U.S. PTO
11/897177
08/28/2007

082807 01919 U.S. PTO

UTILITY PATENT APPLICATION TRANSMITTAL

(Only for new nonprovisional applications under 37 CFR 1.53(b))

Attorney Docket No.	D-3111 CON
First Inventor	Acheampong et al.
Title	Methods of Providing Therapeutic Effects Using Cyclosporin Components
Express Mail Label No.	EV 516292203 US

APPLICATION ELEMENTS

See MPEP chapter 600 concerning utility patent application contents

1. ☒ **Fee Transmittal Form** (e.g., PTO/SB/17)
2. ☐ **Applicant claims small entity status.** See 37 CFR 1.27
3. ☒ **Specification** [*Total Pages* 34]
   Both the claims and abstract must start on a new page.
   (For information on the preferred arrangement, see MPEP 608.01(a))
4. ☐ **Drawing(s)** (*35 U.S.C. 113*) [*Total Sheets*]
5. ☒ **Oath or Declaration** [*Total Sheets* 2]
   a. ☐ Newly executed (original or copy)
   b. ☒ A copy from a prior application (37 CFR 1.63(d)) *(for continuation/divisional with Box 18 completed)*
      i. ☐ DELETION OF INVENTOR(S)
      Signed statement attached deleting inventor(s) name in the prior application, see 37 CFR 1.63(d)(2) and 1.33(b)
6. ☒ **Application Data Sheet**. See 37 CFR 1.76
7. ☐ **CD-ROM or CD-R** in duplicate, large table or Computer Program (*Appendix*)
   ☐ Landscape Table on CD
8. **Nucleotide and/or Amino Acid Sequence Submission** (*if applicable, items a.-c. are required*)
   a. ☐ Computer Readable Form (CRF)
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      ii. ☐ Paper
   c. ☐ Statements verifying identity of above copies

ADDRESS TO: **Commissioner for Patents**
P.O. Box 1450
Alexandria VA 22313-1450

ACCOMPANYING APPLICATION PARTS

9. ☒ **Assignment Papers** (cover sheet & document(s))
   Name of Assignee Allergan, Inc.
10. ☐ **37 CFR 3.73(b) Statement** (*when there is an assignee*) ☐ **Power of Attorney**
11. ☐ **English Translation Document** (*if applicable*)
12. ☐ **Information Disclosure Statement** (PTO/SB/08 or PTO-1449)
    ☐ Copies of citations attached
13. ☐ **Preliminary Amendment**
14. ☒ **Return Receipt Postcard** (MPEP 503) (*Should be specifically itemized*)
15. ☐ **Certified Copy of Priority Document(s)** (*if foreign priority is claimed*)
16. ☐ **Nonpublication Request** under 35 U.S.C. 122(b)(2)(B)(i). Applicant must attach form PTO/SB/35 or equivalent.
17. ☐ **Other**

18. If a CONTINUING APPLICATION, *check appropriate box, and supply the requisite information below and in the first sentence of the specification following the title, or in an Application Data Sheet under 37 CFR 1.76:*

☒ Continuation ☐ Divisional ☒ Continuation-in-part (CIP) of prior application No.: 10/927,857

Prior application information: *Examiner* Cordero Garcia, Marcela *Art Unit* 1654

19. CORRESPONDENCE ADDRESS

☒ The address associated with Customer Number: 33197 *OR* ☐ Correspondence address below

Name					
Address					
City		State		Zip Code	
Country		Telephone		Fax	

Signature	Carlos A. Fisher	*Date*	August 28, 2007
Name (Print/Type)	Carlos A. Fisher	*Registration No. (Attorney/Agent)*	36,510

FEE TRANSMITTAL for FY 2005

Patent fees are subject to annual revision.

☐ Application claims small entity status. See 37 CFR 1.27

TOTAL AMOUNT OF PAYMENT ($) 1400.00

Complete if Known	
Application Number	Not yet known
Filing Date	Herewith
First Named Inventor	Acheampong et al.
Examiner Name	N/A
Art Unit	N/A
Attorney Docket No.	D-3111 CON

METHOD OF PAYMENT *(check all that apply)*

☐ Check ☐ Credit Card ☐ Money Order ☐ None ☐ Other (please identify): ____

☒ Deposit Account Deposit Account Number 01-0885 Deposit Account Name Allergan

For the above-identified deposit account, the Director is hereby authorized to: *(check all that apply)*

☒ Charge fee(s) indicated below ☐ Charge fee(s) indicated below, **except for the filing fee**

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FEE CALCULATION

1. BASIC FILING, SEARCH, AND EXAMINATION FEES

	FILING FEES		SEARCH FEES		EXAMINATION FEES		
		Small Entity		Small Entity		Small Entity	
Application Type	**Fee ($)**	**Fee ($)**	**Fee ($)**	**Fee ($)**	**Fee ($)**	**Fee ($)**	**Fees Paid ($)**
Utility	300	150	500	250	200	100	1000
Design	200	100	100	50	130	65	
Plant	200	100	300	150	160	80	
Reissue	300	150	500	250	600	300	
Provisional	200	100	0	0	0	0	

Subtotal (1) ____

2. EXCESS CLAIM FEES

Fee Description	Fee ($)	Small Entity Fee ($)
Each claim over 20 or, for Reissues, each claim over 20 and more than in the original patent	50	25
Each independent claim over 3 or, for Reissues, each independent claim more than in the original patent	200	100
Multiple Dependent Claims	360	180

Total Claims		Extra Claims		Fee ($)		Fee Paid ($)
24	-20 or HP =	4	x	50		200

HP = highest number of total claims paid for, if greater than 20

Indep. Claims		Extra Claims		Fee ($)		Fee Paid ($)
4	-3 or HP =	1	x	200		200

HP = highest number of independent claims paid for, if greater than 3

Multiple Dependent Claims	
Fee ($)	**Fee Paid ($)**
____	____

Subtotal (2) **400**

3. APPLICATION SIZE FEE

If the specification and drawings exceed 100 sheets of paper, the application size fee due is $250 ($125 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).

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Subtotal (3) **0**

4. OTHER FEE(S)

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☐ Request for Continued Examination: $790 fee ($395 small entity discount)	
☐ Other: ____	

Subtotal (4) **0**

SUBMITTED BY

Name (Print/Type)	Carlos A. Fisher	*Registration No. (Attorney/Agent)*	36,510	*Telephone*	949-450-1750
Signature	Carlos A. Fisher			*Date*	August 28, 2007

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application No.	:	To be assigned	Confirmation No.
Applicant	:	Acheampong et al.	
Filed	:	Herewith	
Title	:	METHODS OF PROVIDING THERAPEUTIC EFFECTS USING CYCLOSPORIN COMPONENTS	
TC/A.U.	:	NA	
Examiner	:	NA	
Docket No.	:	D-3111 CON	
Customer No.	:	33197	

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EXPRESS MAIL CERTIFICATE

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Date: August 28, 2007

Respectfully submitted,

Shawnna Waddell

Shawnna Waddell
Assistant to Carlos A. Fisher
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Name (Print/Type)	Carlos A. Fisher	*Registration No. (Attorney/Agent)*	36,510

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SUBMITTED BY

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4 Venture, Suite 300
Irvine, California 92618
Telephone: 949-450-1750

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.

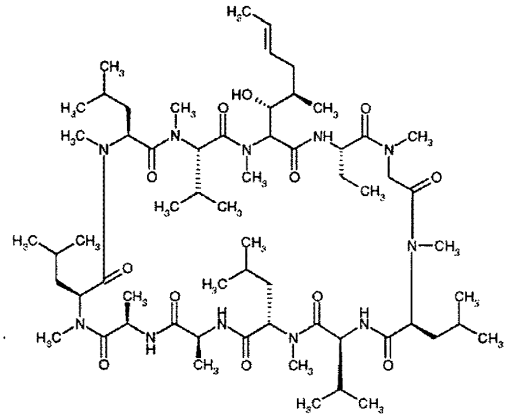
One ml of blood is acidified with 0.2 ml of 0.1 N HCl solution, then extracted with 5 ml of methyl t-butyl ether. After separation from the acidified aqueous layer, the organic phase is neutralized with 2 ml of 0.1 N NaOH, evaporated, reconstituted in a water/acetonitrile-based mobil phase, and injected 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

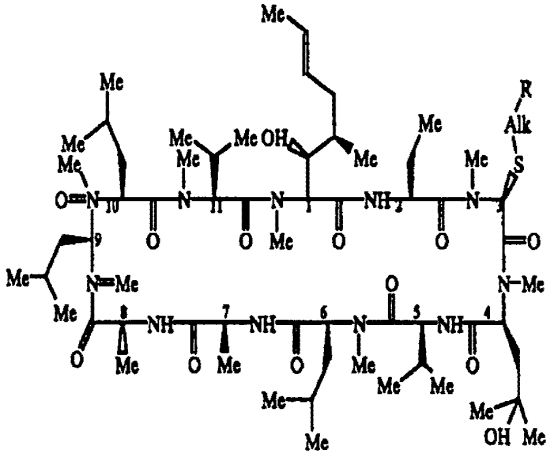


As used herein the term "derivatives" of a cyclosporin refer to compounds having structures sufficiently similar to the cyclosporin so as to function in a manner substantially similar to or substantially identical to the cyclosporin, for example, cyclosporin A, in the present methods. Included, without 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:

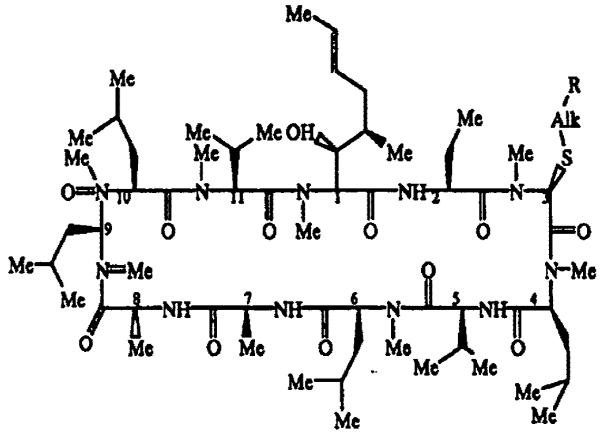
Formula II

(II)



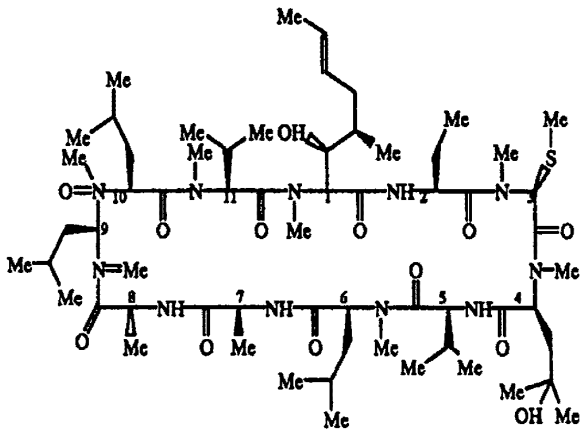
Formula III

(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.

DECLARATION FOR PATENT APPLICATION

D-3111

As a below named inventor, I hereby declare that:

My residence post office address and citizenship are as stated below next to my name.

I believe I am the original first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled **METHODS OF PROVIDING THERAPEUTIC EFFECTS USING CYCLOSPORIN COMPONENTS** the specification of which

(check one) [X] is attached hereto
[ ] was filed on
as US Application Serial Number or PCT International Application Number
and was amended on ___ (if applicable).

I hereby state that I have reviewed and understand the contents of the above identified specification, including the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose information which is material to the patentability as defined in 37 CFR § 1.56.
I hereby claim foreign priority benefits under 35 U.S.C. §119(a)-(d) or §365(b) of any foreign application(s) for patent or inventor's certificate, or §365(a) of any PCT International application which designated at least one country other than the United States, listed below and have also identified below any foreign application for patent or inventor's certificate, or PCT International application having a filing date before that of the application on which priority is claimed. **NONE**

I hereby claim the benefit under 35 U.S.C. §119(e) of any United States provisional application(s) listed below.

Serial No. 60/503,137, September 15, 2003

I hereby claim the benefit under 35 U.S.C. §120 of any United States application(s), or §365(c) of any PCT International application designation the United States, listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States or PCT International application in the manner provided by the first paragraph of 35 U.S.C. §112, I acknowledge the duty to disclose information which is material to patentability as defined in 37 CFR §1.56 which became available between the filing date of the prior application and the national or PCT International filing date of this application. **NONE**

I hereby appoint the following attorney(s) and/or agent(s) to prosecute this application and to transact all business in the Patent and Trademark Office connected therewith: Martin A. Voet, Reg. No. 25,208, Robert Baran, Reg. No. 25,806, Carlos A. Fisher, Reg. No. 36,510, Stephen Donovan, Reg. No. 33,433, Brent A. Johnson, Reg. No. 51,851, Dean G. Stathakis, Reg. No. 54,465, Frank J. Uxa, Reg. No. 25,612, Donald E. Stout, Reg. No. 34,493; Robert D. Buyan, Reg. No. 32,460; Kenton R. Mullins, Reg. No. 36,331; Jo Anne M. Ybaben, Reg. No. 42,243, Linda Allyson Fox, Reg. No. 38,883, and Greg S. Hollrigel, Reg. No. 45,374,

Address all telephone calls to Frank J. Uxa - Telephone: 949-450-1750
Address all correspondence to Frank J. Uxa
4 Venture, Suite 300
Irvine, CA 92618

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.

Full name of sole or first inventor (given name, family name) **ANDREW ACHEAMPONG**

Inventor's signature A Acheampong Date 8/12/04
Residence Irvine, California Citizenship U.S.A.
Post Office Address 16 Wintergreen
Irvine, CA 92604

Full name of second inventor (given name, family name) **DIANE TANG-LIU**

Inventor's signature Diane Tang-Liu Date 8-12-2004
Residence Newport Beach, California Citizenship U.S.A.
Post Office Address 2615 Blackthorn Street
Newport Beach, CA 92660

Continued... Docket No. D-3111

Full name of third Inventor (given name, family name) **JAMES N. CHANG**

Inventor's signature _____ Date 8/12/04
Residence Newport Beach, California Citizenship U.S.A.
Post Office Address 36 Cervantes
Newport Beach, CA 92660

Full name of fourth Inventor (given name, family name) **DAVID F. POWER**

Inventor's signature _____ Date 8/12/04
Residence Trabuco Canyon, California Citizenship U.S.A.
Post Office Address 28335 Quiet Hill Lane
Trabuco Canyon, CA 92679-1131

D-3111

ASSIGNMENT

WHEREAS, we, **ANDREW ACHEAMPONG**, of the County of Orange, State of California, **DIANE TANG-LIU**, of the County of Orange, State of California, **JAMES N. CHANG**, of the County of Orange, State of California and **DAVID F. POWER**, of the County of Orange, State of California, have invented certain new and useful improvements in **METHODS OF PROVIDING THERAPEUTIC EFFECTS USING CYCLOSPORIN COMPONENTS**, which said **ANDREW ACHEAMPONG**, has this 12 day of AUGUST, 2004, which said **DIANE TANG-LIU**, has this 12 day of AUGUST, 2004, which said **JAMES N. CHANG**, has this 12 day of AUGUST, 2004, and which said **DAVID F. POWER** has this 12 day of AUGUST, 2004, executed application papers for United States Letters Patent thereon; and

NOW, THEREFORE, in consideration of ONE DOLLAR ($1.00) and other valuable consideration paid to us by Allergan, Inc., having its principal place of business at 2525 Dupont Drive, Irvine, CA 92612, receipt of which is hereby acknowledged, and intending to be legally bound. we do hereby assign unto said Allergan, Inc., its successors, and assigns, the entire right, title and interest in and to the said invention, said executed application, any divisional, continuation and continuation-in-part of said application, and all Letters Patent of the United States and all foreign countries to be obtained therefore;

We further assign to said Allergan, Inc. the right, optionally in its own name or in the names of its related companies, to apply for, obtain and maintain in all countries foreign to the United States, patent and/or Utility Model applications for said invention, including the full right to claim for any such application the benefits of any priority rights based on said executed United States application;

And we agree to execute further instruments (including divisional, continuation, continuation-in-part or reissue applications or other instruments) proper to effectuate the premises, this agreement to be binding upon my heirs, executors, and administrators;

And we request the Commissioner of Patents and Trademarks of the United States, and any official of any country or countries foreign to the United States whose duty it is to issue patents on applications as aforesaid, to issue Letters Patent in accordance herewith.

Executed this 12 day of August, 2004.

A Acheampong
ANDREW ACHEAMPONG

State of California)
) ss
County of Orange)

On this 12th day of AUGUST, 2004, before me, MARY LOU MCNOWN, personally appeared **ANDREW ACHEAMPONG** ~~personally known to me or~~ proved to me on the basis of satisfactory evidence to be the person(s) whose name(s) ~~is/~~are subscribed to the within instrument and acknowledged to me that ~~he/she/they~~ executed the same in ~~his/her/their~~ authorized capacity~~(ies)~~, and that by ~~his/her/their~~ signature(s) on the instrument the person(s) or the entity upon behalf of which the person(s) acted, executed the instrument.

WITNESS my hand and official seal.

Mary Lou McNown
Notary Public

SEAL

MARY LOU MC NOWN
Commission # 1431736
Notary Public - California
Orange County
My Comm. Expires Aug 16, 2007

Executed this 12th day of August, 2004.

