, 1 page, 14 (11)	☐

Receipt date: 09/11/2013	Application Number	13967179 13967179 - GAU: 1658
INFORMATION DISCLOSURE STATEMENT BY APPLICANT (**Not for submission under 37 CFR 1.99)**	Filing Date	2013-08-14
	First Named Inventor	ACHEAMPONG, ANDREW
	Art Unit	1653
	Examiner Name	TBD
	Attorney Docket Number	17618-US-BCON5-AP

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

	19	DONNENFELD, ERIC D., The Economics Of Using Restasis, Ophthalmology Management, 10/2003, 3 pages, US	☐
	20	DROSOS, A. A. ET AL, Efficacy and Safety of Cyclosporine-A Therapy for Primary Sjogren's Syndrome, Ter. Arkh., 1998, 77-80, 60(4)	☐
	21	DROSOS, A.A. ET AL, Cyclosporin A Therapy in Patients with Primary Sjogren's Syndrome: Results at One Year, Scand J Rheumatology, 1986, 246-249, 61	☐
	22	EISEN, DRORE ET AL, Topical Cyclosporine for Oral Mucosal Disorders, J Am Acad Dermatol, Dec. 1990, 1259-1264, 23	☐
	23	EPSTEIN, JOEL ET AL, Topical Cyclosporine in a Bioadhesive for Treatment of Oral Lichenoid Muscosal Reactions, Oral Surg Oral Med Oral Pathol Oral, 1996, 532-536, 82	☐
	24	ERDMANN, S. ET AL, Pemphigus Vulgaris Der Mund- Und Kehlkopfschleimhaut Pemphigus Vulgaris of the Oral Mucosa and the Larynx, H+G Zeitschrift Fuer Hautkrankheiten, 1997, 283-286, 72(4)	☐
	25	FDA Concludes Restasis (Cyclosporine) Not Effective for Dry Eye (6/18/1999). Accessed online at http://www.dryeyeinfo.org/Restasis_Cyclosporine.htm on 8/14/09. 1 Page	☐
	26	GAETA, G.M. ET AL, Cyclosporin Bioadhesive Gel in the Topical Treatment of Erosive Oral Lichen Planus, International Journal of Immunopathology and Pharmacology, 1994, 125-132, 7(2)	☐
	27	GIPSON, ILENE ET AL, Character of Ocular Surface Mucins and Their Alteration in Dry Eye Disease, The Ocular Surface, April 2004, 131-148, 2(2)	☐
	28	GREMSE, DAVID ET AL, Ulcerative Colitis in Children, Pediatr Drugs, 2002, 807-815, 4(12)	☐
	29	GUNDUZ, KAAN ET AL, Topical Cyclosporin Treatment of Keratoconjunctivitis Sicca in Secondary Sjogren's Syndrome, Acta Ophthalmologica, 1994, 438-442, 72	☐

Receipt date: 09/11/2013	Application Number	13967179 13967179 - GAU: 1658
INFORMATION DISCLOSURE STATEMENT BY APPLICANT (**Not for submission under 37 CFR 1.99)**	Filing Date	2013-08-14
	First Named Inventor	ACHEAMPONG, ANDREW
	Art Unit	1653
	Examiner Name	TBD
	Attorney Docket Number	17618-US-BCON5-AP

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

	30	http://web.archive.org/web/2001030625323/http://www.surfactant.co.kr/surfactants/pegester.html, 2001, 6 Pages, retrieved on 7/05/2008	☐
	31	HUNTER, P.A. ET AL, Cyclosporin A Applied Topically to the Recipient Eye Inhibits Corneal Graft Rejection, Clin Exp Immunol, 1981, 173-177, 45	☐
	32	JUMAA, MUHANNAD ET AL, Physicochemical Properties and Hemolytic Effect of Different Lipid Emulsion Formulations Using a Mixture of Emulsifiers, Pharmaceutica Acta Helvetiae, 1999, 293-301, 73	☐
	33	KANAI, A. ET AL, The Effect on the Cornea of Alpha Cyclodextrin Vehicle for Eye Drops, Transplantation Proceedings, Febraury 1989, 3150-3152, Vol. 21	☐
	34	KANPOLAT, AYFER ET AL, Penetration of Cyclosporin A into the Rabbit Cornea and Aqueous Humor after Topical Drop and Collagen Shield Administration, Cornea/External Disease, April 1994, 119-122, 20(2)	☐
	35	KAUR, RABINDER ET AL, Solid Dispersions of Drugs in Polyocyethylene 40 Stearate: Dissolution Rates and Physico-Chemical Interactions, Journal of Pharmacy and Pharmacology, December 1979, 48P	☐
	36	KUWANO, MITSUAKI ET AL, Cyclosporine A Formulation Affects Its Ocular Distribution in Rabbits, Pharmaceutical Research, January 2002, 108-111, 19(1)	☐
	37	Lambert Technologies Corp. Material Safety Data Sheet for LUMULSE ™ POE-40 MS KP, last revision 8/22/2003. 3 pages	☐
	38	LEIBOVITZ, Z. ET AL., Our Experience In Processing Maize (Corn) Germ Oil, Journal Of The American Oil Chemists Society, 02/1983, 395-399, 80 (2), US	☐
	39	LIXIN, XIE ET AL, Effect Of Cyclosporine A Delivery System in Corneal Transplantation, Chinese Medical Journal, 2002, 110-113, 115 (1), US	☐
	40	LOPATIN, D.E., Chemical Compositions and Functions of Saliva, 8/24/2001, 31 Pages	☐

Receipt date: 09/11/2013	Application Number	13967179 13967179 - GAU: 1658
INFORMATION DISCLOSURE STATEMENT BY APPLICANT (**Not for submission under 37 CFR 1.99)**	Filing Date	2013-08-14
	First Named Inventor	ACHEAMPONG, ANDREW
	Art Unit	1653
	Examiner Name	TBD
	Attorney Docket Number	17618-US-BCON5-AP