DIANE TANG-LIU

State of California)
) ss
County of Orange)

On this 12th day of AUGUST, 2004, before me, MARY LOU MC NOWN, personally appeared **DIANE TANG-LIU** ~~personally known to me or~~ proved to me on the basis of satisfactory evidence to be the person(s) whose name(s) ~~is/are~~ subscribed to the within instrument and acknowledged to me that ~~he/she/they~~ executed the same in ~~his/her/their~~ authorized capacity(~~ies~~), and that by ~~his/her/their~~ signature(s) on the instrument the person(s) or the entity upon behalf of which the person(s) acted, executed the instrument.

WITNESS my hand and official seal.

Mary Lou Mc Nown
Notary Public

MARY LOU MC NOWN
Commission # 1431736
Notary Public - California
Orange County
My Comm. Expires Aug 16, 2007

SEAL

Executed this 12 day of August, 2004.

JAMES N. CHANG

State of California)
) ss
County of Orange)

On this 12th day of AUGUST, 2004, before me, MARY LOU MC NOWN, personally appeared **JAMES N. CHANG** ~~personally known to me or~~ proved to me on the basis of satisfactory evidence to be the person(s) whose name(s) ~~is/are~~ subscribed to the within instrument and acknowledged to me that ~~he/she/they~~ executed the same in ~~his/her/their~~ authorized capacity(~~ies~~), and that by ~~his/her/their~~ signature(s) on the instrument the person(s) or the entity upon behalf of which the person(s) acted, executed the instrument.

WITNESS my hand and official seal.

Mary Lou Mc Nown
Notary Public

SEAL

MARY LOU MC NOWN
Commission # 1431736
Notary Public - California
Orange County
My Comm. Expires Aug 16, 2007

Executed this 12 day of August, 2004.

DAVID F. POWER

State of California)
) ss
County of Orange)

On this 12th day of AUGUST, 2004, before me, MARY LOU McNOWN, personally appeared **DAVID F. POWER** ~~personally known to me or~~ proved to me on the basis of satisfactory evidence to be the person(s) whose name(s) is/are subscribed to the within instrument and acknowledged to me that he/she/they executed the same in his/her/their authorized capacity(ies), and that by his/~~her/their~~ signature(s) on the instrument the person(s) or the entity upon behalf of which the person(s) acted, executed the instrument.

WITNESS my hand and official seal.

Notary Public

SEAL

MARY LOU MC NOWN
Commission # 1451736
Notary Public - California
Orange County
My Comm. Expires Aug 16, 2007

APPLICATION DATA SHEET

Inventor Information

Inventor One Given Name::	Andrew
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City::	Irvine
State or Province::	CA
Postal or Zip Code::	92604
Citizenship Country::	USA

Inventor Two Given Name::	Diane
Family Name::	Tang-Liu
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State or Province::	CA
Postal or Zip Code::	92660
Citizenship Country::	USA

Inventor Three Given Name::	James N.
Family Name::	Chang
Postal Address Line One::	36 Cervantes
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State or Province::	CA
Postal or Zip Code::	92660
Citizenship Country::	USA

Inventor Four Given Name::	David F.
Family Name::	Power
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City::	Trabuco Canyon
State or Province::	CA
Postal or Zip Code::	92679
Citizenship Country::	USA

Correspondence Information

USPTO Customer No.::	33197
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City::	Irvine
State or Province::	CA
Postal or Zip Code::	92618
Telephone::	949-450-1750
Fax::	949-450-1764
Electronic Mail::	fjuxa@patlawyers.com

Application Information

Title Line One::	METHODS OF PROVIDING THERAPEUTIC
Title Line Two::	EFFECTS USING CYCLOSPORIN COMPONTNTS
Total Drawing Sheets::	
Formal Drawings?::	
Application Type::	Utility

Representative Information

Registration Number One::	Martin A. Voet 25,208
Registration Number Two::	Robert Baran 25,806
Registration Number Three:	Carlos A. Fisher.....36,510
Registration Number Four::	Stephen Donovan 33,433
Registration Number Five::	Brent A. Johnson 51,851
Registration Number Six::	Dean G. Stathakis 54,465
Registration Number Seven::	Frank J. Uxa, Jr..... 25,612
Registration Number Eight::	Donald E. Stout 34,493
Registration Number Nine::	Robert D. Buyan 32,460
Registration Number Ten::	Kenton R. Mullins 36,331
Registration Number Eleven::	JoAnne M. Ybaben 42,243
Registration Number Twelve::	Linda Allyson Fox..... 38,883
Registration Number Thirteen::	Greg S. Hollrigel 45,374

Continuity Information

This application is a::	Continuation
>Application Two::	10/927,857
Filing Date::	August 27, 2004
This application claims the Benefit of::	
>Application One::	60/503,137
Filing Date::	September 15, 2003

Assignment Information

Assignee Name One::	Allergan, Inc.
Postal Address Line One::	2525 Dupont Drive
Postal Address Line Two::	
City::	Irvine
State or Province::	CA
Postal or Zip Code::	92612

PATENT APPLICATION SERIAL NO._____

U.S. DEPARTMENT OF COMMERCE
PATENT AND TRADEMARK OFFICE
FEE RECORD SHEET

08/31/2007 WASFAW1 00000009 010885 11897177

01 FC:1011	300.00	DA
02 FC:1111	500.00	DA
03 FC:1311	200.00	DA
04 FC:1202	800.00	DA

PTO-1556
(5/87)

*U.S. Government Printing Office: 2002- 489-267/69033

PTO/SB/06 (02-07)
Approved for use through 02/28/2007. OMB 0651-0032
U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

PATENT APPLICATION FEE DETERMINATION RECORD

Substitute for Form PTO-875

Application or Docket Number: 11897177

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	$150		N/A	$300
SEARCH FEE (37 CFR 1.16(k), (l), or (m))	N/A	N/A	N/A	$250		N/A	$500
EXAMINATION FEE (37 CFR 1.16(o), (p), or (q))	N/A	N/A	N/A	$100		N/A	$200
TOTAL CLAIMS (37 CFR 1.16(i))	36 minus 20 =	16	x $25 =		OR	x $50 =	800
INDEPENDENT CLAIMS (37 CFR 1.16(h))	2 minus 3 =	—	x $100 =			x $200 =	
APPLICATION SIZE FEE (37 CFR 1.16(s))	If the specification and drawings exceed 100 sheets of paper, the application size fee due is $250 ($125 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).		$125			$250	
MULTIPLE DEPENDENT CLAIM PRESENT (37 CFR 1.16(j))			+180 =			+360 =	
* If the difference in column 1 is less than zero, enter "0" in column 2.			TOTAL			TOTAL	1800

APPLICATION AS AMENDED – PART II

AMENDMENT A	(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 ($)	OTHER THAN SMALL ENTITY ADDITIONAL FEE ($)
Total (37 CFR 1.16(i))	*	Minus	**	=	x $25 =		OR	x $50 =	
Independent (37 CFR 1.16(h))	*	Minus	***	=	x $100 =		OR	x $200 =	
Application Size Fee (37 CFR 1.16(s))					$125			$250	
FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))					+180 =		OR	+360 =	
					TOTAL ADD'L FEE		OR	TOTAL ADD'L FEE	

AMENDMENT B	(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA	RATE ($)	ADDITIONAL FEE ($)	OR	RATE ($)	ADDITIONAL FEE ($)
Total (37 CFR 1.16(i))	*	Minus	**	=	x $25 =		OR	x $50 =	
Independent (37 CFR 1.16(h))	*	Minus	***	=	x $100 =		OR	x $200 =	
Application Size Fee (37 CFR 1.16(s))					$125			$250	
FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))					+180 =		OR	+360 =	
					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 number 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	GRP ART UNIT	FIL FEE REC'D	ATTY.DOCKET.NO	TOT CLAIMS	IND CLAIMS
11/897,177	08/28/2007	1654	1800	D-3111 CON	36	2

CONFIRMATION NO. 3860

33197
STOUT, UXA, BUYAN & MULLINS LLP
4 VENTURE, SUITE 300
IRVINE, CA92618

FILING RECEIPT

Date Mailed: 09/14/2007

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 write to the Office of Initial Patent Examination's Filing Receipt Corrections. 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**

Applicant(s)

Andrew Acheampong, Irvine, CA;
Diane Tang-Liu, Newport Beach, CA;
James N. Chang, Newport Beach, CA;
David F. Power, Trabuco Canyon, CA;

Assignment For Published Patent Application

Allergan, Inc., Irvine, CA

Power of Attorney: None

Domestic Priority data as claimed by applicant

This application is a CON of 10/927,857 08/27/2004
which claims benefit of 60/503,137 09/15/2003

Foreign Applications

If Required, Foreign Filing License Granted: 09/14/2007

The country code and number of your priority application, to be used for filing abroad under the Paris Convention, is **US11/897,177**

Projected Publication Date: 12/27/2007

Non-Publication Request: No

Early Publication Request: No

Title

Methods of providing therapeutic effects using cyclosporin compontnts

Preliminary Class

514

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 (1-866-999-4158).

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).

RECEIVED
CENTRAL FAX CENTER
NOV 02 2007

TRANSMITTAL FORM

(to be used for all correspondence after initial filing)

Application Number	11/897,177
Filing Date	August 28, 2007
First Named Inventor	Acheampong et al.
Group Art Unit	1654
Examiner Name	Unknown
Total Number of Pages in This Submission: 5	Attorney Docket Number: D-3111CON

ENCLOSURES (*check all that apply*)

- ☐ Fee Transmittal Form *(in duplicate)*
- ☐ Fee Attached
- ☐ Amendment/Reply
- ☐ After Final
- ☐ Affidavits/declaration(s)
- ☐ Extension of Time Request
- ☐ Express Abandonment Request
- ☐ Information Disclosure Statement
- ☐ Certified Copy of Priority Document(s)
- ☐ Response to Missing Parts/ Incomplete Application
- ☐ Response to Missing Parts under 37 CFR 1.52 or 1.53
- ☐ Drawing(s)
- ☐ Licensing-related Papers
- ☐ Petition
- ☐ Petition to Convert to a Provisional Application
- ☐ Power of Attorney, Revocation Change of Correspondence Address
- ☐ Terminal Disclaimer
- ☐ Request for Refund
- ☐ CD, Number of CD(s) ____
- ☐ Landscape Table on CD
- ☐ After Allowance Communication to TC
- ☐ Appeal Communication to Board of Appeals and Interferences
- ☐ Appeal Communication to TC *(Appeal Notice, Brief, Reply Brief)*
- ☐ Proprietary Information
- ☐ Status Letter
- ☒ Other Enclosure(s) *(please identify below)*

Request for Corrected Filing Receipt

Remarks

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

Firm Name	Stout, Uxa, Buyan & Mullins, LLP		
Signature			
Printed Name	Carlos A. Fisher		
Date	November 2, 2007	Reg. No.	36,510

CERTIFICATE OF TRANSMISSION/MAILING

I hereby certify that this correspondence is being facsimile transmitted to the USPTO at fax number 571-273-8300, or deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Mail Stop Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on the date shown below.

Signature			
Typed or printed name	Shawnna Waddell	Date	Nov. 2, 2007

D-3111CON

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

PATENT

In re application of:
ACHEAMPONG et al) Group Art Unit: 1654
)
Serial No. 11/897,177) Examiner: N/A
)
Filed: August 28, 2007)
)
For: METHODS OF PROVIDING THERAPEUTIC)
EFFECTS USING CYCLOSPORIN)
COMPONENTS)

CERTIFICATE OF FACSIMILE TRANSMISSION

I hereby certify that this correspondence is being transmitted via facsimile to: Commissioner for Patents, PO Box 1450, Alexandria, VA 22313-1450, to fax number 571-273-8300, on the date indicated below

November 1, 2007
Date

Shawnna Waddell

REQUEST FOR CORRECTED FILING RECEIPT

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

Dear Sir:

Please issue a corrected Filing Receipt in the above-identified application to read as follows with regard to the TITLE:

Please change: "Methods of providing therapeutic effects using cyclosporin compontnts"

to: --Methods of providing therapeutic effects using cyclosporin components--.

Therefore, applicant requests that a corrected filing receipt be issued, as set forth above, to properly identify the title. A copy of the filing receipt is enclosed.

Respectfully submitted,

Carlos A. Fisher
Attorney for Applicant
Reg. No. 36,510
4 Venture, Suite 300
Irvine, CA 92618
(949) 450-1750
Facsimile (714) 450-1764

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

APPL NO.	FILING OR 371(c) DATE	ART UNIT	FIL FEE REC'D	ATTY.DOCKET NO	TOT CLMS	IND CLMS
11/897,177	08/28/2007	1654	1800	D-3111 CON	36	2

CONFIRMATION NO. 3860

83197
STOUT, UXA, BUYAN & MULLINS LLP
4 VENTURE, SUITE 300
IRVINE, CA 92618

FILING RECEIPT

"OC000000025840055"

Date Mailed: 09/14/2007

Receipt is acknowledged of this nonprovisional 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 write to the Office of Initial Patent Examination's Filing Receipt Corrections. 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 (if appropriate).**

Applicant(s)

Andrew Acheampong, Irvine, CA;
Diane Tang-Liu, Newport Beach, CA;
James N. Chang, Newport Beach, CA;
David F. Power, Trabuco Canyon, CA;

Assignment For Published Patent Application

Allergan, Inc., Irvine, CA

Power of Attorney: None

Domestic Priority data as claimed by applicant

This application is a CON of 10/927,857 08/27/2004
which claims benefit of 60/503,137 09/15/2003

Foreign Applications

If Required, Foreign Filing License Granted: 09/14/2007

The country code and number of your priority application, to be used for filing abroad under the Paris Convention, is US11/897,177

Projected Publication Date: 12/27/2007

Non-Publication Request: No

Early Publication Request: No

Title

Methods of providing therapeutic effects using cyclosporin compontnts

Preliminary Class

514

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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.

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APPLICATION NUMBER	FILING or 371(c) DATE	GRP ART UNIT	FIL FEE REC'D	ATTY.DOCKET.NO	TOT CLAIMS	IND CLAIMS
11/897,177	08/28/2007	1646	1800	D-3111 CON	36	2

CONFIRMATION NO. 3860

33197
STOUT, UXA, BUYAN & MULLINS LLP
4 VENTURE, SUITE 300
IRVINE, CA 92618

CORRECTED FILING RECEIPT

OC000000026639371

Date Mailed: 11/13/2007

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D-3111CON

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

PATENT

In re application of:
ACHEAMPONG et al.) Group Art Unit: 1654
)
Serial No. 11/897,177) Examiner: N/A
)
Filed: August 28, 2007)
)
For: METHODS OF PROVIDING THERAPEUTIC EFFECTS USING CYCLOSPORIN COMPONENTS)

CERTIFICATE OF MAILING OR FACSIMILE TRANSMISSION
I hereby certify that this correspondence is being facsimile transmitted to the Patent and Trademark Office fax number 571-273-8300, or mailed by first class mail to the Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on or before:

November 14, 2007
Date
Alicia Curran

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

INFORMATION DISCLOSURE STATEMENT

Dear Sir:

Applicant wishes to call to the attention of the Examiner the documents cited on the accompanying Form PTO-1449. No concession is made that these documents are prior art, and applicant expressly reserves the right to antedate the documents as may be appropriate. Applicant requests that each of these documents be made of record in the above-identified application.

Each of the patents and publications cited on the accompanying Form PTO-1449 were cited in related (parent) application Serial No. 10/927,857 filed August 27, 2004. Therefore, no copies of these patents and publications are submitted herewith.

Respectfully submitted,

Carlos A. Fisher
Attorney for Applicant
Reg. No. 36,510
4 Venture, Suite 300
Irvine, CA 92618
(949) 450-1750
Facsimile (949) 450-1764

CAF/ac

Form PTO-1449

INFORMATION DISCLOSURE CITATION IN AN APPLICATION
(Use several sheets if necessary)

Docket No.: D-3111CON	Application No.: 11/897,177
Applicant: Acheampong et al.	
Filing Date: August 28, 2007	Group Art Unit: 1654

U. S. PATENT DOCUMENTS

EXAMINER INITIAL	DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE
	3,278,447	10/1966	McNicholas			
	4,388,307	06/1983	Cavanak			
	4,649,047	03/1987	Kaswan			
	4,814,323	3/1989	Andrieu			
	4,839,342	06/1989	Kaswan			
	4,970,076	11/1990	Horrobin			
	4,990,337	02/1991	Kurihara et al.			
	4,996,193	02/1991	Hewitt et al.			
	5,286,730	02/1994	Caufield et al.			
	5,286,731	02/1994	Caufield et al.			
	5,342,625	08/1994	Hauer et al.			
	5,411,952	05/1995	Kaswan			

FOREIGN PATENT DOCUMENTS

	DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION YES	TRANSLATION NO

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

	AA	Acheampong et al, "Cyclosporine Distribution into the Conjunctiva, Cornea, Lacrimal Gland, and Systemic Blood Following Topical Dosing of Cyclosporine to Rabbit, Dog, and Human Eyes," *Lacrimal Gland, Tear Film, and Dry Eye Syndromes 2 - Basic Science and Clinical Relevance, Plenum Press, New York & London, ©1998, pp. 1001-1004.*
	AB	Acheampong et al, "Distribution of Cyclosporin A in Ocular Tissues After Topical Administration to Albino Rabbits and Beagle Dogs", *Curr Eye Res, Feb 1999, 18(2):91-103b.*
	AC	Angelov et al, "Preclinical Safety Studies of Cyclosporine Ophthalmic Emulsion," *Lacrimal Gland, Tear Film, and Dry Eye Syndromes 2 - Basic Science and Clinical Relevance, Plenum Press, New York & London, ©1998, pp. 991-5.*
	AD	Brewster et al, "Enhanced Delivery of Ganciclovir to the Brain through the Use of Redox Targeting", *Antimicrobial Agents and Chemotherapy, April 1994, 38(4):817-823.*
	AE	Brewster et al, "Intravenous and Oral Pharmacokinetic Evaluation of a 2-Hydroxypropyl-β-cyclodextrin-Based Formulation of Carbamazepine in the Dog: Comparison with Commercially Available Tablets and Suspensions," *J Pharm Sci, March 1997, 86(3):335-9.*

EXAMINER	DATE CONSIDERED

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Form PTO-1449	Docket No.: D-3111CON	Application No.: 11/897,177
INFORMATION DISCLOSURE CITATION IN AN APPLICATION (Use several sheets if necessary)	Applicant: Acheampong et al.	
	Filing Date: August 28, 2007	Group Art Unit: 1654

U. S. PATENT DOCUMENTS

EXAMINER INITIAL	DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE
	5,474,979	12/1995	Ding et al.			
	5,504,068	04/1996	Komiya et al.			
	5,540,931	07/1996	Hewitt et al.			
	5,719,123	02/1998	Morley et al.			
	5,739,105	04/1998	Kim et al.			
	5,807,820	09/1998	Elias			
	5,843,452	12/1998	Wiedmann et al.			
	5,843,891	12/1998	Sherman			
	5,858,401	01/1999	Bhalani et al.			
	5,866,159	02/1999	Hauer et al.			
	5,891,846	04/1999	Ishida et al.			
	5,916,589	06/1999	Hauer et al.			

FOREIGN PATENT DOCUMENTS

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OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

	AA	Brewster et al, "Preparation, Characterization, and Anesthetic Properties of 2-Hydroxypropyl-β - cyclodextrin Complexes of Pregnanolone and Pregnenolone in Rat and Mouse", *J Pharm Sci, October 1995, 84(10):1154-9.*
	AB	Sall et al, "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", *Ophthalmology, April 2000, 107(4):631-9.*
	AC	Small 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", *J Ocul Pharmacol Ther, Oct 2002, 18(5):411-8.*
	AD	Stevenson et al., "Efficacy and Safety of Cyclosporin A Ophthalmic Emulsion in the Treatment of Moderate-to-severe Dry Eye Disease", *Ophthalmology, May 2000, 107(5):967-74.*
	AE	
	AF	

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INFORMATION DISCLOSURE CITATION IN AN APPLICATION
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	5,951,971	09/1999	Kawashima et al.			
	5,962,017	10/1999	Hauer et al.			
	5,981,479	11/1999	Ko et al.			
	5,981,607	11/1999	Ding et al.			
	5,998,365	12/1999	Sherman			
	6,008,191	12/1999	Singh et al.			
	6,008,192	12/1999	Al-Razzak et al.			
	6,022,852	02/2000	Klokkers et al.			
	6,024,978	02/2000	Hauer et al.			
	6,046,163	04/2000	Stuchlik et al.			
	6,159,933	12/2000	Sherman			
	6,254,860	07/2001	Garst			
	6,323,204	11/2001	Burke et al.			

FOREIGN PATENT DOCUMENTS

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U. S. PATENT DOCUMENTS

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	6,346,511	02/2002	Singh et al.			
	6,350,442	02/2002	Garst			
	6,413,547	07/2002	Bennett et al.			
	6,420,355	07/2002	Richter et al.			
	6,468,968	10/2002	Cavanak et al.			
	6,486,124	11/2002	Olbrich et al.			
	2001/0014665	08/2001	Fisher et al.			
	2003/0021816	01/2003	Kang et al.			
	2003/0044452	03/2003	Ueno			
	2003/0060402	03/2003	Cavanak et al.			
	2003/0087813	05/2003	Or et al			
	2003/0104992	06/2003	Or et al			
	2003/0109425	06/2003	Or et al			
	2003/0109426	06/2003	Or et al.			
	2003/0143250	07/2003	Hauer et al.			

FOREIGN PATENT DOCUMENTS

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PATENT AND TRADEMARK OFFICE
FORM PTO-1449

LIST OF ART CITED BY APPLICANT

ATTY. DOCKET: D-3111CON	SERIAL NO.: 11/897,177
APPLICANT: Acheampong et al	TITLE: Methods of Providing Therapeutic Effects Using Cyclosporin Components
FILING DATE: August 28, 2007	GROUP: 1654

U.S. PATENT DOCUMENTS

*EXAMINER INITIAL		DOCUMENT NO.	DATE	NAME	CLASS	SUB-CLASS	FILING DATE (if applicable)
	AA	4,614,736	09/1986	Delevallee et al.			
	AB	5,368,854	11/1994	Rennick			
	AC	6,872,705	03/2005	Lyons			
	AD	2001/0036449 A1	11/2001	Garst			
	AE	2003/0055028 A1	03/2003	Stergiopoulos et al.			
	AF						

FOREIGN PATENT DOCUMENTS

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	BA	DE 19810655	09/1999	Germany			
	BB	WO 03/030834	04/2003	PCT			
	BC						

OTHER ART
(Including Author, Title, Date, Pertinent Pages, etc.)

	CA	T.A. Winter, et al. Scand J Gastroenterol. (1993), 28(8), pages 701-704
	CB	M. Schwab and U. Klotz, Clin. Pharmacokinet. (2001), 40(10), pages 723-751
	CC	J. Rudinger. In: Peptide Hormones, JA Parsons, Ed. (1976) pages 1-7
	CD	D.E. Smilek, et al. Proc. Natl. Acad. Sci. USA (1991) 88, pages 9633-9637
	CE	MBanić, et al. Dig. Dis. Sci. (2002), 47(6), pages 1362-1368
	CF	The Online Medical Dictionary, accessed 7/7/05 and 7/13/05. 6 pages
	CG	W.J. Sandborn, et al. Am. J. Gastroenterol. (1993), 88(5), pages 640-645
	CH	D.H. Present. Am. J. Gastroenterol. (1993) 88(5), pages 627-630
	CI	S. Ardizzone and G.B. Porro. Drugs. (1998), 55(4), pages 519-542
	CJ	W.J. Sandborn, et al. Gastroenterology. (1994), 106(6), pages 1429-1435
	CK	K. Tsubota, et al. Invest. Ophthalmol. Vis. Sci. (1998), 39(9), pages 1551-1559
	CL	A.A. Drosos and N.M. Moutsopoulos. Ter. Arkh. (1998), 60(4), pages 77-80
	CM	A.A. Drosos, et al. Scand. J. Rheumatology (1986) Suppl. 61, pages 246-249
	CN	W.A. van der Reijden, et al. Ann. Rheum. Dis. (1999), 58, pages 465-473
	CO	N.A. Robinson and D. Wray. Australian Dental Journal (2003), 48(4), pages 206-211
	CP	A.M. Pedersen and B. Nauntofte. Expert Opin Pharmacother (2001), 2(9), pages 1415-1436

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	CQ	D.E. Lopatin. Chemical compositions and functions of Saliva. 8/24/2001, 31 pages
	CR	Gunduz et al, "Topical Cyclosporin Treatment of Keratoconjunctivitis Sicca in Secondary Sjogren's Syndrome", Acta Ophthalmologica, Vol. 72, No. 4, 1994, pp 438-442, XP009063039
	CS	Phillips et al, "Cyclosporine Has A Direct Effect on the Differentiation of a Mucin-Secreting Cell Line", Journal of Cellular Physiology, Vol. 184, No. 3, Sept. 2000, pp 400-408, XP009063023
	CT	Gipson et al, "Character of Ocular Surface Mucins and Their Alteration in Dry Eye Disease", The Ocular Surface, Vol. 2, No. 2, April 2004, pp 131-148, XP001208377
	CU	Akpek et al, "A Randomized Trial of Topical Cyclosporin 0.05% in Topical Steroid-Resistant Atopic Keratoconjunctivitis", Ophthalmology, Vol. III, No. 3, March 2004, pp 476-482, XP00906021
	CV	Eisen et al, "Topical Cyclosporine for Oral Mucosal Disorders", Journal of the American Academy of Dermatology, Vol. 23, No. 6, Part 2, Dec. 1990, pp 1259-1264, XP009063043
	CW	Epstein et al, "Topical Cyclosporine in a Bioadhesive for Treatment of Oral Lichenoid Mucosal Reactions. An Open Label Clinical Trial", Oral Surgery, Oral Medicine..., Vol. 82, No. 5, 1996, pp 532-536, XP009063045
	CX	Erdmann et al, "Pemphigus Vulgaris Der Mund-Und Kehlopfschleimhaut Pemphigus Vulagris of the Oral Mucosa and the Larynx", H+G Zeitschrift Fuer Hautkrankheiten, Vol. 72. No. 4, 1997, pp 283-296, XP009063042
	CY	Brinkmeier et al, "Pyodermatitis-Pyostomatitis Vegetans: A Clinical Course of Two Decades with Response to Cyclosporine and Low-Dose Prednisolone", Acta Dermato-Venereologica, Vol. 81, No. 2, May 2001, pp 134-136
	CZ	Gremse et al, "Ulcerative Colitis in Children. Medical Management", Pediatric Drugs, Vol. 4, No. 12, 2002, pp 807-815, XP009063025
	CAA	Gaeta G.M. et al, "Cyclosporin bioadhesive gel in the topical treatment of erosive lichen planus" International Journal of Immunopathology and Pharmacology, Vol. 7, No. 2, 1994, pages 125-132.
	CBB	Kuwano et al., "Cyclosporine A Formulation Affects its Ocular Distribution in Rabbits", Pharm Res., January 2002, Vol. 19, No. 1, pages 108-111.
	CCC	Ding et al., Cyclosporine Ophthalmic o/w Emulsion: Formulation and Emulsion Characterization. Pharmaceutical Research 1997. 14(11, suppl):S41 (2 pages).

EXAMINER_____ DATE CONSIDERED _____

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

UNITED STATES PATENT AND TRADEMARK OFFICE

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APPLICATION NUMBER	FILING OR 371(c) DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO./TITLE
11/897,177	08/28/2007	Andrew Acheampong	D-3111 CON

CONFIRMATION NO. 3860

33197
STOUT, UXA, BUYAN & MULLINS LLP
4 VENTURE, SUITE 300
IRVINE, CA92618

Title: Methods of providing therapeutic effects using cyclosporin components

Publication No. US-2007-0299004-A1
Publication Date: 12/27/2007

NOTICE OF PUBLICATION OF APPLICATION

The above-identified application will be electronically published as a patent application publication pursuant to 37 CFR 1.211, et seq. The patent application publication number and publication date are set forth above.

The publication may be accessed through the USPTO's publically available Searchable Databases via the Internet at www.uspto.gov. The direct link to access the publication is currently http://www.uspto.gov/patft/.

The publication process established by the Office does not provide for mailing a copy of the publication to applicant. A copy of the publication may be obtained from the Office upon payment of the appropriate fee set forth in 37 CFR 1.19(a)(1). Orders for copies of patent application publications are handled by the USPTO's Office of Public Records. The Office of Public Records can be reached by telephone at (703) 308-9726 or (800) 972-6382, by facsimile at (703) 305-8759, by mail addressed to the United States Patent and Trademark Office, Office of Public Records, Alexandria, VA 22313-1450 or via the Internet.

In addition, information on the status of the application, including the mailing date of Office actions and the dates of receipt of correspondence filed in the Office, may also be accessed via the Internet through the Patent Electronic Business Center at www.uspto.gov using the public side of the Patent Application Information and Retrieval (PAIR) system. The direct link to access this status information is currently http://pair.uspto.gov/. Prior to publication, such status information is confidential and may only be obtained by applicant using the private side of PAIR.

Further assistance in electronically accessing the publication, or about PAIR, is available by calling the Patent Electronic Business Center at 1-866-217-9197.

Pre-Grant Publication Division, 703-605-4283

UNITED STATES PATENT AND TRADEMARK OFFICE

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
11/897,177	08/28/2007	Andrew Acheampong	D-3111 CON	3860

33197 7590 01/08/2008

STOUT, UXA, BUYAN & MULLINS LLP
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IRVINE, CA 92618

EXAMINER	
CORDERO GARCIA, MARCELA M	
ART UNIT	**PAPER NUMBER**
1654	

MAIL DATE	DELIVERY MODE
01/08/2008	PAPER

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.

Office Action Summary	Application No.	Applicant(s)	
	11/897,177	ACHEAMPONG ET AL.	
	Examiner	Art Unit	
	Marcela M. Cordero Garcia	1654	

-- 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 1 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 _____.

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

3)☐ 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

4)☒ Claim(s) 1-36 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

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

8)☒ Claim(s) 1-36 are subject to restriction and/or election requirement.

Application Papers

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

10)☐ 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).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

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).

a)☐ All b)☐ Some * c)☐ None of:

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) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-20, drawn to a method of treating dry eye, classified, e.g., in class 514, subclass 11.

II. Claims 21-36, drawn to a composition, classified, e.g., in class 514, subclass 2.

The inventions are distinct, each from the other because of the following reasons:

Inventions II and I are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product. See MPEP § 806.05(h). In the instant case, the compositions of cyclosporin may also be used to study the stability of cyclosporin in pharmaceutical compositions.

The search for each of the above inventions is not co-extensive particularly with regard to the literature search. Further, a reference which would anticipate the invention of one Group would not necessarily anticipate or even make obvious another Group. Finally, the consideration for patentability is different in each case. Thus, it would be an undue burden to examine all of the above inventions in one application.

Because these inventions are distinct for the reasons given above and the search required for each Group is not necessarily required for the other Groups, restriction for examination purposes as indicated is proper.

Applicant is advised that the response to this requirement, to be complete, must include an election of the invention to be examined even though the requirement be traversed.

The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and the product claims are subsequently found allowable, withdrawn process claims that depend from or otherwise require all the limitations of the allowable product claim will be considered for rejoinder. All claims directed to a nonelected process invention must require all the limitations of an allowable product claim for that process invention to be rejoined.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103 and 112. Until all claims to the elected product are found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowable product claim will not be rejoined. See MPEP § 821.04(b). Additionally, in order to retain the right to rejoinder in accordance with the above policy, applicant is advised that the process claims should be amended during

prosecution to require the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder**. Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

This application contains claims directed to the following patentably distinct species: the many and multiple hydrophobic components, cyclosporin components and weight ratios within the instantly claimed methods and compositions. The species are independent or distinct because they are drawn to materially different hydrophobic components and cyclosporin components which have different chemical structures, or to materially different ratios which have different amounts of hydrophobic with respect to cyclosporin and therefore have different and distinct compositions.

The search for each of the above inventions is not co-extensive particularly with regard to the literature search. Further, a reference which would anticipate the invention of one species would not necessarily anticipate or even make obvious another species. Finally, the consideration for patentability is different in each case. Thus, it would be an undue burden to examine all of the above inventions in one application.

Because these species are distinct for the reasons given above and the search required for each species is not necessarily required for the other species, restriction for examination purposes as indicated is proper.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species [i.e., elect a single and specific cyclosporin, a single and specific hydrophobic component and a single and specific weight ratio] for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, claims 1-36 are generic.

Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which depend from or otherwise require all the limitations of an allowable generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

Applicant is advised that the reply to this requirement to be complete must include (i) an election of a species or invention to be examined even though the requirement be traversed (37 CFR 1.143) and (ii) identification of the claims encompassing the elected invention.

The election of an invention or species may be made with or without traverse. To reserve a right to petition, the election must be made with traverse. If the reply does not

distinctly and specifically point out supposed errors in the restriction requirement, the election shall be treated as an election without traverse.

Should applicant traverse on the ground that the inventions or species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the inventions or species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C.103(a) of the other invention.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

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-Th 7:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia J. Tsang can be reached on (571) 272-0562. 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
Patent Examiner
Art Unit 1654

MMCG 01/08

/Cecilia Tsang/
Supervisory Patent Examiner, Art Unit 1654

TRANSMITTAL FORM

(to be used for all correspondence after initial filing)

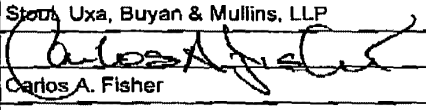
Application Number	11/897,177
Filing Date	August 28, 2007
First Named Inventor	Acheampong et al.
Group Art Unit	1654
Examiner Name	Cordero Garcia, Marcela M.
Total Number of Pages In This Submission: 3	Attorney Docket Number: D-3111 CON

ENCLOSURES (*check all that apply*)

- ☐ Fee Transmittal Form
  - ☐ Fee Attached
- ☒ Amendment/Reply
  - ☐ After Final
  - ☐ Affidavits/declaration(s)
- ☐ Extension of Time Request
- ☐ Express Abandonment Request
- ☐ Information Disclosure Statement
- ☐ Certified Copy of Priority Document(s)
- ☐ Response to Missing Parts/ Incomplete Application
  - ☐ Response to Missing Parts under 37 CFR 1.52 or 1.53
- ☐ Drawing(s)
- ☐ Licensing-related Papers
- ☐ Petition
- ☐ Petition to Convert to a Provisional Application
- ☐ Power of Attorney, Revocation Change of Correspondence Address
- ☐ Terminal Disclaimer
- ☐ Request for Refund
- ☐ CD, Number of CD(s) ____
  - ☐ Landscape Table on CD
- ☐ After Allowance Communication to TC
- ☐ Appeal Communication to Board of Appeals and Interferences
- ☐ Appeal Communication to TC (*Appeal Notice, Brief, Reply Brief*)
- ☐ Proprietary Information
- ☐ Status Letter
- ☐ Other Enclosure(s) (*please identify below*)

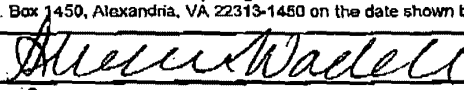
Remarks

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

Firm Name	Stout, Uxa, Buyan & Mullins, LLP		
Signature			
Printed Name	Carlos A. Fisher		
Date	February 6, 2008	Reg. No.	36,510

CERTIFICATE OF TRANSMISSION/MAILING

I hereby certify that this correspondence is being facsimile transmitted to the USPTO at fax number 571-273-8300, or deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Mail Stop Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on the date shown below.