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

	41	LYONS, R.T. ET AL, Influence of Three Emulsion Formulation Parameters on the Ocular Bioavailability of Cyclosporine A in Albino Rabbits, Am Assoc Pharm Sci, 2000, 1 Page, 2(4)	☐
	42	PEDERSEN, ANNE MARIE ET AL, Primary Sjogren's Syndrome: Oral Aspects on Pathogenesis, Diagnostic Criteria, Clinical Features and Approaches for Therapy, Expert Opin Pharma, 2001, 1415-1436, 2(9)	☐
	43	PHILLIPS, THOMAS ET AL, Cyclosporine Has a Direct Effect on the Differentiation of a Mucin-Secreting Cell Line, Journal of Cellular Physiology, 2000, 400-408, 184	☐
	44	PRESENT, D.H. ET AL, Cyclosporine and Other Immunosuppressive Agents: Current and Future Role in the Treatment of Inflammatory Bowel Disease, American Journal of Gastroenterology, 1993, 627-630, 88(5)	☐
	45	Restasis ® Product Information Sheet, Allergan, Inc., 2009, 5 Pages	☐
	46	Restasis® Increasing Tear Production, Retrieved on 08/14/2009, http://www.restasisprofessional.com/_clinical/clinical_increasing.htm 3 pages	☐
	47	ROBINSON, N.A. ET AL, Desquamative Gingivitis: A Sign of Mucocutaneous Disorders - a Review, Australian Dental Journal, 2003, 205-211, 48(4)	☐
	48	RUDINGER, J., Characteristics of the Amino Acids as Components of a Peptide Hormone Sequence, Peptide Hormones, 1976, 1-7	☐
	49	SALL, KENNETH ET AL, Two Multicenter, Randomized Studies of the Efficacy and Safety of Cyclosporine Ophthalmic Emulsion in Moderate to Severe Dry Eye Disease, Ophthalmology, 2000, 631-639, 107	☐
	50	SANDBORN, WILLIAM ET AL, A Placebo-Controlled Trial of Cyclosporine Enemas for Mildly to Moderately Active Left-Sided Ulcerative Colitis, Gastroenterology, 1994, 1429-1435, 106	☐
	51	SANDBORN, WILLIAM ET AL, Cyclosporine Enemas for Treatment-Resistant, Mildly to Moderately Active, Left-Sided Ulcerative Colitis, American Journal of Gastroenterology, 1993, 640-645, 88(5)	☐

Receipt date: 09/11/2013	Application Number	13967179 13967179 - GAU: 1658
INFORMATION DISCLOSURE STATEMENT BY APPLICANT (**Not for submission under 37 CFR 1.99)**	Filing Date	2013-08-14
	First Named Inventor	ACHEAMPONG, ANDREW
	Art Unit	1653
	Examiner Name	TBD
	Attorney Docket Number	17618-US-BCON5-AP

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

	52	SCHWAB, MATTHIAS ET AL, Pharmacokinetic Considerations in the Treatment of Inflammatory Bowel Disease, Clin Pharm, 2001, 723-751, 60(10)	☐
	53	SECCHI, ANTONIO ET AL, Topical Use of Cyclosporine in the Treatment of Vernal Keratoconjunctivitis, American Journal of Ophthalmology, December 1990, 641-645, 110	☐
	54	SMALL, DAVE ET AL, The Ocular Pharmacokinetics of Cyclosporine in Albino Rabbits and Beagle Dogs, Ocular Drug Delivery and Metabolism, 1999, 54	☐
	55	SMALL, DAVID ET AL, Blood Concentrations of Cyclosporin A During Long-Term Treatment With Cyclosporin A ophthalmic Emulsions in Patients with Moderate to Severe Dry Eye Disease, Journal of Ocular Pharmacology and Therapeutics, 2002, 411-418, 18(5)	☐
	56	SMILEK, DAWN ET AL, A Single Amino Acid Change in a Myelin Basic Protein Peptide Confers the Capacity to Prevent Rather Than Induce Experimental Autoimmune Encephalomyelitis, Proc. Natl. Acad. Sci., Nov 1991, 9633-9637, 88	☐
	57	STEPHENSON, MICHELLE, The Latest Uses Of Restasis, Review Of Ophthalmology, 12/30/2005, 7 Pages, US	☐
	58	STEVENSON, DARA ET AL, Efficacy and Safety of Cyclosporin A ophthalmic Emulsion in the Treatment of Moderate-to-Severe Dry Eye Disease, Ophthalmology, 2000, 967-974, 107	☐
	59	TESAVIBUL, N. ET AL, Topical Cyclosporine A (CsA) for Ocular Surface Abnormalities in Graft Versus Host Disease Patients, Invest Ophthalmol Vis Sci, Feb 1996, S1026, 37(3)	☐
	60	The Online Medical Dictionary, Derivative, Analog, Analogue, Xerostomia, accessed 7/7/2005 and 7/13/2005, 6 Pages	☐
	61	TIBELL, A. ET AL., Cyclosporin A In Fat Emulsion Carriers: Experimental Studies On Pharmacokinetics And Tissue Distribution, Pharmacology & Toxicology, 1995, 115-121, 76, US	☐
	62	TSUBOTA, KAZUO ET AL, Use of Topical Cyclosporin A in a Primary Sjogren's Syndrome Mouse Model, Invest Ophthalmol Vis Sci, Aug. 1998, 1551-1559, 39(9)	☐

Receipt date: 09/11/2013	Application Number	13967179 13967179 - GAU: 1658
INFORMATION DISCLOSURE STATEMENT BY APPLICANT (**Not for submission under 37 CFR 1.99)**	Filing Date	2013-08-14
	First Named Inventor	ACHEAMPONG, ANDREW
	Art Unit	1653
	Examiner Name	TBD
	Attorney Docket Number	17618-US-BCON5-AP

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

	63	VAN DER REIJDEN, WILLY ET AL, Treatment of Oral Dryness Related Complaints (Xerostomia) in Sjogren's Syndrome, Ann Rheum Dis, 1999, 465-473, 58	☐
	64	WINTER, T.A. ET AL, Cyclosporin A Retention Enemas in Refractory Distal Ulcerative Colitis and 'Pouchitis', Scand J Gastroenterol, 1993, 701-704, 28	☐
	65	U.S. Pending Application: 13/967,189 Filed on August 14, 2013	☐
	66	U.S. Pending Application: 13/961,818 Filed on August 07, 2013	☐
	67	U.S. Pending Application: 13/961,828 Filed on August 07, 2013	☐
	68	U.S. Pending Application: 13/961,835 Filed on August 07, 2013	☐
	69	U.S. Pending Application: 13/961,808 Filed on August 07, 2013	☐
	70	U.S. Pending Application: 13/967,163 Filed on August 14, 2013	☐
	71	U.S. Pending Application: 13/967,168 Filed on August 14, 2013	☐
	72	U.S. Re-Examination Application: 90/009,944 Filed on August, 27, 2011	☐

If you wish to add additional non-patent literature document citation information please click the Add button

Receipt date: 09/11/2013	Application Number	13967179 13967179 - GAU: 1658
INFORMATION DISCLOSURE STATEMENT BY APPLICANT (**Not for submission under 37 CFR 1.99)**	Filing Date	2013-08-14
	First Named Inventor	ACHEAMPONG, ANDREW
	Art Unit	1653
	Examiner Name	TBD
	Attorney Docket Number	17618-US-BCON5-AP

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

EXAMINER SIGNATURE			
Examiner Signature	/Marcela Cordero Garcia/	Date Considered	10/07/2013

*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: 09/11/2013	Application Number	13967179 13967179 - GAU: 1658
INFORMATION DISCLOSURE STATEMENT BY APPLICANT (**Not for submission under 37 CFR 1.99)**	Filing Date	2013-08-14
	First Named Inventor	ACHEAMPONG, ANDREW
	Art Unit	1653
	Examiner Name	TBD
	Attorney Docket Number	17618-US-BCON5-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)	2013-09-11
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 record s.