Signature			
Typed or printed name	Shawnna Waddell	Date	Feb. 6, 2008

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Appl. No. : 11/897,177 Confirmation No. 3860
Applicant : ACHEAMPONG ET AL.
Filed : AUGUST 28, 2007
Title : METHODS OF PROVIDING THERAPEUTIC EFFECTS USING CYCLOSPORIN COMPONENTS

TC/A.U. : 1654
Examiner : Cordero Garcia, Marcela M.

Docket No. : D-3111 CON
Customer No. : 33197

CERTIFICATE OF FACSIMILE TRANSMISSION

I hereby certify that this paper is being facsimile transmitted to the Patent and Trademark Office fax number 571-273-8300 on the date shown below.

Date: February 6, 2008
Name: Shawnna Waddell

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

REPLY TO RESTRICTION REQUIREMENT

Sir:

In response to the Restriction Requirement mailed January 8, 2008, Applicants have the following comments.

Claims 1-36 are currently pending. The Examiner has required restriction between Group I (claims 1-20; drawn to a method for the treatment of dry eye) and Group II (claims 21-26, drawn to compositions).

Applicants hereby elect to prosecute Examiner's Group I, claims 1-20.

Additionally, the Examiner has made an election of species requirement. Applicants provisionally elect the species wherein the cyclosporin component is cyclosporin A, the hydrophobic component is castor oil, and wherein the weight ratio of cyclosporin A to castor oil is 0.04. All presently pending claims 1-20 are readable upon this species.

As this reply is being filed within the time period set for response to the Restriction Requirement, no fee is thought due in connection with this communication. However, if Applicants are in error in this regard, please use Deposit Account 01-0885 for the payment of any fee now due.

Should any matters remain unresolved, applicant requests the Examiner to telephone applicant's attorney at the telephone number given below.

Respectfully submitted,

Date: 2/6/08

Carlos A. Fisher
Attorney for Applicant
Registration No. 36,510
4 Venture, Suite 300
Irvine, California 92618
(949) 450-1750
(949) 450-1764 Facsimile

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
11/897,177	08/28/2007	Andrew Acheampong	D-3111 CON	3860

33197 7590 05/30/2008

STOUT, UXA, BUYAN & MULLINS LLP
4 VENTURE, SUITE 300
IRVINE, CA 92618

EXAMINER	
CORDERO GARCIA, MARCELA M	
ART UNIT	**PAPER NUMBER**
1654	
MAIL DATE	**DELIVERY MODE**
05/30/2008	PAPER

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.

Office Action Summary	Application No.	Applicant(s)	
	11/897,177	ACHEAMPONG ET AL.	
	Examiner	Art Unit	
	MARCELA M. CORDERO GARCIA	1654	

-- 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 *06 February 2008*.

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

3)☐ 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

4)☒ Claim(s) *1-36* is/are pending in the application.

4a) Of the above claim(s) *21-36* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-20* is/are rejected.

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

8)☐ Claim(s) *1-20* are subject to restriction and/or election requirement.

Application Papers

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

10)☐ 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).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

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).

a)☐ All b)☐ Some * c)☐ None of:

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) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

U.S. Patent and Trademark Office

DETAILED ACTION

Claims 1-36 are pending in the application.

Election/Restrictions

Applicant's election of claims 1-20 (Group I) in the reply filed on 2/6/08 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

In addition, Applicant has elected the species wherein the cyclosporin component is cyclosporin A, the hydrophobic component is castor oil, and wherein the weight ratio of cyclosporin A to castor oil is 0.04. Claims 1-20 are readable upon the elected species.

Claims 1-20 are presented for examination on the merits. Claims 21-36 are withdrawn as not drawn to the elected Group.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> 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.

Claims 4-6 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. Claims 4-5 are rendered vague and indefinite by the phrase "substantially no detectable concentration" since the metes and bounds for such limitation are not well defined and there is no definition in the disclosure encompassing what the term "substantially" means. All other claims that

depend directly or indirectly from rejected claims and are, therefore, also rejected under USC 112, second paragraph for the reasons set forth above.

Claim Rejections - 35 USC § 103

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.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-20 are rejected under 35 U.S.C. 103(a) as being obvious over Ding et al. (US 5,474,979 cited in the IDS of 11/14/07).

Ding et al. teach 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 cyclosporin component in a therapeutically effective amount of less than 0.1% by weight, the weight ratio of the cyclosporin component (cyclosporin A, e.g., Example 1D and column 3, lines 30-37) to the hydrophobic component (castor oil, a vegetable oil) is 0.08 (see, e.g., Example 1D). Ding et al. also teach embodiment 1B which has 0.2% of cyclosporin and a 0.04

ratio of cyclosporin/castor oil. Additionally, embodiment 1E has 0.05% of cyclosporin A and 0.08 ratio cyclosporin/castor oil. Ding et al. do teach that an embodiment having both less than 0.1 % of cyclosporin and wherein the weight ratio of the cyclosporin component to the hydrophobic component can be less than 0.08 (0.12 to 0.02). In addition, Ding et al. teach in claim 8 a pharmaceutical emulsion consisting of between about 0.05% and about 0.40% by weight cyclosporin A (which reads upon the limitation “less than 0.1 % by weight cyclosporin A” of instant claim 1) and between 0.625 and about 5.0 % castor oil. The corresponding lower and upper rations for the range is 0.05%/5.0% = 0.01 weight ratio of cyclosporin A/castor oil, which reads upon the limitation in claim 1 “the weight ratio of he cyclosporin A to the castor oil being less than 0.08”. The limitations of claim 2: “dry eye syndrome” and of claim 3: “effective in treating dry eye syndrome” are taught, e.g., in column 5, lines 10-14. The limitation of claim 4: “wherein the blood of the human or animal has substantially no detectable concentration of cyclosporin component” and of claim 5: ”wherein the blood of the human or animal has substantially no detectable concentration of the cyclosporin component as measure using a validated liquid chromatography/mass spectrometry-mass spectrometry analytical method" and the limitation of claim 6: “0.1 ng/mL or less” necessarily read upon the method of Ding et al. since it teaches overlapping steps/concentrations. The limitation of claims 7-8: “cyclosporin A" is taught, e.g., in Example 1. The limitation of claim 9: “wherein the cyclosporin component is solubilized in the hydrophobic component present in the composition" is taught in column 3, lines 21-23. The limitations of claim 10: “wherein

the hydrophobic component is present in the composition in an amount greater than 0.625% by weight“, of claim 11: "oily material", of claim 12: "vegetable oils" and of claim 13: "castor oil" are taught, e.g., in Examples 1A-D which teach 5.00%, 2.5% and 1.25% of hydrophobic component (castor oil). The limitation of claim 14: “topically administering the composition to the eye" is taught, e.g., in column 5, lines 15-18 and claim 8 of Ding et al. The limitation of claim 15: “whrein the composition comprises an effective amount of an emulsifier component” is taught in column 3, lines 38-4 and 50-56. The limitations of claim 16-17: “tonicity" and "organic tonicity component" are taught in column 4, lines 12-19. The limitation of claim 18: “polyelectrolyte component in an amount effective in stabilizing the composition” is taught in column 3, lines 64-67 and column 4, lines 1-12. The limitation of claims 19-20 drawn to ph ranges of "of about 7.0 to about 8.0" and “of about 7.2 to about 7.6” are taught, e.g., in Example 1A-1E and in claim 8 of Ding et al.

Ding et al. do not expressly teach an embodiment comprising both less than 0.1% of cyclosporin A and less than 0.08 cyclosporin A/castor oil ratio. The closest embodiments are 1D comprising 0.10% of cyclosporin A and 0.08 cyclosporin A/castor oil ratio; 1E comprising 0.05% of cyclosporin A and 0.08 cyclosporin A/castor oil ratio and 1B comprising 0.20% cyclosporin A and 0.04 cyclosporin A/castor oil ratio. While Ding et al. does teach a method of treating an eye of an animal comprising: administering an eye of the animal a composition..., Ding et al. did not apply the composition to an eye of a human. It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the

compositions of Ding et al. (such as 1E) by increasing the amount of castor oil or decreasing the cyclosporin concentration in order to reduce the ratio of the cyclosporin component to hydrophobic component from 0.08 to, e.g., 0.04 as taught by Ding et al. (see, e.g., column 3, lines 18-20) and exemplified in embodiment 1B. The skilled artisan would have been motivated to do so because such proportions were taught by the Ding et al. patent. There would have been a reasonable expectation of success, given that compositions with a higher amount of castor oil are encompassed by the Ding et al. claims (e.g., claim 8, embodiment 1B) and because optimizing the ratio of cyclosporin/hydrophobic components to below 0.08 (i.e., 0.02 to 0.12, which reads upon the range of ratios of 0.02 to 0.08) was taught by Ding et al. (e.g., column 3, lines 18-20) and embodiment 1B (which has 0.04). The adjustment of particular conventional working conditions (e.g., using all the ratios and proportions taught by Ding. et al., applying to a human population instead of a rabbit population within such method) is deemed merely a matter of judicious selection and routine optimization that is well within the purview of the skilled artisan. As such, it would have been obvious to one skilled in the art at the time of invention to determine all optimum and operable conditions [e.g., formulation ranges and proportions, patient population (e.g., column 1, lines 10-15)], because such conditions are art-recognized result-effective variables that are routinely determined and optimized in the art through routine experimentation ("[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation.". *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233,

235 (CCPA 1955). See MPEP 2145.05). One would have been motivated to determine all optimum and operable conditions in order to achieve the safest and most effective method in the most efficient manner. One would have had a reasonable expectation for success because such modifications are routinely determined and optimized in the art through routine experimentation.

From the teaching of the references, 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.

Conclusion

No claim is allowed.

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

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, Cecilia J. Tsang can be reached on (571) 272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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/Marcela M Cordero Garcia/
Primary Examiner, Art Unit 1654

MMCG 05/08

Notice of References Cited	Application/Control No. 11/897,177	Applicant(s)/Patent Under Reexamination ACHEAMPONG ET AL.	
	Examiner MARCELA M. CORDERO	Art Unit 1654	Page 1 of 1

U.S. PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Name	Classification
*	A	US-6,656,460	12-2003	Benita et al.	424/78.04
*	B	US-2003/0108626	06-2003	Benita et al.	424/731
*	C	US-2005/0014691	01-2005	Bakhit et al.	514/012
*	D	US-2005/0059583	03-2005	Acheampong et al.	514/011
*	E	US-2007/0027072	02-2007	Tien et al.	514/011
*	F	US-2007/0087962	04-2007	Tien et al.	514/011
*	G	US-2007/0299004	12-2007	Acheampong et al.	514/011
*	H	US-2008/0039378	02-2008	Graham et al.	514/011
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FOREIGN PATENT DOCUMENTS

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*A copy of this reference is not being furnished with this Office action. (See MPEP § 707.05(a).)
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Search Notes	Application/Control No.	Applicant(s)/Patent under Reexamination	
	11/897,177	ACHEAMPONG ET AL.	
	Examiner	Art Unit	
	MARCELA M. CORDERO GARCIA	1654	

SEARCHED			
Class	Subclass	Date	Examiner
none	none		

INTERFERENCE SEARCHED			
Class	Subclass	Date	Examiner

SEARCH NOTES (INCLUDING SEARCH STRATEGY)		
	DATE	EXMR
STN searched by STIC (available via PAIR / SCORE)	5/22/2008	MMCG
EAST searched (attached)	5/23/2008	MMCG
also ran PALM Inventor search	5/23/2008	MMCG

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Docket No.: D-3111CON	Application No.: 11/897,177
Applicant: Acheampong et al.	
Filing Date: August 28, 2007	Group Art Unit: 1654

U. S. PATENT DOCUMENTS

EXAMINER INITIAL	DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE
	3,278,447	10/1966	McNicholas			
	4,388,307	06/1983	Cavanak			
	4,649,047	03/1987	Kaswan			
	4,814,323	3/1989	Andrieu			
	4,839,342	06/1989	Kaswan			
	4,970,076	11/1990	Horrobin			
	4,990,337	02/1991	Kurihara et al.			
	4,996,193	02/1991	Hewitt et al.			
	5,286,730	02/1994	Caufield et al.			
	5,286,731	02/1994	Caufield et al.			
	5,342,625	08/1994	Hauer et al.			
	5,411,952	05/1995	Kaswan			

FOREIGN PATENT DOCUMENTS

	DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION YES	TRANSLATION NO

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

	AA	Acheampong et al, "Cyclosporine Distribution into the Conjunctiva, Cornea, Lacrimal Gland, and Systemic Blood Following Topical Dosing of Cyclosporine to Rabbit, Dog, and Human Eyes," *Lacrimal Gland, Tear Film, and Dry Eye Syndromes 2 - Basic Science and Clinical Relevance, Plenum Press, New York & London, ©1998, pp. 1001-1004.*
	AB	Acheampong et al, "Distribution of Cyclosporin A in Ocular Tissues After Topical Administration to Albino Rabbits and Beagle Dogs", *Curr Eye Res, Feb 1999, 18(2):91-103b.*
	AC	Angelov et al, "Preclinical Safety Studies of Cyclosporine Ophthalmic Emulsion," *Lacrimal Gland, Tear Film, and Dry Eye Syndromes 2 - Basic Science and Clinical Relevance, Plenum Press, New York & London, ©1998, pp. 991-5.*
	AD	Brewster et al, "Enhanced Delivery of Ganciclovir to the Brain through the Use of Redox Targeting", *Antimicrobial Agents and Chemotherapy, April 1994, 38(4):817-823.*
	AE	Brewster et al, "Intravenous and Oral Pharmacokinetic Evaluation of a 2-Hydroxypropyl-β-cyclodextrin-Based Formulation of Carbamazepine in the Dog: Comparison with Commercially Available Tablets and Suspensions," *J Pharm Sci, March 1997, 86(3):335-9.*

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Form PTO-1449	Docket No.: D-3111CON	Application No.: 11/897,177
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U. S. PATENT DOCUMENTS

EXAMINER INITIAL	DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE
	5,474,979	12/1995	Ding et al.			
	5,504,068	04/1996	Komiya et al.			
	5,540,931	07/1996	Hewitt et al.			
	5,719,123	02/1998	Morley et al.			
	5,739,105	04/1998	Kim et al.			
	5,807,820	09/1998	Elias			
	5,843,452	12/1998	Wiedmann et al.			
	5,843,891	12/1998	Sherman			
	5,858,401	01/1999	Bhalani et al.			
	5,866,159	02/1999	Hauer et al.			
	5,891,846	04/1999	Ishida et al.			
	5,916,589	06/1999	Hauer et al.			

FOREIGN PATENT DOCUMENTS

	DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION YES	TRANSLATION NO

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

	AA	Brewster et al, "Preparation, Characterization, and Anesthetic Properties of 2-Hydroxypropyl-β - cyclodextrin Complexes of Pregnanolone and Pregnenolone in Rat and Mouse", *J Pharm Sci, October 1995, 84(10):1154-9.*
	AB	Sall et al, "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", *Ophthalmology, April 2000, 107(4):631-9.*
	AC	Small 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", *J Ocul Pharmacol Ther, Oct 2002, 18(5):411-8.*
	AD	Stevenson et al., "Efficacy and Safety of Cyclosporin A Ophthalmic Emulsion in the Treatment of Moderate-to-severe Dry Eye Disease", *Ophthalmology, May 2000, 107(5):967-74.*
	AE	
	AF	

EXAMINER	DATE CONSIDERED

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U. S. PATENT DOCUMENTS

EXAMINER INITIAL	DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE
	5,951,971	09/1999	Kawashima et al.			
	5,962,017	10/1999	Hauer et al.			
	5,981,479	11/1999	Ko et al.			
	5,981,607	11/1999	Ding et al.			
	5,998,365	12/1999	Sherman			
	6,008,191	12/1999	Singh et al.			
	6,008,192	12/1999	Al-Razzak et al.			
	6,022,852	02/2000	Klokkers et al.			
	6,024,978	02/2000	Hauer et al.			
	6,046,163	04/2000	Stuchlik et al.			
	6,159,933	12/2000	Sherman			
	6,254,860	07/2001	Garst			
	6,323,204	11/2001	Burke et al.			