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.

EAST Search History

EAST Search History (Prior Art)

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
S3	377	cyclosporin same castor	US-PGPUB; USPAT; EPO; JPO; DERWENT	ADJ	ON	2013/10/04 16:09
S4	12	cyclosporin same castor same polysorbate same pemulen	US-PGPUB; USPAT; EPO; JPO; DERWENT	ADJ	ON	2013/10/05 09:54
S5	19	cyclosporin same "0.05" same castor same "1.25"	US-PGPUB; USPAT; EPO; JPO; DERWENT	ADJ	ON	2013/10/05 09:59
S6	89	cyclosporin same castor same polysorbate	US-PGPUB; USPAT; EPO; JPO; DERWENT	ADJ	ON	2013/10/05 10:21
S7	4	cyclosporin same castor same polysorbate same pemulen same hydroxide	US-PGPUB; USPAT; EPO; JPO; DERWENT	ADJ	ON	2013/10/05 10:21
S8	104	"5474979"	US-PGPUB; USPAT; EPO; JPO; DERWENT	ADJ	ON	2013/10/05 12:06
S9	2	"5474979".pn.	US-PGPUB; USPAT; EPO; JPO; DERWENT	ADJ	ON	2013/10/05 12:06

10/7/2013 2:09:53 PM

Connecting via Winsock to STN at stnc.cas.org on port 23

Welcome to STN International! Enter x:x

LOGINID:SSSPTA1654MCG

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * * * Welcome to STN International * * * * * * * * * *

NEWS	1	FEB 1	Instructor-led and on-demand STN training options available from CAS
NEWS	2	MAY 23	Get the Latest Version of STN Express, Version 8.5.1!
NEWS	3	DEC 10	New SDI STANDARD Option Streamlines SDI Set-ups on STN
NEWS	4	JAN 17	Cooperative Patent Classification (CPC) Search and Display Capabilities Now Available in CA/CAplus Family of Databases and USPAT Databases on STN
NEWS	5	JAN 23	INPADOC: CPC Backfile Data Now Available
NEWS	6	JAN 28	Reloaded MEDLINE on STN Now Includes 2013 MeSH Vocabulary and New Fields
NEWS	7	JAN 31	INPADOC Databases Enhanced with Calculated Expiration Dates
NEWS	8	JAN 31	INPADOC Enhanced with Citing Patent Information
NEWS	9	JAN 31	INPAFAMDB Enhanced with Patent Family Counts
NEWS	10	FEB 6	Enhancements to COMPENDEX
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
NEWS	14	MAR 22	Cooperative Patent Classification (CPC) Added to USPATOLD on STN
NEWS	15	MAR 25	SciSearch on STN Now Includes New Fields Find Grant Information More Easily
NEWS	16	APR 29	Embase Alert (EMBAL) Enhanced with Articles-in-Press Content and Optimized for Use as a Companion Database for Embase
NEWS	17	APR 30	Derwent WPI: The New Cooperative Patent Classification Is Now Available
NEWS	18	MAY 21	STN Updated to Reflect Streamlining of CAS Roles
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
NEWS	23	JUL 24	Find the Most Comprehensive and Timely Results When Searching the Newly Enhanced Embase Alert(TM) together with Embase(TM)
NEWS	24	JUL 31	New PV Cluster on STN(R) Simplifies Pharmacovigilance Alerting and Searching
NEWS	25	AUG 09	DWPI Manual Code Revision - submit your suggestions
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
NEWS	28	SEP 10	CAS Expands Coverage of Philippines Patents
NEWS	29	SEP 13	STN on the Web Enhanced with Updated Structure and BLAST Plug-ins
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

```
 NEWS 32  OCT 04  Impacts of U.S. Government Shutdown on STN Databases

 NEWS EXPRESS 23 MAY 2012 CURRENT WINDOWS VERSION IS V8.5.1,
              AND CURRENT DISCOVER FILE IS DATED 22 JULY 2013.

 NEWS HOURS    STN Operating Hours Plus Help Desk Availability
 NEWS LOGIN    Welcome Banner and News Items
 NEWS TRAINING Find instructor-led and self-directed training opportunities

Enter NEWS followed by the item number or name to see news on that
specific topic.

  All use of STN is subject to the provisions of the STN customer
  agreement.  This agreement limits use to scientific research.  Use
  for software development or design, implementation of commercial
  gateways, or use of CAS and STN data in the building of commercial
  products is prohibited and may result in loss of user privileges
  and other penalties.

* * * * * * * * * * * * * * * * STN  Columbus  * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 14:10:54 ON 07 OCT 2013

=> (cyclosporin or cyclosporine) (10a) ("castor oil") (10a) polysorbate
THIS COMMAND NOT AVAILABLE IN THE CURRENT FILE
Some commands only work in certain files.  For example, the EXPAND
command can only be used to look at the index in a file which has an
index.  Enter "HELP COMMANDS" at an arrow prompt (=>) for a list of
commands which can be used in this file.

=> file biosis embase medline pubmed
'PUBMED' IS NOT A VALID FILE NAME
Enter "HELP FILE NAMES" at an arrow prompt (=>) for a list of files
that are available.  If you have requested multiple files, you can
specify a corrected file name or you can enter "IGNORE" to continue
accessing the remaining file names entered.
ENTER A FILE NAME OR (IGNORE):ignore
COST IN U.S. DOLLARS                            SINCE FILE      TOTAL
                                                   ENTRY    SESSION
FULL ESTIMATED COST                                 2.16       2.16

FILE 'BIOSIS' ENTERED AT 14:16:25 ON 07 OCT 2013
Copyright (c) 2013 The Thomson Corporation

FILE 'EMBASE' ENTERED AT 14:16:25 ON 07 OCT 2013
Copyright (c) 2013 Elsevier B.V. All rights reserved.

FILE 'MEDLINE' ENTERED AT 14:16:25 ON 07 OCT 2013

=> file biosis embase medline caplus
COST IN U.S. DOLLARS                            SINCE FILE      TOTAL
                                                   ENTRY    SESSION
FULL ESTIMATED COST                                 3.67       5.83

FILE 'BIOSIS' ENTERED AT 14:16:34 ON 07 OCT 2013
Copyright (c) 2013 The Thomson Corporation

FILE 'EMBASE' ENTERED AT 14:16:34 ON 07 OCT 2013
Copyright (c) 2013 Elsevier B.V. All rights reserved.

FILE 'MEDLINE' ENTERED AT 14:16:34 ON 07 OCT 2013
```