FOREIGN PATENT DOCUMENTS

	DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION	

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

	AA	
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Filing Date: August 28, 2007	Group Art Unit: 1654

U. S. PATENT DOCUMENTS

EXAMINER INITIAL	DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE
	6,346,511	02/2002	Singh et al.			
	6,350,442	02/2002	Garst			
	6,413,547	07/2002	Bennett et al.			
	6,420,355	07/2002	Richter et al.			
	6,468,968	10/2002	Cavanak et al.			
	6,486,124	11/2002	Olbrich et al.			
	2001/0014665	08/2001	Fisher et al.			
	2003/0021816	01/2003	Kang et al.			
	2003/0044452	03/2003	Ueno			
	2003/0060402	03/2003	Cavanak et al.			
	2003/0087813	05/2003	Or et al			
	2003/0104992	06/2003	Or et al			
	2003/0109425	06/2003	Or et al			
	2003/0109426	06/2003	Or et al.			
	2003/0143250	07/2003	Hauer et al.			

FOREIGN PATENT DOCUMENTS

	DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION YES	TRANSLATION NO

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

	AA	
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Sheet 5 of 6

LIST OF ART CITED BY APPLICANT

ATTY. DOCKET: D-3111CON	SERIAL NO.: 11/897,177
APPLICANT: Acheampong et al	TITLE: Methods of Providing Therapeutic Effects Using Cyclosporin Components
FILING DATE: August 28, 2007	GROUP: 1654

U.S. PATENT DOCUMENTS

*EXAMINER INITIAL		DOCUMENT NO.	DATE	NAME	CLASS	SUB-CLASS	FILING DATE (if applicable)
	AA	4,614,736	09/1986	Delevallee et al.			
	AB	5,368,854	11/1994	Rennick			
	AC	6,872,705	03/2005	Lyons			
	AD	2001/0036449 A1	11/2001	Garst			
	AE	2003/0055028 A1	03/2003	Stergiopoulos et al.			
	AF						

FOREIGN PATENT DOCUMENTS

		DOCUMENT NO.	DATE	COUNTRY	CLASS	SUB-CLASS	TRANSLATION (yes/no)
	BA	DE 19810655	09/1999	Germany			
	BB	WO 03/030834	04/2003	PCT			
	BC						

OTHER ART
(Including Author, Title, Date, Pertinent Pages, etc.)

	CA	T.A. Winter, et al. Scand J Gastroenterol. (1993), 28(8), pages 701-704
	CB	M. Schwab and U. Klotz, Clin. Pharmacokinet. (2001), 40(10), pages 723-751
	CC	J. Rudinger. In: Peptide Hormones, JA Parsons, Ed. (1976) pages 1-7
	CD	D.E. Smilek, et al. Proc. Natl. Acad. Sci. USA (1991) 88, pages 9633-9637
	CE	MBanić, et al. Dig. Dis. Sci. (2002), 47(6), pages 1362-1368
	CF	The Online Medical Dictionary, accessed 7/7/05 and 7/13/05. 6 pages
	CG	W.J. Sandborn, et al. Am. J. Gastroenterol. (1993), 88(5), pages 640-645
	CH	D.H. Present. Am. J. Gastroenterol. (1993) 88(5), pages 627-630
	CI	S. Ardizzone and G.B. Porro. Drugs. (1998), 55(4), pages 519-542
	CJ	W.J. Sandborn, et al. Gastroenterology. (1994), 106(6), pages 1429-1435
	CK	K. Tsubota, et al. Invest. Ophthalmol. Vis. Sci. (1998), 39(9), pages 1551-1559
	CL	A.A. Drosos and N.M. Moutsopoulos. Ter. Arkh. (1998), 60(4), pages 77-80
	CM	A.A. Drosos, et al. Scand. J. Rheumatology (1986) Suppl. 61, pages 246-249
	CN	W.A. van der Reijden, et al. Ann. Rheum. Dis. (1999), 58, pages 465-473
	CO	N.A. Robinson and D. Wray. Australian Dental Journal (2003), 48(4), pages 206-211
	CP	A.M. Pedersen and B. Nauntofte. Expert Opin Pharmacother (2001), 2(9), pages 1415-1436

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LIST OF ART CITED BY APPLICANT

ATTY. DOCKET: D-3111CON	SERIAL NO.: 11/897,177
APPLICANT: Acheampong et al	TITLE: Methods of Providing Therapeutic Effects Using Cyclosporin Components
FILING DATE: August 28, 2007	GROUP: 1654

	CQ	D.E. Lopatin. Chemical compositions and functions of Saliva. 8/24/2001, 31 pages
	CR	Gunduz et al, "Topical Cyclosporin Treatment of Keratoconjunctivitis Sicca in Secondary Sjogren's Syndrome", Acta Ophthalmologica, Vol. 72, No. 4, 1994, pp 438-442, XP009063039
	CS	Phillips et al, "Cyclosporine Has A Direct Effect on the Differentiation of a Mucin-Secreting Cell Line", Journal of Cellular Physiology, Vol. 184, No. 3, Sept. 2000, pp 400-408, XP009063023
	CT	Gipson et al, "Character of Ocular Surface Mucins and Their Alteration in Dry Eye Disease", The Ocular Surface, Vol. 2, No. 2, April 2004, pp 131-148, XP001208377
	CU	Akpek et al, "A Randomized Trial of Topical Cyclosporin 0.05% in Topical Steroid-Resistant Atopic Keratoconjunctivitis", Ophthalmology, Vol. III, No. 3, March 2004, pp 476-482, XP00906021
	CV	Eisen et al, "Topical Cyclosporine for Oral Mucosal Disorders", Journal of the American Academy of Dermatology, Vol. 23, No. 6, Part 2, Dec. 1990, pp 1259-1264, XP009063043
	CW	Epstein et al, "Topical Cyclosporine in a Bioadhesive for Treatment of Oral Lichenoid Mucosal Reactions. An Open Label Clinical Trial", Oral Surgery, Oral Medicine..., Vol. 82, No. 5, 1996, pp 532-536, XP009063045
	CX	Erdmann et al, "Pemphigus Vulgaris Der Mund-Und Kehlopfschleimhaut Pemphigus Vulagris of the Oral Mucosa and the Larynx", H+G Zeitschrift Fuer Hautkrankheiten, Vol. 72. No. 4, 1997, pp 283-296, XP009063042
	CY	Brinkmeier et al, "Pyodermatitis-Pyostomatitis Vegetans: A Clinical Course of Two Decades with Response to Cyclosporine and Low-Dose Prednisolone", Acta Dermato-Venereologica, Vol. 81, No. 2, May 2001, pp 134-136
	CZ	Gremse et al, "Ulcerative Colitis in Children. Medical Management", Pediatric Drugs, Vol. 4, No. 12, 2002, pp 807-815, XP009063025
	CAA	Gaeta G.M. et al, "Cyclosporin bioadhesive gel in the topical treatment of erosive lichen planus" International Journal of Immunopathology and Pharmacology, Vol. 7, No. 2, 1994, pages 125-132.
	CBB	Kuwano et al., "Cyclosporine A Formulation Affects its Ocular Distribution in Rabbits", Pharm Res., January 2002, Vol. 19, No. 1, pages 108-111.
	CCC	Ding et al., Cyclosporine Ophthalmic o/w Emulsion: Formulation and Emulsion Characterization. Pharmaceutical Research 1997. 14(11, suppl):S41 (2 pages).

EXAMINER /Marcela M Cordero Garcia/ DATE CONSIDERED 04/24/2008

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SERIAL NUMBER	FILING or 371(c) DATE	CLASS	GROUP ART UNIT	ATTORNEY DOCKET NO.
11/897,177	08/28/2007 RULE	514	1654	D-3111 CON

APPLICANTS

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James N. Chang, Newport Beach, CA;
David F. Power, Trabuco Canyon, CA;

**** CONTINUING DATA **************************

This application is a CON of 10/927,857 08/27/2004
which claims benefit of 60/503,137 09/15/2003

**** FOREIGN APPLICATIONS **************************

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Foreign Priority claimed	35 USC 119(a-d) conditions met	Verified and Acknowledged	Met after Allowance	STATE OR COUNTRY	SHEETS DRAWINGS	TOTAL CLAIMS	INDEPENDENT CLAIMS
☐ Yes ☑ No	☐ Yes ☑ No	/MARCELA M CORDERO GARCIA/ Examiner's Signature	☐ Initials	CA	0	36	2

ADDRESS

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TITLE

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EAST Search History

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
S25	271	cyclosporin same "castor oil"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2008/05/22 14:26
S26	68	cyclosporin same "castor oil" same emulsion	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2008/05/22 16:11
S27	29	cyclosporin same "castor oil" same emulsion and method.clm.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2008/05/22 16:11

5/23/08 2:28:59 PM

EAST Search History

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
S28	21	cyclosporin same "castor oil" same emulsion and method. clm. and allergan	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2008/05/22 16:12
S29	18	cyclosporin same "castor oil" same emulsion and method. clm. and allergan and cyclosporin.clm.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2008/05/22 16:19
S31	9	cyclosporin same "castor oil" same emulsion and method. clm. and allergan and cyclosporin.clm. and eye.clm.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2008/05/22 16:22

5/23/08 2:36:24 PM

Docket No. 17618CON (AP)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Appl. No.	: 11/897,177	Confirmation No.	3860
Applicant	: ACHEAMPONG ET AL.		
Filed	: AUGUST 28, 2007		
Title	: Methods Of Providing Therapeutic Effects Using Cyclosporin Components		
TC/A.U.	: 1654		
Examiner	: Cordero Garcia, Marcela M.		
Docket No.	: D-3111 CON		
Customer No.	: 33197		

TRANSMITTAL

Commissioner for Patents
Alexandria, VA 22313-1450

Dear Sir:

Transmitted herewith is a Reply to the Office Action dated May 30, 2008 on the above-identified application.
[X] Reply (14 pages)
[X] The fee has been calculated as shown below:

CLAIMS	**COLUMN A** *Claims Remaining After Amendment*	**COLUMN B** *Highest Number Previously Paid*	**COLUMN C** *Present Extra*	*Rate*	*Additional Fee*
Total	20	36	0	x $50	$0.00
Independent	1	2	0	x $210	$0.00
[ ] First Presentation of Multiple Dep. Claim x $280 = $.00					
Time Extension Fees:					$.00
Total Due:					$0.00

The Commissioner is hereby authorized to charge payment of extension of time fees or any other fees required, or credit any overpayment, to Deposit Account No. 01-0885.

Date: Respectfully submitted,

Date: September 2, 2008

/John E. Wurst/
John E. Wurst
Reg. No. 40,283
Attorney of Record

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Appl. No.	: 11/897,177	Confirmation No. 3860
Applicant	: ACHEAMPONG ET AL.	
Filed	: AUGUST 28, 2007	
Title	: METHODS OF PROVIDING THERAPEUTIC EFFECTS USING CYCLOSPORIN COMPONENTS	
TC/A.U.	: 1654	
Examiner	: Cordero Garcia, Marcela M.	
Docket No.	: D-3111 CON	
Customer No.	: 33197	

Electronically Filed

AMENDMENT

Sir:

Applicants have received and carefully reviewed the Office Action mailed May 30, 2008 in this matter. As a result of this careful review Applicant have the following comments.

The **Status of the Claims** begin on page 2 of this communication.

The **Remarks** begin on page 8 of this communication.

The **Conclusion** begins on page 8 of this communication.

STATUS OF THE CLAIMS

The following claim listing shall supercede any previous listing of the claims.

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

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

5. (Currently Amended) 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. (Original) 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. (Original) The method of claim 1 wherein the cyclosporin component comprises a material selected from cyclosporin A, derivatives of cyclosporin A and mixtures thereof.

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

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

10. (Original) 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. (Original) The method of claim 1 wherein the hydrophobic component comprises an oily material.

12. (Original) 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. (Original) The method of claim 1 wherein the hydrophobic component comprises castor oil.

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

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

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

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

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

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

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

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

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

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

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

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

28. (Withdrawn) 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. (Withdrawn) The composition of claim 21 wherein the hydrophobic component comprises castor oil.

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

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

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

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

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

35. (Withdrawn) 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. (Withdrawn) 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.

REMARKS

Applicants have carefully reviewed the above-referenced Office Action and have the following comments.

Claim 4 has been amended to remove the word "substantially".

Rejection of claims 4-5 under 35 USC §112

Claims 4-5 were rejected as allegedly being indefinite through the use of the phrase "substantially no detectable concentration". Applicants have amended claims 4 and 5 to delete the word "substantially"; in addition, claim 5 has been amended to remove a redundancy. As a result of these amendments, this rejection is now moot.

Rejection of claims 1-20 under 35 USC §103

Claims 1-20 have been rejected as allegedly obvious pursuant to Ding et al. U.S. Patent No. 5,474,979 (hereinafter "Ding"). Applicants traverse this rejection for the following reasons.

An invention is patentable unless the invention is lacking in utility or novelty, or is obvious. The burden of proving that an invention lacks one of these requirements is placed upon one who challenges the patentability of an invention; *see e.g.*, 35 USC §101 ("whoever invents or discovers any new and useful process, machine, manufacture or composition

of matter . . . may obtain a patent therefor subject to the conditions and requirements of this title.")

Obviousness is determined from the point of view of a person of ordinary skill in the art at the time the invention was made. *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. __, 82 U.S.P.Q.2d 1385 (2007). *Graham v. John Deere Co.*, 383 U.S. 1, 148 U.S.P.Q. 459 (1966) sets forth the standards used in determining whether a claimed invention is obvious under 35 U.S.C. §103(a): "the scope and content of the prior art are to be determined; differences between the prior art and the claims at issue are to be ascertained; and the level of ordinary skill in the pertinent art resolved. Against this background, the obviousness or non-obviousness of the subject matter is determined." 383 U.S. at 17, 148 U.S.P.Q. at 467.

The Scope and Content of the Prior Art

The Examiner has characterized the prior art (Ding) as having disclosed a method of treating an eye of a human or animal comprising administering 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. Applicants respectfully disagree.

The Examiner has cited Example 1D of Ding for this proposition. However, Example 1D has a weight ratio of the cyclosporin component to the hydrophobic component (castor oil) of 0.08, rather than less than 0.8. Furthermore, Example 1D

contains 0.1% (w/v) a cyclosporin component, rather than less than 0.1%.

The Office Action attempts to anticipate this objection by citing Example 1B of Ding. However, this Example is a composition that contains 0.2% of a cyclosporin component and 5.00% castor oil, yielding a cyclosporin to castor oil ratio of 0.04. However, of course, the cyclosporin concentration of 0.2% is more than twice the concentration (less than 0.1%) permitted by the present claims.

The Office Action also attempts to meet the deficiencies of Examples 1D and 1B by also citing the composition of Example 1E of Ding. However, this composition, the only composition disclosed by Ding to contain less than 0.1% cyclosporin A, also has a ratio of cyclosporin A to hydrophobic component of 0.08, rather than less than this amount.

Furthermore, the present claims require the concentration of a cyclosporin component used in the claimed method to be a "therapeutically effective concentration" less than 0.1%. However, Ding provides absolutely no suggestion that a concentration of a cyclosporin component less than 0.1% would be therapeutically effective at all. Ding mentions three times (in column 5, lines 15-32) that the formulations of Examples 1A-1D, which have cyclosporin A concentrations of 0.1% or to 0.4%, are bioavailable, non-toxic, and therapeutically effective. However, conspicuously absent from all these data is any mention of the composition of Example 1E.

As stated above, obviousness of determined from the point of view of a person of ordinary skill in the art at the time that the invention was made. Moreover, ascertaining the differences between the claimed invention and the prior art requires interpreting the claim language, see MPEP § 2111, and considering both the invention and the prior art as a whole." *See e.g.*, MPEP §2141.

Ding's conspicuous omission from mention of Example 1E as a formulation having therapeutic effectiveness cannot simply be ignored; it is part of the prior art as a whole. And a person of ordinary skill in the art would certainly consider this omission, repeated by Ding three times, as intentional. Thus, Ding, like any prior art reference, must be considered for all it teaches, particularly when, as here, it so obviously teaches away from the claimed invention.

The Office Action next alleges that claim 8 of Ding teaches than a composition has less than 0.1% cyclosporin and the weight ratio of a cyclosporin component to hydrophobic component "can be" less than 0.08. Claim 8 of Ding is drawn to an emulsion containing, among other ingredients, between about 0.05% and about 0.40% cyclosporin A, and about 0.625% and about 5.0% castor oil, both by weight. Claim 8 does not expressly mention ratios of a cyclosporin component to hydrophobic component; however, if ratios are to be calculated from these ingredients, it is true that the lowest ratio implied by these concentrations would be about 0.05/5.0 = 0.01, and the highest ratio would be about 0.4/0.625=0.64.

Even if claim 8 were interpreted to implicitly disclose a range of ratios of about 0.01 to about 0.64, the Office Action neither alleges, nor does Ding teach, that compositions having less than 0.1% a cyclosporin component are therapeutically effective. Indeed, Claim 8 says nothing about therapeutic effectiveness at all claimed concentrations, and it is unreasonable to assume that it does, since a patent claim need not cover only operative embodiments. *See e.g., Atlas Powder Co. v. E.I. du Pont de Nemours & Co.*, 750 F.2d 1569, 1577, 224 USPQ 409, 414 (Fed. Cir. 1984). (Holding that the presence of inoperative embodiments within the scope of a claim does not necessarily render a claim unpatentable). If a patent claim may encompass inoperative embodiments, then by definition, the teaching of that patent claim cannot, without more, be that every embodiment encompassed by the claim is operative.

Therefore, a person of ordinary skill in the art would clearly not be justified in believing that claim 8 of Ding suggests that formulations containing less than 0.1% are therapeutically effective, or in ignoring the repeated suggestions in Ding that Example 1E is not therapeutically effective.