FILE 'CAPLUS' ENTERED AT 14:16:34 ON 07 OCT 2013
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

=> (cyclosporin or cyclosporine) (10a) ("castor oil") (10a) polysorbate
L1 12 (CYCLOSPORIN OR CYCLOSPORINE) (10A) ("CASTOR OIL") (10A) POLYSOR
BATE

=> d ibib abs total hitseq

L1 ANSWER 1 OF 12 BIOSIS COPYRIGHT (c) 2013 The Thomson Corporation on STN
ACCESSION NUMBER: 2006:456121 BIOSIS
DOCUMENT NUMBER: PREV200600453000
TITLE: Stable bioavailability of cyclosporin A, regardless of food intake, from soft gelatin capsules containing a new self-nanoemulsifying formulation.
AUTHOR(S): Yang, S. G.; Kim, D. D.; Chung, S. J.; Shim, C. K. [Reprint Author]
CORPORATE SOURCE: Seoul Natl Univ, Coll Pharm, Dept Pharmaceut, San 56-1,Shinlim Dong, Seoul 151742, South Korea
shimck@snu.ac.kr
SOURCE: International Journal of Clinical Pharmacology and Therapeutics, (MAY 2006) Vol. 44, No. 5, pp. 233-239.
ISSN: 0946-1965.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 13 Sep 2006
Last Updated on STN: 13 Sep 2006

AB Aim: We recently succeeded in preparing soft gelatin capsules containing a new self-nanoemulsifying formulation consisting of cyclosporin A (CsA), triacetin, polyoxyl 40 hydrogenated castor oil, polysorbate 20, medium chain triglycerides and medium chain mono- and diglycerides. The soft capsules containing the new formulation exhibited a significantly improved physical stability in terms of the appearance of the gelatin capsule shells and the composition of the fill mass during long-term storage, compared to commercially available soft capsules containing CsA, in which ethanol was employed as a cosolvent of CsA. In the present study, the influence of a fat-rich meal on the bioavailability of CsA from the soft capsule containing the new formulation (test drug) was evaluated and the results compared to those obtained with a representative soft capsule of CsA. Volunteers and methods: A randomized, open-label, 3-way crossover study was performed in the test capsules and reference soft capsules, in a fasted state or after a fat-rich breakfast. 18 healthy male volunteers received a single dose of the reference formulation (Neoral, Novartis AG, Basel, Switzerland) or test formulation (2 capsules each, 200 mg as CsA) with 240 ml of water with a 1-week washout period between the treatments, after a fat-rich (670 kcal, 45 g fat) breakfast (for the test drug, Treatment A; for the reference drug, Treatment B) or a 12-h fasting (for the test drug, Treatment Q. Serial blood samples, collected over a 24-h period after the administration, were assayed for blood CsA concentrations using a specific monoclonal radioimmunoassay. Results: The differences in bioavailability parameters (i.e., AUC(0-24h), AUC(0-infinity) and C-max) between the treatments were within the range of 80 - 125% of the reference treatment. An analysis of variance (ANOVA) revealed no significant differences ($p > 0.05$) between subjects, formulations or periods. The 90% confidence intervals (CI) indicated that the differences between the treatments (Treatments A and B, Treatments A and Q were also within the criteria. Conclusion: These results indicate that the bioavailability of CsA from the test drug is equivalent to reference in the fed state, and is likely to be less influenced by a fat-rich meal. Therefore, the new formulation of CsA using triacetin

appears to have an advantage over the commercial soft capsules of CsA using a volatile cosolvent such as ethanol.

L1 ANSWER 2 OF 12 EMBASE COPYRIGHT (c) 2013 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2006216678 EMBASE
TITLE: Stable bioavailability of cyclosporin A, regardless of food intake, from soft gelatin capsules containing a new self-nanoemulsifying formulation.
AUTHOR: Yang, S.G.; Kim, D.D.; Chung, S.J.; Shim, C.-K., Dr. (correspondence)
CORPORATE SOURCE: Research Institute of Pharmaceutical Sciences, College of Pharmacy, Seoul National University, San 56-1, Shinlim-dong, Kwanak-gu, Seoul 151-742, Korea, Republic of. shimck@snu.ac.kr
AUTHOR: Shim, C.-K., Dr. (correspondence)
CORPORATE SOURCE: Department of Pharmaceutics, College of Pharmacy, Seoul National University, San 56-1, Shinlim-dong, Kwanak-gu, Seoul 151-742, Korea, Republic of. shimck@snu.ac.kr
SOURCE: International Journal of Clinical Pharmacology and Therapeutics, (May 2006) Vol. 44, No. 5, pp. 233-239. Refs: 22
ISSN: 0946-1965 CODEN: ICTHEK
COUNTRY: Germany
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 030 Clinical and Experimental Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered Embase: 30 May 2006
Last Updated on Embase: 6 Sep 2007

AB Aim: We recently succeeded in preparing soft gelatin capsules containing a new self-nanoemulsifying formulation consisting of cyclosporin A (CsA), triacetin, polyoxyl 40 hydrogenated castor oil, polysorbate 20, medium chain triglycerides and medium chain mono- and diglycerides. The soft capsules containing the new formulation exhibited a significantly improved physical stability in terms of the appearance of the gelatin capsule shells and the composition of the fill mass during long-term storage, compared to commercially available soft capsules containing CsA, in which ethanol was employed as a cosolvent of CsA. In the present study, the influence of a fat-rich meal on the bioavailability of CsA from the soft capsule containing the new formulation (test drug) was evaluated and the results compared to those obtained with a representative soft capsule of CsA. Volunteers and methods: A randomized, open-label, 3-way crossover study was performed in the test capsules and reference soft capsules, in a fasted state or after a fat-rich breakfast. 18 healthy male volunteers received a single dose of the reference formulation (Neoral, Novartis AG, Basel, Switzerland) or test formulation (2 capsules each, 200 mg as CsA) with 240 ml of water with a 1-week washout period between the treatments, after a fat-rich (670 kcal, 45 g fat) breakfast (for the test drug, Treatment A; for the reference drug, Treatment B) or a 12-h fasting (for the test drug, Treatment C). Serial blood samples, collected over a 24-h period after the administration, were assayed for blood CsA concentrations using a specific monoclonal radioimmunoassay. Results: The differences in bioavailability parameters (i.e., AUC0-24h, AUC0-∞ and Cmax) between the treatments were within the range of 80-125% of the reference treatment. An analysis of variance (ANOVA) revealed no significant differences ($p > 0.05$) between subjects, formulations or periods. The 90% confidence intervals (CI) indicated that the differences between the treatments (Treatments A and B, Treatments A and C) were also within the criteria. Conclusion: These results indicate that the

bioavailability of CsA from the test drug is equivalent to reference in the fed state, and is likely to be less influenced by a fat-rich meal. Therefore, the new formulation of CsA using triacetin appears to have an advantage over the commercial soft capsules of CsA using a volatile cosolvent such as ethanol. .COPYRGT. 2006 Dustri-Verlag Dr. K. Feistle.