To establish *prima facie* obviousness of a claimed invention, all the claim features must be taught or suggested by the prior art. *In re Royka*, 490 F.2d 981, 180 USPQ 580 (CCPA 1974). Applicants submit that the claims as a whole, comprising a method employing a composition having a therapeutically effective amount of a cyclosporin component less than 0.1% and a ratio of a cyclosporin component to a hydrophobic component of less than 0.08 is not taught or

suggested by Ding. Indeed, Ding teaches against such compositions, which must be considered as non-obvious in light thereof.

CONCLUSION

As this reply is being filed within the shortened statutory time period, no fee is thought due in connection with this communication. However, if Applicants are in error in this regard, please use Deposit Account 05-4004 for the payment of any fee now due.

Should any matters remain unresolved, applicant requests the Examiner to telephone applicant's attorney at the telephone number given below.

No fee is believed due at this time. The Commissioner is authorized to charge any fee which may be required in connection with this Amendment to Deposit Account No. 01-0885.

Respectfully submitted,

September 2, 2008

/John E. Wurst/
John E. Wurst
Reg. No. 40,283
Attorney of Record

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Facsimile
~~ELECTRONICALLY~~ FILED 9/2/08

M. Butler

PTO/SB/06 (07-06)
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PATENT APPLICATION FEE DETERMINATION RECORD

Substitute for Form PTO-875

Application or Docket Number	Filing Date	☐ To be Mailed
11/897,177	08/28/2007	

APPLICATION AS FILED – PART I

	(Column 1)	(Column 2)	SMALL ENTITY ☐		OR	OTHER THAN SMALL ENTITY	
FOR	NUMBER FILED	NUMBER EXTRA	RATE ($)	FEE ($)		RATE ($)	FEE ($)
☐ BASIC FEE (37 CFR 1.16(a), (b), or (c))	N/A	N/A	N/A			N/A	
☐ SEARCH FEE (37 CFR 1.16(k), (i), or (m))	N/A	N/A	N/A			N/A	
☐ EXAMINATION FEE (37 CFR 1.16(o), (p), or (q))	N/A	N/A	N/A			N/A	
TOTAL CLAIMS (37 CFR 1.16(i))	minus 20 =	*	X $ =		OR	X $ =	
INDEPENDENT CLAIMS (37 CFR 1.16(h))	minus 3 =	*	X $ =			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 $250 ($125 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			TOTAL	

APPLICATION AS AMENDED – PART II

		(Column 1)		(Column 2)	(Column 3)	SMALL ENTITY		OR	OTHER THAN SMALL ENTITY	
AMENDMENT	09/02/2008	CLAIMS REMAINING AFTER AMENDMENT		HIGHEST NUMBER PREVIOUSLY PAID FOR	PRESENT EXTRA	RATE ($)	ADDITIONAL FEE ($)		RATE ($)	ADDITIONAL FEE ($)
	Total (37 CFR 1.16(i))	* 36	Minus	** 36	= 0	X $ =		OR	X $50=	0
	Independent (37 CFR 1.16(h))	* 2	Minus	***2	= 0	X $ =		OR	X $210=	0
	☐ 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	0

		(Column 1)		(Column 2)	(Column 3)					
AMENDMENT		CLAIMS REMAINING AFTER AMENDMENT		HIGHEST NUMBER PREVIOUSLY PAID FOR	PRESENT EXTRA	RATE ($)	ADDITIONAL FEE ($)		RATE ($)	ADDITIONAL FEE ($)
	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 number found in the appropriate box in column 1.

Legal Instrument Examiner:
/TERRY MALLOY ROSS/

This collection of information is required by 37 CFR 1.16. 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 12 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.

TRANSMITTAL FORM

(to be used for all correspondence after initial filing)

Application Number	11/897,177
Filing Date	August 28, 2007
First Named Inventor	Acheampong
Group Art Unit	1654
Examiner Name	Cordero Garcia, M
Total Number of Pages in This Submission: 2	Attorney Docket Number: D-3111CON (17618CON)

ENCLOSURES *(check all that apply)*

- ☐ Fee Transmittal Form *(in duplicate)*
  - ☐ Fee Attached
- ☐ Amendment/Reply
  - ☐ After Final
  - ☐ Affidavits/declaration(s)
- ☐ Extension of Time Request
- ☐ Express Abandonment Request
- ☐ Information Disclosure Statement
- ☐ Certified Copy of Priority Document(s)
- ☐ Response to Missing Parts/ Incomplete Application
  - ☐ Response to Missing Parts under 37 CFR 1.52 or 1.53
- ☐ Drawing(s)
- ☐ Licensing-related Papers
- ☐ Petition
- ☐ Petition to Convert to a Provisional Application
- ☐ Power of Attorney, Revocation Change of Correspondence Address
- ☐ Terminal Disclaimer
- ☐ Request for Refund
- ☐ CD, Number of CD(s) ____
  - ☐ Landscape Table on CD
- ☐ After Allowance Communication to TC
- ☐ Appeal Communication to Board of Appeals and Interferences
- ☐ Appeal Communication to TC *(Appeal Notice, Brief, Reply Brief)*
- ☐ Proprietary Information
- ☐ Status Letter
- ☒ Other Enclosure(s) *(please identify below)*

Change of Correspondence Address

Remarks

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

Firm Name	Stout, Uxa, Buyan & Mullins, LLP		
Signature			
Printed Name	Frank J. Uxa		
Date	9/8/08	Reg. No.	25,612

CERTIFICATE OF TRANSMISSION/MAILING

I hereby certify that this correspondence is being facsimile transmitted to the USPTO at fax number 571-273-8300, or deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Mail Stop Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on the date shown below.

Signature			
Typed or printed name	JANET McGHEE	Date	9/8/08

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U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

CHANGE OF CORRESPONDENCE ADDRESS
Application

Address to:
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Alexandria, VA 22313-1450

Application Number	11/897,177
Filing Date	August 28, 2007
First Named Inventor	Acheampong
Art Unit	1654
Examiner Name	Cordero Garcia, M
Attorney Docket Number	D-3111CON (17618CON)

Please change the Correspondence Address for the above-identified patent application to:

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I am the:

☐ Applicant/Inventor

☐ Assignee of record of the entire interest.
Statement under 37 CFR 3.73(b) is enclosed. (Form PTO/SB/96).

☑ Attorney or agent of record. Registration Number 25,612.

☐ Registered practitioner named in the application transmittal letter in an application without an executed oath or declaration. See 37 CFR 1.33(a)(1). Registration Number_____.

Signature

Typed or Printed Name Frank J. Uxa

Date 9/8/08 | Telephone 949-450-1750

NOTE: Signatures of all the inventors or assignees of record of the entire interest or their representative(s) are required. Submit multiple forms if more than one signature is required, see below*.

☑ *Total of 1 forms are submitted.

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
11/897,177	08/28/2007	Andrew Acheampong	D-3111 CON	3860

51957 7590 12/12/2008

ALLERGAN, INC.
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IRVINE, CA 92612-1599

EXAMINER	
CORDERO GARCIA, MARCELA M	
ART UNIT	PAPER NUMBER
1654	

MAIL DATE	DELIVERY MODE
12/12/2008	PAPER

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.

Office Action Summary	Application No.	Applicant(s)	
	11/897,177	ACHEAMPONG ET AL.	
	Examiner	Art Unit	
	MARCELA M. CORDERO GARCIA	1654	

-- 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 *02 September 2008*.

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

3)☐ 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

4)☒ Claim(s) *1-36* is/are pending in the application.

4a) Of the above claim(s) *21-36* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-20* is/are rejected.

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

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

Application Papers

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

10)☐ 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).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

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).

a)☐ All b)☐ Some * c)☐ None of:

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) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

U.S. Patent and Trademark Office

DETAILED ACTION

This Office Action is in response to the reply received on 2 September 2008.

Claims1-36 are pending in the application.

Claims 1-20 are presented for examination on the merits as they read upon the elected species wherein the cyclosporin component is cyclosporin A, the hydrophobic component is castor oil, and wherein the weight ratio of cyclosporin A to castor oil is 0.04. Claims 21-36 are withdrawn as drawn to a non-elected group.

Any rejection from the previous office action, which is not restated here, is withdrawn.

Rejection maintained

Claim Rejections - 35 USC § 103

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.

> This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-20 are rejected under 35 U.S.C. 103(a) as being obvious over Ding et al. (US 5,474,979 cited in the IDS of 11/14/07).

Ding et al. teach 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 cyclosporin component in a therapeutically effective amount of less than 0.1% by weight, the weight ratio of the cyclosporin component (cyclosporin A, e.g., Example 1D and column 3, lines 30-37) to the hydrophobic component (castor oil, a vegetable oil) is 0.08 (see, e.g., Example 1D). Ding et al. also teach embodiment 1B which has 0.2% of cyclosporin and a 0.04 ratio of cyclosporin/castor oil. Additionally, embodiment 1E has 0.05% of cyclosporin A and 0.08 ratio cyclosporin/castor oil. Ding et al. do teach that an embodiment having both less than 0.1 % of cyclosporin and wherein the weight ratio of the cyclosporin component to the hydrophobic component can be less than 0.08 (0.12 to 0.02). In addition, Ding et al. teach in claim 8 a pharmaceutical emulsion consisting of between about 0.05% and about 0.40% by weight cyclosporin A (which reads upon the limitation "less than 0.1 % by weight cyclosporin A" of instant claim 1) and between 0.625 and about 5.0 % castor oil. The corresponding lower and upper rations for the range is 0.05%/5.0% = 0.01 weight ratio of cyclosporin A/castor oil, which reads upon the limitation in claim 1 "the weight ratio of he cyclosporin A to the castor oil being less than 0.08". The limitations of claim 2: "dry eye syndrome" and of claim 3: "effective in treating dry eye syndrome" are taught, e.g., in column 5, lines 10-14. The limitation of claim 4: "wherein the blood of the human or animal has substantially no detectable concentration of cyclosporin component" and of claim 5: "wherein the blood of the human or animal has substantially no detectable concentration of the cyclosporin component as measure using a validated liquid chromatography/mass spectrometry-mass spectrometry analytical method" and the limitation of claim 6: "0.1 ng/mL or less" necessarily read upon the method of Ding et al. since it teaches overlapping steps/concentrations. The limitation of claims 7-8: "cyclosporin A" is taught, e.g., in Example 1. The limitation of claim 9:

“wherein the cyclosporin component is solubilized in the hydrophobic component present in the composition" is taught in column 3, lines 21-23. The limitations of claim 10: “wherein the hydrophobic component is present in the composition in an amount greater than 0.625% by weight“, of claim 11: "oily material", of claim 12: "vegetable oils" and of claim 13: "castor oil" are taught, e.g., in Examples 1A-D which teach 5.00%, 2.5% and 1.25% of hydrophobic component (castor oil). The limitation of claim 14: “topically administering the composition to the eye" is taught, e.g., in column 5, lines 15-18 and claim 8 of Ding et al. The limitation of claim 15: “whrein the composition comprises an effective amount of an emulsifier component” is taught in column 3, lines 38-4 and 50-56. The limitations of claim 16-17: “tonicity" and "organic tonicity component" are taught in column 4, lines 12-19. The limitation of claim 18: “polyelectrolyte component in an amount effective in stabilizing the composition” is taught in column 3, lines 64-67 and column 4, lines 1-12. The limitation of claims 19-20 drawn to ph ranges of "of about 7.0 to about 8.0" and “of about 7.2 to about 7.6” are taught, e.g., in Example 1A-1E and in claim 8 of Ding et al.

Ding et al. do not expressly teach an embodiment comprising both less than 0.1% of cyclosporin A and less than 0.08 cyclosporin A/castor oil ratio. The closest embodiments are 1D comprising 0.10% of cyclosporin A and 0.08 cyclosporin A/castor oil ratio; 1E comprising 0.05% of cyclosporin A and 0.08 cyclosporin A/castor oil ratio and 1B comprising 0.20% cyclosporin A and 0.04 cyclosporin A/castor oil ratio. While Ding et al. does teach a method of treating an eye of an animal comprising: administering an eye of the animal a composition, Ding et al. did not apply the composition to an eye of a human. It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the compositions of Ding et

al. (such as 1E) by increasing the amount of castor oil or decreasing the cyclosporin concentration in order to reduce the ratio of the cyclosporin component to hydrophobic component from 0.08 to, e.g., 0.04 as taught by Ding et al. (see, e.g., column 3, lines 18-20) and exemplified in embodiment 1B. The skilled artisan would have been motivated to do so because such proportions were taught by the Ding et al. patent. There would have been a reasonable expectation of success, given that compositions with a higher amount of castor oil are encompassed by the Ding et al. claims (e.g., claim 8, embodiment 1B) and because optimizing the ratio of cyclosporin/hydrophobic components to below 0.08 (i.e., 0.02 to 0.12, which reads upon the range of ratios of 0.02 to 0.08) was taught by Ding et al. (e.g., column 3, lines 18-20) and embodiment 1B (which has 0.04). The adjustment of particular conventional working conditions (e.g., using all the ratios and proportions taught by Ding. et al., applying to a human population instead of a rabbit population within such method) is deemed merely a matter of judicious selection and routine optimization that is well within the purview of the skilled artisan. As such, it would have been obvious to one skilled in the art at the time of invention to determine all optimum and operable conditions [e.g., formulation ranges and proportions, patient population (e.g., column 1, lines 10-15)], because such conditions are art-recognized result-effective variables that are routinely determined and optimized in the art through routine experimentation ("[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation.". *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). See MPEP 2145.05). One would have been motivated to determine all optimum and operable conditions in order to achieve the safest and most effective method in the most efficient manner. One would have had a reasonable

expectation for success because such modifications are routinely determined and optimized in the art through routine experimentation.

From the teaching of the references, 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.

Applicants' arguments

An invention is patentable unless the invention is lacking in utility or novelty, or is obvious. The burden of proving that an invention lacks one of these requirements is placed upon one who challenges the patentability of an invention; see e.g., 35 USC 101 ("whoever invents or discovers any new and useful process, machine, manufacture or composition of matter … may obtain a patent therefor subject to the conditions and requeriments of this title.")

The examiner has characterized the prior art (Ding) as having disclosed a method of treating an eye of a human or animal comprising administering a composition in the form of an emulsion comprising water, a hydrophobic component and a cyclosporin component in a therapeutical 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, rather than less than 0.8. Furthermore, Example 1D contains 0.1 % w/v a cyclosporin component, rather than 01%.

The Office Action attempts to anticipate this objection by citin Example 1B of Ding. However, this Example is a composition that contains 0.2% of a cyclosporin component and

5.00% castor oil, yielding an cyclosporin to castor oil ratio of 0.04. However, of course, the cyclosporin concentration of 0.2% is more than twice the concentration (less than 0.1%) permitted by the present claims.

The Office Action also attempts to meet the deficiencies of Examples 1D and IB by also citing the composition of Example 1E of Ding. However, this composition, the only composition disclosed by Ding to contain less than 0.1% cyclosporin A, also has a ratio of cyclosporin A to hydrophobic component of 0.08 rather than less than this amount.

Furthermore, the present claims require the concentration of a cyclosporin component used in the claimed method to be a "therapeutically effective concentration" less than 0.1%. However, Ding provides absolutely no suggestion that a concentration of a cyclosporin component less than 0.1% would be therapeutically effective at all. Ding mentions three times (in column 5, lines 15-32) that the formulations of Examples 1A-!D, which have cyclosporin A concentrations of 0.1% or to 0.4%, are bioavailable, non-toxic and therapeutically effective. However, conspicuously absent from all these date is any mention of the composition of Example 1E.

Ding's conspicuous omission from mention of Example 1E as a formulation having therapeutic effectivenes cannot simply be ignored; it is part of the prior art as a whole. And a person of ordinary skill in the art would certainly consider this omission, repeated by Ding three times, as intentional. Thus, Ding, like any prior art reference, must be considered for all it teaches, particularly when, as here, it so obviously teaches away from the invention.

The Office Action next alleges that claim 8 of Ding teaches than a composition has less than 0.1% cyclosporin and the weight ratio of a cyclosporin component to hydrophobic

component "can be" less than 0.08. Claim 8 is drawn to an emulsion containing, among other ingredients, between about 0.05% and about 0.40% cyclosporin A, and about 0.625% and about 5.0% castor oil, both by weight. Claim 8 does not expressly mention ratios of a cyclosporin component to hydrophobic component; however, if ratios are to be calculated from these ingredients, it is true that the lowest ratios implied by these concentrations would be about 0.05/5.0 = 0.01, and the highest ratio would be about 4.0/ 0.625 = 0.64.

Even if claim 8 were interpreted to implicitly disclose the range of ratios of about 0.01 to about 0.64, the Office actions neither alleges, nor does Ding teach that compositions having less than 0.1% of a cyclosporin component are therapeutically effective. Indeed, claim 8 says nothing about therapeutic effectiveness at all claimed concentrations, and it is unreasonable to assume that it does, since a patent claim need not cover only operative embodiments. *See e.g., Atlas Powder Col. V. E.I. du Pont de Nemours & Co.,* 750 F.2d 1569, 1577, 224 USPQ 409, 414 (Fed. Cir. 1984). (Holding that the presence of inoperative embodiments within the scope of a claim does not necessarily render a claim unpatentable). If a patent claim may encompass inoperative embodiments, then, by definition, the teaching of that patent claim cannot, without more, be that every embodiment encompassed by the claim is operative.

Therefore, a person of ordinary skill in the art would clearly not be justified in believing that claim 8 of Ding suggests that formulations containing less than 0.1% are therapeutically effective.

To establish prima facie obviousness of a claimed invention, all the claim features must be taught or suggested by the prior art. *In re Royka*, 490 F. 2d 981, 180 USPQ 580 (CCPA 1974). Applicants submit that the claims a a whole, comprising a method employing a composition

having a therapeutically effective amount of a cyclosporin component less than 0.1% and a ratio of cyclosporin component to a hydrophobic component of less than 0.08 is not taught or suggested by Ding. Indeed, Ding teaches against such compositions, which must be considered as non-obvious in light thereof.

Response to Arguments

Applicants' arguments have been carefully considered but not deemed persuasive for the following reasons.

The Ding reference teaches that cyclosporins are immunosuppressant and enhance or restore lacrimal gland tearing and minimizing the problems related to unpleasant sensation and syndrome exacerbation by reducing the oil content and dispersing the oil phase in water into an emulsion. The emulsions of Ding utilize higher fatty acid glycerides but in combination with polysorbate 80 which results in an emulsion with a high comfort level and low irritation potential suitable for delivery of medications to sensitive areas such as ocular tissues. Ding teaches nonirritating pharmaceutical compositions with high comfort level and low irritation potential suitable for delivery to sensitive areas such as ocular tissues comprises cyclosporin in admixture with an emulsifying amount of a higher fatty acid glycerol and polysorbate 80. More particularly, the composition comprises cyclosporin A and the higher fatty acid glyceride may comprise castor oil. (e.g., columns 1-3).

The Ding reference goes on to teach, preferably, the weight ratio of the castor oil to the polysorbate 80 is between about 0.3 to about 30, and a weight ratio of the cyclosporing to castor oil is below 0.16. More preferably, the weight ratio of castor oil to polysorbate 80 is between 0.5 and 12.5, and the weight ratio of cyclosporin to castor oil is between 0.12 and .02 (e.g., column

3). Additionally, Ding provides Examples 1-4 which further illustrate their invention (columns 4-5) which include treating keratoconjuctivitis sicca (dry eye) syndrome and Examples 1A-1D were also tested for ocular bioavailability in rabbits, and the therapeutic level of cyclosporin was found in the tissues of interest after dosage (e,g,, column 5). Applicants argue that he fact that Example 1E was not recorded as tested for ocular bioavailability implies that the composition of Example 1E (having 0.05% cyclosporin) did not have any therapeutic effectiveness and that therefore, the Ding reference teaches away from such compositions or methods of use. However, nowhere in the Ding reference it is expressly stated that such compositions having less than 0.10% would be inoperative. Moreover, at column 5, at lines 10-15, Ding teaches that "[t]he formulations set forth in Examples 1-4 were made for treatment of keratoconjunctivitis sicca (dry eye syndrome)…". Therefore it is clear that such compositions, including Examples 1A thru 1E (having as low as 0.05% of cyclosporin) were all intended as therapeutic compositions. Additionally, Applicants' claim that having less cyclosporin than 0.1 % would render the embodiment inoperable is not deemed persuasive for the following reasons: Please note that Example 1D encompasses 0.10 % of cyclosporin and shows ocular bioavailability at a therapeutic level. (e.g., column 5, lines 15-25). Therefore, one skilled in the art at the time the invention was made would have concluded that there would be a reasonable expectation of success that a composition having slightly less than 0.10% cyclosporin (e.g., 0.09%) and slightly less than 0.08 cyclosporin/castor oil (e.g., 0.07) would still maintain therapeutic activity when topically applied to the eye, especially in light of the teachings of Ding describing preferred embodiments for nonirritating pharmaceutical compositions with high comfort level and low irritation potential suitable for delivery to sensitive areas such as ocular tissues with weight ratios

of cyclosporin/castor oil more preferably between 0.12 and 0.02 (e.g., column 3, lines 15-20) and the teachings of claim 8 that encompass pharmaceutical emulsions for topical application encompassing 0.05% cyclosporin or more (which reads upon the instantly claimed "less than 0.1% of cyclosporin") and as low as 0.01 ratio of cyclosporin to castor oil (which reads upon the instantly claimed "less than 0.08" weight ratio of cyclosporin/castor oil). Therefore, the obviousness rejection in view of Ding is maintained.

Conclusion

No claim is allowed.

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

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

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, Cecilia J. Tsang can be reached on (571) 272-0562. 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.

/Cecilia Tsang/
Supervisory Patent Examiner, Art Unit 1654
MMCG 12/08

/Marcela M Cordero Garcia/
Examiner, Art Unit 1654

Search Notes	Application/Control No.	Applicant(s)/Patent Under Reexamination
	11897177	ACHEAMPONG ET AL.
	Examiner	Art Unit
	MARCELA M CORDERO GARCIA	1654

SEARCHED			
Class	Subclass	Date	Examiner
none	none	12/01/08	MMCG

SEARCH NOTES		
Search Notes	Date	Examiner
updated	12/01/08	MMCG

INTERFERENCE SEARCH			
Class	Subclass	Date	Examiner

17618CON1(AP)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Acheampong et al	Examiner: Marcela M. Cordero Garcia
Serial No.: 11/897,177	Group Art Unit: 1654
Filed: August 28, 2007	Confirmation No.: 3860
For: METHODS OF PROVIDING THERAPEUTIC EFFECTS USING CYCLOSPORIN COMPONENTS	Customer No.: 051957

Response

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

Dear Sir:

The Applicants respond as follows to the Office Action of December 12, 2008 (the "Office Action"):

A listing of claims begins on page 2 of this paper.

Remarks begin on page 7 of this paper.

CLAIMS

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

1. (Currently amended) 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~~ hydrophobic component, and a cyclosporin component in a therapeutically effective amount ~~of less than 0.1%~~ equal to or less than 0.05% by weight of the composition, wherein the weight ratio of the cyclosporin component to the hydrophobic component is less than 0.08.

2. (Original) 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. (Original) The method of claim 1 wherein the administering step is effective in treating dry eye syndrome.

4. (Previously presented) The method of claim 1 wherein the blood of the human or animal has no detectable concentration of the cyclosporin component.

5. (Previously presented) 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 analytical method.

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

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

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

10. (Original) 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. (Original) The method of claim 1 wherein the hydrophobic component comprises an oily material.

12. (Original) 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. (Original) The method of claim 1 wherein the hydrophobic component comprises castor oil.

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

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

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

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

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

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

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

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

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

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

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

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

28. (Withdrawn) 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. (Withdrawn) The composition of claim 21 wherein the hydrophobic component comprises castor oil.

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

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

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

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

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

35. (Withdrawn) 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. (Withdrawn) 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.

37. (New) The method of claim 1, where the cyclosporin component is in a therapeutically effective amount of less than 0.05% by weight of the composition.

REMARKS

The Office action sets forth a single rejection. The examiner rejected the claims under 35 U.S.C. § 103(a), arguing that they are obvious in light of the Ding reference (US 5,474,979). The applicants respectfully disagree.

The Ding reference discloses various cyclosporin compositions. One composition contains the claimed amount of cyclosporin (0.05%, Example 1E), but does not, as required by the pending claims, contain a hydrophobic component in amount such that the ratio of cyclosporin to the hydrophobic component is less than 0.08. Another composition contains cyclosporin and a hydrophobic component in a ratio that is less than 0.08, but contains more than the claimed amount of cyclosporin (0.20%, Example 1B). The examiner has selected one feature from a particular example, a different feature from a different example, and combines them to arrive at the claimed invention. The applicants respectfully submit that doing so is possible only with the applicants specification as a guide – that without the benefit of this hindsight, one of ordinary skill in the art would not have made this combination with the expectation that it would be successful.

There is no reason, according to the Ding reference, to reduce the absolute amount of cyclosporin and increase its amount in proportion to the oil. The claims, as amended, are directed to methods of treating an eye using compositions containing 0.5% or less of cyclosporin. This is at the bottom (amended claim 1), or below (new claim 37), the range of cyclosporin compositions disclosed in the Ding reference. As the applicants note in their application:

> 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.

Specification, at ¶ 0005. There is good reason to do this, since, as the Ding reference describes,

> Another drawback of [prior art] formulations is that they contain a high concentration of oils, and oils exacerbate the symptoms of certain ocular surface diseases such as dry eyes, indicated by cyclosporin. Therefore, these oily formulations may not be clinically acceptable.

Col. 2, lns. 46-50. *See also* Ding reference, at col. 2, lns. 5-7 ("if oily preparations containing cyclosporin are applied directly to the eyes, irritation or a clouding of visual field may result."). Hence, the Ding reference suggests that where one decreases the amount of cyclosporin, one should correspondingly decrease the amount of oil.

The applicants' invention, in contrast, does precisely the opposite: it does not decrease the amount of oil in proportion to the amount of cyclosporin, but *increases* it. Example 1A of the Ding reference discloses a formulation comprising cyclosporin 0.40% and castor oil 5.00%; in a formulation containing 0.05% cyclosporin, then, one could use 0.625% castor oil (Example 1E of Ding), and achieve the same ratio of cyclosporin to castor oil (0.08) The applicants teach that one can do the opposite, instead: in one example, they disclose a formulation containing 0.05% cyclosporin, but, instead of a correspondingly lower amount of castor oil, they disclose that one can use twice as much of it (1.25%; Example I, Composition II), a ratio of cyclosporin to castor oil of 0.04.

It is true that the Ding reference also discloses a formulation having 0.20% cyclosporin and 5.0% castor oil, a ratio of 0.04 (Example IB). But the Ding reference contemplates the use of such a ratio with an amount of cyclosporin that it four times as much as the highest permitted by the claims of the present invention (0.05%). Moreover, the amount of castor oil, 5.0%, is the highest the Ding reference discloses (Examples 1-4), and, in claim 8, the most it claims. The Ding reference suggests only that one should not formulate cyclosporin using more than 5.0% castor oil. It does not suggest that, when reducing the amount

of cyclosporin, one should not decrease but *increase* the relative amount of castor oil or other hydrophobic component, as in the applicant's invention.

For the foregoing reasons, the applicants respectfully request that the examiner withdraw the obviousness rejection.

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,

/JOEL B. GERMAN/

Date: June 05, 2009

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Electronic Acknowledgement Receipt

EFS ID:	5461177
Application Number:	11897177
International Application Number:	
Confirmation Number:	3860
Title of Invention:	Methods of providing therapeutic effects using cyclosporin components
First Named Inventor/Applicant Name:	Andrew Acheampong
Customer Number:	51957
Filer:	Joel B. German/Bonnie Ferguson
Filer Authorized By:	Joel B. German
Attorney Docket Number:	17618CON (AP)
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Time Stamp:	12:16:51
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		17618CON1Response060509toOfficeaction.pdf	88496 382281dcd46015ae87d1e4d21ad326bb748443ec	yes	9

	Multipart Description/PDF files in .zip description		
	Document Description	**Start**	**End**
	Amendment After Final	1	1
	Amendment Copy Claims/Response to Suggested Claims	2	6
	Applicant Arguments/Remarks Made in an Amendment	7	9
Warnings:			
Information:			
	Total Files Size (in bytes):	88496	

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New Applications Under 35 U.S.C. 111
If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

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

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

PTO/SB/30 (01-08)
Approved for use through 03/31/2008. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Request for Continued Examination (RCE) Transmittal

Address to:
Mail Stop RCE
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Application Number	11/897,177
Filing Date	August 28, 2007
First Named Inventor	Andrew Acheampong
Art Unit	1654
Examiner Name	Marcela M. Cordero Garcia
Attorney Docket Number	17618CON1(AP)

This is a Request for Continued Examination (RCE) under 37 CFR 1.114 of the above-identified application.
Request for Continued Examination (RCE) practice under 37 CFR 1.114 does not apply to any utility or plant application filed prior to June 8, 1995, or to any design application. See Instruction Sheet for RCEs (not to be submitted to the USPTO) on page 2.

1. Submission required under 37 CFR 1.114 Note: If the RCE is proper, any previously filed unentered amendments and amendments enclosed with the RCE will be entered in the order in which they were filed unless applicant instructs otherwise. If applicant does not wish to have any previously filed unentered amendment(s) entered, applicant must request non-entry of such amendment(s).

   a. ☐ Previously submitted. If a final Office action is outstanding, any amendments filed after the final Office action may be considered as a submission even if this box is not checked.

      i. ☐ Consider the arguments in the Appeal Brief or Reply Brief previously filed on _____

      ii. ☐ Other _____

   b. ☑ Enclosed

      i. ☑ Amendment/Reply

      ii. ☐ Affidavit(s)/ Declaration(s)

      iii. ☐ Information Disclosure Statement (IDS)

      iv. ☐ Other _____

2. Miscellaneous

   a. ☐ Suspension of action on the above-identified application is requested under 37 CFR 1.103(c) for a period of _____ months. (Period of suspension shall not exceed 3 months; Fee under 37 CFR 1.17(i) required)

   b. ☐ Other _____

3. Fees The RCE fee under 37 CFR 1.17(e) is required by 37 CFR 1.114 when the RCE is filed.

   a. ☑ The Director is hereby authorized to charge the following fees, any underpayment of fees, or credit any overpayments, to Deposit Account No. 01-0885. I have enclosed a duplicate copy of this sheet.

      i. ☑ RCE fee required under 37 CFR 1.17(e)

      ii. ☑ Extension of time fee (37 CFR 1.136 and 1.17)

      iii. ☐ Other _____

   b. ☐ Check in the amount of $ _____ enclosed

   c. ☐ Payment by credit card (Form PTO-2038 enclosed)

WARNING: Information on this form may become public. Credit card information should not be included on this form. Provide credit card information and authorization on PTO-2038.

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT REQUIRED

Signature	/Joel B. German/	Date	June 5, 2009
Name (Print/Type)	Joel B. German	Registration No.	48,676

CERTIFICATE OF MAILING OR TRANSMISSION

I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Mail Stop RCE, Commissioner for Patents, P. O. Box 1450, Alexandria, VA 22313-1450 or facsimile transmitted to the U.S. Patent and Trademark Office on the date shown below.

Signature			
Name (Print/Type)		Date	

Electronic Patent Application Fee Transmittal

Application Number:	11897177
Filing Date:	28-Aug-2007
Title of Invention:	Methods of providing therapeutic effects using cyclosporin components
First Named Inventor/Applicant Name:	Andrew Acheampong
Filer:	Joel B. German/Bonnie Ferguson
Attorney Docket Number:	17618CON (AP)

Filed as Large Entity

Utility under 35 USC 111(a) Filing Fees

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Basic Filing:				
Pages:				
Claims:				
Miscellaneous-Filing:				
Petition:				
Patent-Appeals-and-Interference:				
Post-Allowance-and-Post-Issuance:				
Extension-of-Time:				

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Miscellaneous:				
Request for continued examination	1801	1	810	810
		Total in USD ($)		**810**

Electronic Acknowledgement Receipt

EFS ID:	5461467
Application Number:	11897177
International Application Number:	
Confirmation Number:	3860
Title of Invention:	Methods of providing therapeutic effects using cyclosporin components
First Named Inventor/Applicant Name:	Andrew Acheampong
Customer Number:	51957
Filer:	Joel B. German/Bonnie Ferguson
Filer Authorized By:	Joel B. German
Attorney Docket Number:	17618CON (AP)
Receipt Date:	05-JUN-2009
Filing Date:	28-AUG-2007
Time Stamp:	12:43:14
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	Deposit Account
Payment was successfully received in RAM	$810
RAM confirmation Number	8014
Deposit Account	010885
Authorized User	

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)

1	Request for Continued Examination (RCE)	6-5-09-17618CON1Rce.pdf	72687 62ae29a0071740f4b1c18a2eb4d34d0f9eced48c	no	1
Warnings:					
This is not a USPTO supplied RCE SB30 form.					
Information:					
2	Fee Worksheet (PTO-875)	fee-info.pdf	30293 fcda2cd244c1ad4c3d6bba57a1b1abc70c07b13a	no	2
Warnings:					
Information:					
			Total Files Size (in bytes):	102980	

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.

PTO/SB/06 (07-06)
Approved for use through 1/31/2007. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
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PATENT APPLICATION FEE DETERMINATION RECORD

Substitute for Form PTO-875

Application or Docket Number	Filing Date	☐ To be Mailed
11/897,177	08/28/2007	

APPLICATION AS FILED – PART I

	(Column 1)	(Column 2)	SMALL ENTITY ☐		OR	OTHER THAN SMALL ENTITY	
FOR	NUMBER FILED	NUMBER EXTRA	RATE ($)	FEE ($)		RATE ($)	FEE ($)
☐ BASIC FEE (37 CFR 1.16(a), (b), or (c))	N/A	N/A	N/A			N/A	
☐ SEARCH FEE (37 CFR 1.16(k), (i), or (m))	N/A	N/A	N/A			N/A	
☐ EXAMINATION FEE (37 CFR 1.16(o), (p), or (q))	N/A	N/A	N/A			N/A	
TOTAL CLAIMS (37 CFR 1.16(i))	minus 20 =	*	X $ =		OR	X $ =	
INDEPENDENT CLAIMS (37 CFR 1.16(h))	minus 3 =	*	X $ =			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 $250 ($125 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			TOTAL	

APPLICATION AS AMENDED – PART II

AMENDMENT	06/05/2009	(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA	SMALL ENTITY RATE ($)	ADDITIONAL FEE ($)	OR	OTHER THAN SMALL ENTITY RATE ($)	ADDITIONAL FEE ($)
	Total (37 CFR 1.16(i))	* 37	Minus	** 36	= 1	X $ =		OR	X $52=	52
	Independent (37 CFR 1.16(h))	* 2	Minus	***3	= 0	X $ =		OR	X $220=	0
	☐ 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	**52**

AMENDMENT		(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA	RATE ($)	ADDITIONAL FEE ($)	OR	RATE ($)	ADDITIONAL FEE ($)
	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 number found in the appropriate box in column 1.