L1 ANSWER 3 OF 12 MEDLINE ® on STN
ACCESSION NUMBER: 2006296965 MEDLINE
DOCUMENT NUMBER: PubMed ID: 16724578
TITLE: Stable bioavailability of cyclosporin A, regardless of food intake, from soft gelatin capsules containing a new self-nanoemulsifying formulation.
AUTHOR: Yang S G; Kim D D; Chung S J; Shim C K
CORPORATE SOURCE: Research Institute of Pharmaceutical Sciences and College of Pharmacy, Seoul National University, Seoul, Korea.
SOURCE: International journal of clinical pharmacology and therapeutics, (2006 May) Vol. 44, No. 5, pp. 233-9. Journal code: 9423309. ISSN: 0946-1965. L-ISSN: 0946-1965.
PUB. COUNTRY: Germany: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RANDOMIZED CONTROLLED TRIAL) (CLINICAL TRIAL)
LANGUAGE: English
FILE SEGMENT: MEDLINE; Priority Journals
ENTRY MONTH: 200707
ENTRY DATE: Entered STN: 27 May 2006
Last Updated on STN: 12 Dec 2006
Entered Medline: 20 Jul 2007

AB AIM: We recently succeeded in preparing soft gelatin capsules containing a new self-nanoemulsifying formulation consisting of cyclosporin A (CsA), triacetin, polyoxyl 40 hydrogenated castor oil, polysorbate 20, medium chain triglycerides and medium chain mono- and diglycerides. The soft capsules containing the new formulation exhibited a significantly improved physical stability in terms of the appearance of the gelatin capsule shells and the composition of the fill mass during long-term storage, compared to commercially available soft capsules containing CsA, in which ethanol was employed as a cosolvent of CsA. In the present study, the influence of a fat-rich meal on the bioavailability of CsA from the soft capsule containing the new formulation (test drug) was evaluated and the results compared to those obtained with a representative soft capsule of CsA.

VOLUNTEERS AND METHODS: A randomized, open-label, 3-way crossover study was performed in the test capsules and reference soft capsules, in a fasted state or after a fat-rich breakfast. 18 healthy male volunteers received a single dose of the reference formulation (Neoral, Novartis AG, Basel, Switzerland) or test formulation (2 capsules each, 200 mg as CsA) with 240 ml of water with a 1-week washout period between the treatments, after a fat-rich (670 kcal, 45 g fat) breakfast (for the test drug, Treatment A; for the reference drug, Treatment B) or a 12-h fasting (for the test drug, Treatment C). Serial blood samples, collected over a 24-h period after the administration, were assayed for blood CsA concentrations using a specific monoclonal radioimmunoassay.

RESULTS: The differences in bioavailability parameters (i.e., AUC(0-24h), AUC(0-infinity) and C(max)) between the treatments were within the range of 80-125% of the reference treatment. An analysis of variance (ANOVA) revealed no significant differences ($p > 0.05$) between subjects, formulations or periods. The 90% confidence intervals (CI) indicated that the differences between the treatments (Treatments A and B, Treatments A and C) were also within the criteria.

CONCLUSION: These results indicate that the bioavailability of CsA from the test drug is equivalent to reference in the fed state, and is likely to be less influenced by a fat-rich meal. Therefore, the new formulation of CsA using triacetin appears to have an advantage over the commercial soft capsules of CsA using a volatile cosolvent such as ethanol.

L1 ANSWER 4 OF 12 CAPLUS COPYRIGHT 2013 ACS on STN
ACCESSION NUMBER: 2013:569214 CAPLUS
DOCUMENT NUMBER: 158:545244
TITLE: Topical oil-in-water emulsion compositions for enhancing nail health comprising immunomodulator such as cyclosporine
INVENTOR(S): Walt, John G.
PATENT ASSIGNEE(S): Allergan, Inc., USA
SOURCE: PCT Int. Appl., 115pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2013052424	A2	20130411	WO 2012-US58333	20121001

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2011-61543758 P 20111005

AB The present invention is directed to compns. and methods for enhancing the health of nails and cuticles in a mammal, including humans. The compns. may be administered topically to the nail bed, nail matrix and cuticle in an amount effective to enhance nail health. The composition is also effective in strengthening and growing nails. Thus, the disclosed compns. comprised immunomodulator such as cyclosporine, antiinflammatory such as ketorolac, castor oil, surfactant, glycerin, polysorbate 80 and carbomer.

L1 ANSWER 5 OF 12 CAPLUS COPYRIGHT 2013 ACS on STN
ACCESSION NUMBER: 2007:119452 CAPLUS
DOCUMENT NUMBER: 146:190563
TITLE: Pharmaceutical compositions comprising cyclosporins
INVENTOR(S): Tien, Walter L.; Graham, Richard; Chang, James N.
PATENT ASSIGNEE(S): Allergan, Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 4pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

US 20070027072 A1 20070201 US 2005-161218 20050727
US 7501393 B2 20090310
WO 2007016073 A1 20070208 WO 2006-US28788 20060725
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
US 20090131307 A1 20090521 US 2009-361335 20090128
PRIORITY APPLN. INFO.: US 2005-161218 A 20050727
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB A composition is described herein comprising cyclosporin A, Polysorbate 80, a polyoxyethylene stearate, and an oil; wherein the composition is an emulsion which is ophthalmically acceptable. Methods of treating diseases or conditions using the compns., and medicaments related thereto, are also disclosed herein. Thus, a composition contains purite 100 ppm cyclosporin A 0.1, castor oil 0.5, PEG stearate 1.0, Polysorbate-80 0.5, glycerin 1.4, boric acid 0.6, CM-cellulose 0.5, and water qs to 100%.
OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)
REFERENCE COUNT: 108 THERE ARE 108 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 6 OF 12 CAPLUS COPYRIGHT 2013 ACS on STN
ACCESSION NUMBER: 2007:63260 CAPLUS
DOCUMENT NUMBER: 146:149038
TITLE: Opthalmic emulsion comprising cyclosporin
INVENTOR(S): Chang, James N.; Olejnik, Orest; Firestone, Bruce A.
PATENT ASSIGNEE(S): Allergan, Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 24pp., Cont.-in-part of U.S. Ser. No. 181,409.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20070015694	A1	20070118	US 2005-255821	20051019
US 7288520	B2	20071030		
US 20070015690	A1	20070118	US 2005-181178	20050713
US 7297679	B2	20071120		
US 20070015710	A1	20070118	US 2005-181187	20050713
US 7276476	B2	20071002		
US 20070015691	A1	20070118	US 2005-181409	20050713
US 20070015692	A1	20070118	US 2005-181428	20050713
US 7202209	B2	20070410		
US 20070015693	A1	20070118	US 2005-181509	20050713
US 20070149447	A1	20070628	US 2007-679934	20070228
US 8536134	B2	20130917		
US 20080009436	A1	20080110	US 2007-857223	20070918
US 8211855	B2	20120703		
US 20080070834	A1	20080320	US 2007-940652	20071115

US 20120270805 A1 20121025 US 2012-13536479 20120628
PRIORITY APPLN. INFO.: US 2005-181178 A2 20050713
US 2005-181187 A2 20050713
US 2005-181409 A2 20050713
US 2005-181428 A2 20050713
US 2005-181509 A2 20050713
US 2005-255821 A3 20051019
US 2007-857223 A1 20070918
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB A composition is disclosed herein comprising from about 0.001% to about 0.4% cyclosporin A, castor oil, and a surfactant selected from the group consisting of alc. ethoxylated, alcs., alkyl glycosides, alkyl polyglycosides, alkylphenol ethoxylates, amine oxides, block polymers, carboxylated alc. or alkylphenol ethoxylates, carboxylic adds/fatty acids, cellulose derivs., ethoxylated alcs., ethoxylated alkylphenols, ethoxylated aryl phenols, ethoxylated fatty acids, ethoxylated fatty acids, ethoxylated fatty esters and oils, fatty alcs., fatty esters, glycol esters, lanolin-based derivs., lecithin and lecithin derivs., lignin and lignin derivs., Me esters, monoglycerides and derivs., phospholipids, polyacrylic acids, polyethylene glycols, polyethylene oxide-polypropylene oxide copolymers, polyethylene oxides, polymeric surfactants, polypropylene oxides, propoxylated alcs., propoxylated alkyl phenols, propoxylated fatty acids, protein-based surfactants, sarcosine derivs., silicone-based surfactants, sorbitan derivs., stearates, sucrose and glucose esters and derivs., and combinations thereof. For example, emulsion was prepared containing cyclosporin A 0.1%, castor oil 1%, clove oil 0.7%, Polysorbate-80 1%, diglycerol 0.7%, glycerin 2%, CM-cellulose 0.5%, sodium hydroxide to adjust pH (7.2) and water as needed.
OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)
REFERENCE COUNT: 89 THERE ARE 89 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 7 OF 12 CAPLUS COPYRIGHT 2013 ACS on STN
ACCESSION NUMBER: 2007:58577 CAPLUS
DOCUMENT NUMBER: 146:149007
TITLE: Composition comprising cyclosporin A
INVENTOR(S): Chang, James N.; Olejnik, Orest; Firestone, Bruce A.
PATENT ASSIGNEE(S): Allergan, Inc., USA
SOURCE: PCT Int. Appl., 32 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007008894	A2	20070118	WO 2006-US26881	20060712
WO 2007008894	A3	20070628		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

US 20070015690	A1	20070118	US 2005-181178	20050713
US 7297679	B2	20071120		
US 20070015710	A1	20070118	US 2005-181187	20050713
US 7276476	B2	20071002		
US 20070015691	A1	20070118	US 2005-181409	20050713
US 20070015692	A1	20070118	US 2005-181428	20050713
US 7202209	B2	20070410		
US 20070015693	A1	20070118	US 2005-181509	20050713
AU 2006268264	A1	20070118	AU 2006-268264	20060712
CA 2602452	A1	20070118	CA 2006-2602452	20060712
EP 1901711	A2	20080326	EP 2006-786892	20060712
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR				
JP 2009501228	T	20090115	JP 2008-521528	20060712
BR 2006013533	A2	20110118	BR 2006-13533	20060712
US 20070149447	A1	20070628	US 2007-679934	20070228
US 8536134	B2	20130917		
US 20080070834	A1	20080320	US 2007-940652	20071115
US 20080207494	A1	20080828	US 2007-917448	20071213
US 8288348	B2	20121016		

PRIORITY APPLN. INFO.:	US 2005-181178	A	20050713
	US 2005-181187	A	20050713
	US 2005-181409	A	20050713
	US 2005-181428	A	20050713
	US 2005-181509	A	20050713
	WO 2006-US26881	W	20060712

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB Cyclosporin A compns. are disclosed herein comprising an oil and a surfactant. These are useful in the treatment of dry eye disease. Thus, composition was prepared containing cyclosporin A 0.1, castor oil 1, clove oil 0.7, polysorbate-80 1, diglycerol 0.7, glycerin 2, CM-cellulose 0.5 and water as needed.

OS.CITING REF COUNT: 6 THERE ARE 6 CAPLUS RECORDS THAT CITE THIS RECORD (6 CITINGS)

L1 ANSWER 8 OF 12 CAPLUS COPYRIGHT 2013 ACS on STN

ACCESSION NUMBER: 2006:590857 CAPLUS

DOCUMENT NUMBER: 145:443655

TITLE: Stable bioavailability of cyclosporin A, regardless of food intake, from soft gelatin capsules containing a new self-nanoemulsifying formulation

AUTHOR(S): Yang, S. G.; Kim, D. D.; Chung, S. J.; Shim, C. K.

CORPORATE SOURCE: Research Institute of Pharmaceutical Sciences and College of Pharmacy, Seoul National University, Seoul, S. Korea

SOURCE: International Journal of Clinical Pharmacology and Therapeutics (2006), 44(5), 233-239
CODEN: ICTHEK; ISSN: 0946-1965

PUBLISHER: Dustri-Verlag Dr. Karl Feistle

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Aim: We recently succeeded in preparing soft gelatin capsules containing a new self-nanoemulsifying formulation consisting of cyclosporin A (CsA), triacetin, polyoxyl 40 hydrogenated castor oil, polysorbate 20, medium chain triglycerides and medium chain mono- and diglycerides. The soft capsules containing the new formulation exhibited a significantly improved phys. stability in terms of the appearance of the gelatin capsule shells and the composition of the fill mass during long-term storage, compared to com. available soft capsules containing CsA, in which ethanol was employed as a cosolvent of CsA. In the present study, the influence of a fat-rich meal on the bioavailability of CsA from the soft capsule containing the new formulation (test drug) was evaluated and the results compared to those

obtained with a representative soft capsule of CsA. Volunteers and methods: A randomized, open-label, 3-way crossover study was performed in the test capsules and reference soft capsules, in a fasted state or after a fat-rich breakfast. 18 Healthy male volunteers received a single dose of the reference formulation (Neoral, Novartis AG, Basel, Switzerland) or test formulation (2 capsules each, 200 mg as CsA) with 240 mL of water with a 1-wk washout period between the treatments, after a fat-rich (670 kcal, 45 g fat) breakfast (for the test drug, Treatment A; for the reference drug, Treatment B) or a 12-h fasting (for the test drug, Treatment C). Serial blood samples, collected over a 24-h period after the administration, were assayed for blood CsA concns. using a specific monoclonal RIA. Results: The differences in bioavailability parameters (i.e., AUC0-24h, AUC0-∞ and Cmax) between the treatments were within the range of 80 - 125% of the reference treatment. An anal. of variance (ANOVA) revealed no significant differences ($p > 0.05$) between subjects, formulations or periods. The 90% confidence intervals (CI) indicated that the differences between the treatments (Treatments A and B, Treatments A and C) were also within the criteria. Conclusion: These results indicate that the bioavailability of CsA from the test drug is equivalent to reference in the fed state, and is likely to be less influenced by a fat-rich meal. Therefore, the new formulation of CsA using triacetin appears to have an advantage over the com. soft capsules of CsA using a volatile cosolvent such as ethanol.

OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)

REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 9 OF 12 CAPLUS COPYRIGHT 2013 ACS on STN

ACCESSION NUMBER: 2000:494420 CAPLUS

DOCUMENT NUMBER: 133:198474

TITLE: Effect of Polyoxyl 35 castor oil and Polysorbate 80 on the intestinal absorption of digoxin in vitro

AUTHOR(S): Cornaire, Gilles; Woodley, John F.; Saivin, Sylvie; Legendre, Jean-Yves; Decourt, Sylvie; Cloarec, Alix; Houin, Georges

CORPORATE SOURCE: Laboratoire de Cinetique des Xenobiotiques, Faculte des Sciences Pharmaceutiques, Toulouse, Fr.

SOURCE: Arzneimittel-Forschung (2000), 50(6), 576-579
CODEN: ARZNAD; ISSN: 0004-4172

PUBLISHER: Editio Cantor Verlag

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Surfactants are classically used to improve the solubilization of lipophilic drugs such as digoxin. Polysorbate 80 and Cremophor EL (Polyoxyl 35 castor oil) are such surfactants but they may also modulate the action of P-glycoprotein, an energy-dependent "counter-transport" system implicated in the phenomenon of multidrug resistance in cancer cells. P-glycoprotein is also present in the intestine on the apical membrane of mature enterocytes and can potentially reduce the absorption of a wide range of drugs. In this study, using the improved everted gut sac method, the effects of Polysorbate 80, Cremophor EL and cyclosporin on the absorption of digoxin were studied. An increase in the uptake of digoxin in the presence of these 3 products was shown. Cremophor EL and Polysorbate 80 had no toxic effects at the concns. used. Surfactants such as Cremophor EL and Polysorbate 80 should not only support solubilization but can also modulate the P-glycoprotein system to improve the bioavailability of poorly absorbed drugs.

OS.CITING REF COUNT: 27 THERE ARE 27 CAPLUS RECORDS THAT CITE THIS RECORD (27 CITINGS)

REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 10 OF 12 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

L1 ANSWER 11 OF 12 CAPLUS COPYRIGHT 2013 ACS on STN
ACCESSION NUMBER: 1993:588539 CAPLUS
DOCUMENT NUMBER: 119:188539
ORIGINAL REFERENCE NO.: 119:33511a,33514a
TITLE: Leaching of diethylhexyl phthalate from polyvinyl chloride containers by selected drugs and formulation components
AUTHOR(S): Pearson, Stephen D.; Trissel, Lawrence A.
CORPORATE SOURCE: Houston Biotechnol., Inc., Woodlands, TX, USA
SOURCE: American Journal of Hospital Pharmacy (1993), 50(7), 1405-9
CODEN: AJHPA9; ISSN: 0002-9289
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Diethylhexyl phthalate (DEHP) was leached from polyvinyl chloride containers by polysorbate 80, poloxyethylated castor oil, cyclosporine, miconazole, teniposide, chlordiazepoxide HCl, etoposide, and the vehicles used in the formulation of taxol and taxotere. DEHP was detectable immediately in some cases and increased in concentration over the 24-h
study period. Drugs that leach DEHP should be prepared in non-PVC containers and administered through non-PVC tubing.
OS.CITING REF COUNT: 47 THERE ARE 47 CAPLUS RECORDS THAT CITE THIS RECORD (47 CITINGS)

L1 ANSWER 12 OF 12 CAPLUS COPYRIGHT 2013 ACS on STN
ACCESSION NUMBER: 1993:261059 CAPLUS
DOCUMENT NUMBER: 118:261059
ORIGINAL REFERENCE NO.: 118:45259a,45262a
TITLE: Ophthalmic solutions containing cyclosporin and surfactants
INVENTOR(S): Hata, Kunio; Murano, Masaru; Ueda, Shogo
PATENT ASSIGNEE(S): Sankyo Co, Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 4 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE

```
     ---------------     ----  --------    ---------------------   --------
     JP 05058906          A    19930309    JP 1991-226990          19910906
PRIORITY APPLN. INFO.:                     JP 1991-226990          19910906
AB   Aqueous ophthalmic solns. contain cyclosporin (I) and surfactants chosen
     from polysorbate, polyoxyethylene hydrogenated castor oil, and
     polyoxyethylene fatty acid esters.  The solns. show good stability and do
     not irritate the eyes.  I 0.5, polyoxyethylene hydrogenated castor oil 20,
     NaCl 8 g, antiseptic, and H2O to 1000 mL were mixed to give an ophthalmic
     solution
OS.CITING REF COUNT:     2     THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD
                               (2 CITINGS)


=> d his

     (FILE 'HOME' ENTERED AT 14:10:54 ON 07 OCT 2013)

     FILE 'BIOSIS, EMBASE, MEDLINE' ENTERED AT 14:16:25 ON 07 OCT 2013

     FILE 'BIOSIS, EMBASE, MEDLINE, CAPLUS' ENTERED AT 14:16:34 ON 07 OCT 2013
L1           12 (CYCLOSPORIN OR CYCLOSPORINE) (10A) ("CASTOR OIL") (10A) POLYSO

=> logoff h
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                      55.99      61.82

 SESSION WILL BE HELD FOR 120 MINUTES
STN INTERNATIONAL SESSION SUSPENDED AT 14:18:02 ON 07 OCT 2013
```

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

BIB DATA SHEET

CONFIRMATION NO. 8654

SERIAL NUMBER	FILING or 371(c) DATE RULE	CLASS	GROUP ART UNIT	ATTORNEY DOCKET NO.
13/967,179	08/14/2013	514	1658	17618CON5B (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 13/961,818 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 ☐ Yes ☑ No 35 USC 119(a-d) conditions met ☐ Yes ☑ No Verified and Acknowledged /MARCELA M CORDERO GARCIA/ Examiner's Signature	☐ Met after Allowance Initials	STATE OR COUNTRY	SHEETS DRAWINGS	TOTAL CLAIMS	INDEPENDENT CLAIMS
		CA	0	25	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		
2300	FEES: Authority has been given in Paper No._____ to charge/credit DEPOSIT ACCOUNT No._____ for following:	☐ All Fees ☐ 1.16 Fees (Filing) ☐ 1.17 Fees (Processing Ext. of time) ☐ 1.18 Fees (Issue) ☐ Other _____ ☐ Credit

DRAFT CLAIM AMENDMENT
U.S. Patent Application No. 13/967,179
Attorney Ref: 17618CON5B (AP)
FOR DISCUSSION PURPOSES ONLY

37. (**Currently Amended**) A method of treating dry eye disease, the method comprising topically administering to the eye of [[[the]] a human in need thereof 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~~ 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 effective in treating dry eye disease.

60. (**Currently Amended**) A method of treating dry eye disease, the method comprising the step of topically administering to an eye of a human in need thereof an emulsion, the 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 effective in treating dry eye disease.

Docket No. 17618CON5B (AP)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Acheampong, *et al.*	Examiner: Marcela M Cordero Garcia
Serial No.: 13/967,179	Group Art Unit: 1658
Filed: August 14, 2013	Confirmation No. 8654
For: METHODS OF PROVIDING THERAPEUTIC EFFECTS USING CYCLOSPORIN COMPONENTS	Customer No.: 51957

RESPONSE TO NON FINAL OFFICE ACTION DATED OCTOBER 11, 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 11, 2013.

Amendments to the claims begin at page 2;

Summary of the Interview begins at page 7;

Remarks follow on page 8.

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 method of treating dry eye disease, the method comprising topically administering to the eye of ~~the~~ a human in need thereof 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~~ 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 effective in treating dry eye disease.

38. (Previously Presented) The method of Claim 37, wherein the emulsion further comprises a tonicity agent or a demulcent component.

39. (Previously Presented) The method of Claim 38, wherein the tonicity agent or the demulcent component is glycerine.

40. (Previously Presented) The method of Claim 37, wherein the emulsion further comprises a buffer.

41. (Previously Presented) The method of Claim 40, wherein the buffer is sodium hydroxide.

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

43. (Previously Presented) The method of Claim 37, wherein the emulsion comprises polysorbate 80 in an amount of about 1.0% by weight.

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

45. (Previously Presented) The method of Claim 37, wherein the emulsion further comprises glycerine in an amount of about 2.2% by weight and a buffer.

46. (Previously Presented) The method of Claim 45, wherein the buffer is sodium hydroxide.

47. (**Currently Amended**) The method of Claim 37, wherein, when the emulsion 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 cyclosporin A.

48. (Previously Presented) The method of Claim 42, wherein the emulsion has a pH in the range of about 7.2 to about 7.6.

49. (**Currently Amended**) The method of Claim 37, wherein the emulsion is as substantially therapeutically effective as a[[n]] second emulsion administered to a human in need thereof at a frequency of twice a day, the second emulsion comprising cyclosporin A in an amount of 0.1% by weight and castor oil in an amount of 1.25% by weight.

50. (**Currently Amended**) The method of Claim 37, wherein the emulsion achieves at least as much therapeutic effectiveness as a[[n]] second emulsion administered to a human in need thereof a frequency of twice a day, the second emulsion comprising

cyclosporin A in an amount of 0.1% by weight and castor oil in an amount of 1.25% by weight.

51. (**Currently Amended**) The method of Claim 37, 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 compared to a[[n]] second emulsion that contains only 50% as much castor oil.

52. (**Currently Amended**) The method of Claim 37, wherein the emulsion, when administered to the eye of a human, demonstrates a reduction in adverse events in the human, relative to a[[n]] second emulsion administered to a human in need thereof a frequency of twice a day, the second emulsion comprising cyclosporin A in an amount of 0.1% by weight and castor oil in an amount of 1.25% by weight.

53. (**Currently Amended**) The method of Claim 52, wherein the adverse events ~~include~~ are side effects.

54. (**Currently Amended**) A method of reducing side effects in a human ~~suffering from~~ being treated for dry eye syndrome, the method comprising the step of topically administering to the eye of the human in need thereof an emulsion at a frequency of twice a day, wherein the 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~~ acrylate/C10-30 alkyl acrylate cross-polymer 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;

wherein the topical ophthalmic emulsion has a pH in the range of about 7.2 to about 7.6.

55. (Previously Presented) The method of Claim 54, wherein the buffer is sodium hydroxide.

56. (Previously Presented) The method of Claim 54, wherein the tonicity component or the demulcent component is glycerine.

57. (**Currently Amended**) The method of Claim 54, wherein, when the emulsion is administered to the eye of a human ~~in an effective amount in~~ for treating dry eye syndrome, the blood of the human has substantially no detectable concentration of the cyclosporin A.

58. (Canceled)

59. (Previously Presented) The method of Claim 54, wherein the emulsion is effective in treating dry eye disease.

60. (**Currently Amended**) A method of treating dry eye disease, the method comprising the step of topically administering to an eye of a human in need thereof an emulsion at a frequency of twice a day, the 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 effective in treating dry eye disease.

61. (Previously Presented) The method of Claim 60, wherein the emulsion has a pH in the range of about 7.2 to about 7.6.

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 method were presented. Data and information regarding the claimed method'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).

Proposed Amendments

It was proposed to amend Claims 54 to recite a range of pH in the claimed method.

Principal Arguments and Other Matters

The Applicants presented data demonstrating unexpected results, commercial success, and satisfaction of a long felt need of the claimed methods. 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 data and arguments discussed at the interview.

REMARKS

This Reply responds to the Office Action sent October 11, 2013 , in which the Office Action rejected Claims 37-61. Claim 58 is newly cancelled. Claims 37, 44, 47, 49-54, 57, and 60 have been amended. Thus, Claims 37-57 and 59-61 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 37-61 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 37-61 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 methods 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 Methods Provide Surprising and Unexpected Results

As discussed in the interview with the Examiner, the claimed methods 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 methods 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 methods 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 methods demonstrated an *8-fold* increase in relative efficacy for the Schirmer Tear Test ("STT") 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 methods 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.