Legal Instrument Examiner:
/MARY PEOPLES/

Document code: WFEE

United States Patent and Trademark Office
Sales Receipt for Accounting Date: 06/10/2009

MPEOPLES SALE #00000001 Mailroom Dt: 06/05/2009 010885 11897177
01 FC : 1202 52.00 DA

17618CON1(AP)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Acheampong et al	Examiner: Marcela M. Cordero Garcia
Serial No.: 11/897,177	Group Art Unit: 1654
Filed: August 28, 2007	Confirmation No.: 3860
For: METHODS OF PROVIDING THERAPEUTIC EFFECTS USING CYCLOSPORIN COMPONENTS	Customer No.: 051957

Amendment

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

Dear Sir:

The Applicants submit with this paper a list of amended claims at page 2. Remarks follow at page 5.

CLAIMS

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

1. (Currently amended) A method of treating ~~an eye of a human or animal comprising:~~ a condition selected from vernal conjunctivitis and atopic keratoconjunctivitis, the method 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 equal to or less than 0.05% by weight of the composition, wherein the weight ratio of the cyclosporin component to the hydrophobic component is less than 0.08.

2. (Original) 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. (Original) The method of claim 1 wherein the administering step is effective in treating dry eye syndrome.

4. (Previously presented) The method of claim 1 wherein the blood of the human or animal has no detectable concentration of the cyclosporin component.

5. (Previously presented) 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 analytical method.

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

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

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

10. (Original) 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. (Original) The method of claim 1 wherein the hydrophobic component comprises an oily material.

12. (Original) 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. (Original) The method of claim 1 wherein the hydrophobic component comprises castor oil.

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

15. (Original) The method of claim 1 wherein the composition comprises

an effective amount of an emulsifier component.

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

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

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

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

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

21. – 36 (canceled).

37. (Previously presented) The method of claim 1, where the cyclosporin component is in a therapeutically effective amount of less than 0.05% by weight of the composition.

REMARKS

The applicants have reviewed the prosecution history of the present application and co-pending application no. 10/927,857, and have found significant errors. The purpose of this filing is to bring those errors to the attention of the examiner, to file an IDS, and to submit new claims.

The Ding reference and obviousness

The present application describes two compositions at Example 1. Composition II is as follows:

Present Application

	Composition II
Cyclosporin A	0.05 %
Castor Oil	1.25 %
Polysorbate 80	1.00 %
Pemulin®	0.05 %
Glycerine	2.20 %
NaOH	qs
Purified water	qs
pH	7.2-7.6
Ratio cyclosporin to castor oil	0.04

A method of using composition II fell within the scope of the original claims that the applicants previously presented for prosecution.

In a final action dated December 12, 2008, the Office rejected the claims under 35 U.S.C. § 103 in view of U.S. Patent No. 5,474,979 (the "Ding reference"). The Ding reference discloses at Examples 1B, 1D, and 1E the compositions shown on the following page.

Ding Reference

	Example 1B	Example 1D	Example 1E
Cyclosporin A	0.40 %	0.05 %	0.05 %
Castor Oil	5.00 %	0.625 %	0.625 %
Polysorbate 80	1.00 %	1.00 %	1.00 %
Pemulin®	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
Ratio cyclosporin to castor oil	0.08	0.08	0.08

The only difference between Composition II of the present application, and Examples 1D and 1E of the Ding reference, is that Example 1D has more cyclosporin, and Example 1E has less castor oil. The only difference between Composition II and Example 1B of the Ding reference, is that Example 1B has less cyclosporin and less castor oil, although both compositions have cyclosporin and castor oil in the same proportion. Stated differently, Composition II has the same amount of cyclosporin as Example 1E, the same amount of castor oil as Example 1D, and the same proportion of cyclosporin to castor oil as Example 1B. As shown on the following page, the compositions are otherwise the same.

Compositions of the Ding reference compared to

Composition II of the present application '

	Ding *et al.* Example 1B	Ding *et al.* Example 1D	Ding *et al.* Example 1E	Composition II
Cyclosporin A	0.20 %	0.10 %	**0.05 %**	**0.05 %**
Castor Oil	5.00 %	**1.250 %**	0.625 %	**1.250 %**
Polysorbate 80	1.00 %	1.00 %	1.00 %	1.00 %
Pemulin®	0.05 %	0.05 %	0.05 %	0.05 %
Glycerine	2.20 %	2.20 %	2.20 %	2.20 %
NaOH	qs	qs	qs	qs
Purified water	qs	qs	qs	qs
pH	7.2-7.6	7.2-7.6	7.2-7.6	7.2-7.6
cyclosporin : castor oil	**0.04**	0.08	0 .08	**0.04**

The Office argued that the differences between the compositions disclosed in the Ding reference and the compositions of the present application were obvious:

> It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the composition of Ding et al. by increasing the amount of castor oil or decreasing the cyclosporine concentration. . . . [O]ne skilled in the art would readily envisage the claimed composition. The skilled artisan would have been motivated to do so because such proportions were taught by the Ding et al. patent. There would have been a reasonable expectation of success, given that compositions with a higher amount of castor oil are encompassed by the Ding et al. claims and because optimizing the ratio of cyclosporine/hydrophobic components to below 0.08 was taught by Ding et al.

Office action dated December 12, 2008, at 4-5 (parenthetical text omitted).

The applicants concede that it would have been obvious to modify examples 1A-1E of the Ding reference to arrive at Composition II of the present

application. The differences are insignificant. One need only use the cyclosporin concentration of Example 1E (0.05%), the castor oil concentration of Example 1D (1.250%), and the remaining ingredients of those examples. As the examiner correctly observes, one of ordinary skill in the art "would readily envisage" such a composition, especially in view of Example 1B: having selected 0.05% as the concentration of cyclosporin, Example 1B (wherein the ratio of cyclosporin to castor oil is 0.04) teaches that the concentration of castor oil should be 1.250% (0.05% / 1.250% = 0.04). The applicants concede that in making this selection (0.05% cyclosporin and 1.250% castor oil) there would have been a reasonable expectation of success; the differences between Examples 1A-1E and Composition II are too small to believe otherwise.

The formulation of Composition II is squarely within the teaching of the Ding reference, and the Office should disregard any statements by the applicants suggesting otherwise, whether in this application or in co-pending application no. 10/927,857.

The Ding reference and 0.05% cyclosporin

Counsel for the applicants attempted to distinguish the Ding reference by arguing that it does not disclose any therapeutically effective compositions comprising less than 0.10% cyclosporin. That argument is in error. It urges an interpretation of the Ding reference that the applicants do not accept.

Counsel for the applicants had advanced a case based not on evidence but on speculation: the Ding reference states that Examples 1A-1D were tested for ocular bioavailability; it does not state that Example 1E (cyclosporin 0.05%) was tested for ocular bioavailability; therefore, Ding *et al.* did not consider a 0.05% cyclosporin composition to be therapeutically effective. The examiner rejected this argument, and the applicants concede that the examiner was correct to do so.

Hence, the Office should disregard the following argument from the Amendment of September 8, 2008 and all statements filed in connection with this application or co-pending application no. 10/927,857 in support of that argument:

> Ding provides absolutely no suggestion that a concentration of a cyclosporin component less than 0.1% would be therapeutically effective at all. Ding mentions three times (in column 5, lines 15-32) that the formulations of Examples 1A-1D, which have cyclosporin A concentrations of 0.1% or to 0.4%, are bioavailable, non-toxic, and therapeutically effective. However, conspicuously absent from all these data is any mention of the composition of Example 1E.
>
> . . .
>
> Ding's conspicuous omission from mention of Example 1E as a formulation having therapeutic effectiveness cannot simply be ignored . . . a person of ordinary skill in the art would certainly consider this omission, repeated by Ding three times, as intentional.
>
> Thus, Ding . . . obviously teaches away from the claimed invention.

Applicants' Amendment, filed September 8, 2008, at 10-11 (emphasis omitted). Those statements are incorrect, and do not reflect the applicants' position.

Counsel's argument was based on an unfounded negative implication. It is the equivalent of arguing, for example, that because Ding *et al.* fail to state that their compositions are chemically stable, that one should expect them to explode; that because they fail to state that their compositions are not radioactive, that they are radioactive; or that because nowhere do Ding *et al.* state that the compositions will *not* give a patient x-ray vision, that one may conclude that the compositions will allow a patient to see through walls. Counsel's logic elevates speculation above evidence, and permits one to draw any conclusion, no matter how incredible.

Counsel for the applicants had not identified any reason to believe that the compositions of the Ding reference would be ineffective using cyclosporin in

amounts less than 0.10%. The Ding reference expressly discloses a composition comprising 0.05% cyclosporin; it describes its testing; and it claims its use. As the examiner aptly points out:

> nowhere in the Ding reference it is expressly stated that such compositions having less than 0.10% [cyclosporin] would be inoperative. Moreover . . . Ding teaches that "the formulations set forth in Examples 1-4 were made for treatment of keratoconjunctivitis sicca (dry eye syndrome) . . ." Therefore it is clear that such compositions, including Examples 1A thru 1E (having as low as 0.05% of cyclosporin) were all intended as therapeutic compositions.

Office action dated December 12, 2008, at 10 (emphasis omitted). The applicants concede that the examiner is correct.

In sum, the notion that that "Ding provides absolutely no suggestion that a concentration of a cyclosporin component less than 0.1% would be therapeutically effective at all," Applicants' Amendment, filed September 8, 2008, at 10-11, is incorrect. It improperly characterizes the Ding reference, and the Office should disregard any statements made in support of that characterization, whether in this application or in or co-pending application no. 10/927,857.

Claim amendments

In view of the foregoing, the applicants have amended the claims to recite a method of treating a condition selected from vernal conjunctivitis and atopic keratoconjunctivitis; the claims that the applicant previously presented were directed to a "method of treating an eye." Support for the conditions vernal keratoconjunctivitis and atopic keratoconjunctivitis may be found at paragraph 0031 of the present application.

Information Disclosure Statement

Composition II of Example I of the present application describes the formulation of Restasis®, a treatment for dry eye. Restasis® has been on sale in the United States since approximately April, 2003. The applicants submit with this paper an IDS with the prescribing information that Restasis is sold with.

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,

/JOEL B. GERMAN/

Date: June 15, 2009

JOEL B. GERMAN
Attorney of Record

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17618CON1(AP)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Acheampong et al	Examiner: Marcela M. Cordero Garcia
Serial No.: 11/897,177	Group Art Unit: 1654
Filed: August 28, 2007	Confirmation No.: 3860
For: METHODS OF PROVIDING THERAPEUTIC EFFECTS USING CYCLOSPORIN COMPONENTS	Customer No.: 051957

INFORMATION DISCLOSURE STATEMENT

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

Dear Sir:

In accordance with the provisions of 37 C.F.R. 1.56, 1.97, and 1.98, the attention of the Patent and Trademark Office is hereby directed to the documents listed on the attached form PTO-SB/08b (formerly 1449). It is respectfully requested that the documents be expressly considered during the prosecution of this application, and that the documents be made of record therein and appear among the "References Cited" on any patent to issue therefrom.

While these documents may be material pursuant to 37 C.F.R. §1.56, their disclosure is not intended to constitute an admission that the documents are prior art in regard to this invention. The filing of this Statement should not be construed to mean that a search has been conducted or that no other material documents or information exists. Please do not hesitate to contact the undersigned should any questions arise regarding this Statement.

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,

/JOEL B. GERMAN/

Date: June 15, 2009

JOEL B. GERMAN
Attorney of Record
Registration Number 48,676

Please direct all inquiries and correspondence to:
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Irvine, California 92612
Tel: (714) 246-4920 Fax: (714) 246-4249

FORM PTO-1449 U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE	ATTY. DOCKET NO.	SERIAL NO.
INFORMATION DISCLOSURE STATEMENT BY APPLICANT	17618CON1(AP)	11/897,177
(USE SEVERAL SHEETS IF NECESSARY)	APPLICANT: Andrew Acheampong	
	FILING DATE: August 28, 2007	GROUP: 1654

U.S. PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE (IF APPROPRIATE)

FOREIGN PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION	
							YES	NO

EXAMINER INITIAL		**OTHER DOCUMENTS** (INCLUDING AUTHOR, TITLE, DATE, PERTINENT PAGES, ETC.)
		Restasis Product Information Sheet - 5 pages

EXAMINER	DATE CONSIDERED

***EXAMINER**: INITIAL IF CITATION CONSIDERED, WHETHER OR NOT CITATION IS IN CONFORMANCE WITH MPEP 609; DRAW LINE THROUGH CITATION IF NOT IN CONFORMANCE AND NOT CONSIDERED, INCLUDE COPY OF THIS FORM WITH NEXT COMMUNICATION TO APPLICANT.

Electronic Acknowledgement Receipt

EFS ID:	5514333
Application Number:	11897177
International Application Number:	
Confirmation Number:	3860
Title of Invention:	Methods of providing therapeutic effects using cyclosporin components
First Named Inventor/Applicant Name:	Andrew Acheampong
Customer Number:	51957
Filer:	Joel B. German/Bonnie Ferguson
Filer Authorized By:	Joel B. German
Attorney Docket Number:	17618CON (AP)
Receipt Date:	15-JUN-2009
Filing Date:	28-AUG-2007
Time Stamp:	13:21:24
Application Type:	Utility under 35 USC 111(a)

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Submitted with Payment	no

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1		17618CONResponse061509.pdf	89088 db740e7f01fd5229983944ff856c45d2d1582be	yes	11

	Multipart Description/PDF files in .zip description				
	Document Description	**Start**	**End**		
	Amendment/Req. Reconsideration-After Non-Final Reject	1	1		
	Claims	2	4		
	Applicant Arguments/Remarks Made in an Amendment	5	11		
Warnings:					
Information:					
2	Transmittal Letter	17618CON-IDS-Trans6-15-09.pdf	56095 a04b1066c74c3b61d5e1d58e973386abaa9d0652	no	2
Warnings:					
Information:					
3	Information Disclosure Statement (IDS) Filed (SB/08)	17618CON1-1449-6-15-09.pdf	58398 3f9f4c999722209a16f74b8c3303c7c05c2467d9	no	1
Warnings:					
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4	NPL Documents	RestasisProductInfoSheetsb.pdf	62345 604160268435ab09d0183919a20f9a4d97bb6f79	no	5
Warnings:					
Information:					
		Total Files Size (in bytes):	265926		

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New Applications Under 35 U.S.C. 111
If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

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

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

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
11/897,177	08/28/2007	Andrew Acheampong	17618CON (AP)	3860

51957 7590 08/17/2009

ALLERGAN, INC.
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EXAMINER	
CORDERO GARCIA, MARCELA M	
ART UNIT	PAPER NUMBER
1654	
MAIL DATE	DELIVERY MODE
08/17/2009	PAPER

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.

Office Action Summary	Application No.	Applicant(s)	
	11/897,177	ACHEAMPONG ET AL.	
	Examiner	Art Unit	
	MARCELA M. CORDERO GARCIA	1654	

-- 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 *05 June 2009 and 15 June 2009*.

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

3)☐ 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

4)☒ Claim(s) *1-20 and 37* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-20 and 37* is/are rejected.

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

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

Application Papers

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

10)☐ 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).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

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).

a)☐ All b)☐ Some * c)☐ None of:

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) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *06/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

U.S. Patent and Trademark Office

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 6/5/09 has been entered.

2. Claims 1-20 and 37 are pending in the application. The claims were amended twice. The first amendment was filed on 6/5/09 with the RCE filing. The base claim was amended as follows:

> 1. (Currently amended) 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~~ hydrophobic component, and a cyclosporin component in a therapeutically effective amount ~~of less than 0.1%~~ equal to or less than 0.05% by weight of the composition, wherein the weight ratio of the cyclosporin component to the hydrophobic component is less than 0.08.
>
> Subsequently a second amendment was filed (6/15/09) as follows:
>
> 1. (Currently amended) A method of treating ~~an eye of a human or animal comprising:~~ a condition selected from vernal conjunctivitis and atopic keratoconjunctivitis, the method 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 equal to or less than 0.05% by weight of the composition, wherein the weight ratio of the cyclosporin component to the hydrophobic component is less than 0.08.

3. Any rejection from the previous office action, which is not restated here, is withdrawn.

New grounds of rejection necessitated by Applicant's amendment

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> 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.

5. Claims 2-3 are rendered vague and indefinite for lacking antecedent basis in the limitations as set forth below:

Claim 2 recites the limitations "treating a condition selected from the group consisting of dry eye syndrome, phacoanaphylactic endophthalmitis, uveitis, [...] and corneal graft rejection" in lines 2-4. There is insufficient antecedent basis for these limitations in the claim.

Claim 3 recites the limitation "treating dry eye syndrome" in line 2. There is insufficient antecedent basis for these limitations in the claim, since dry eye syndrome (i.e., keratoconjunctivitis sicca) is a different disease from the diseases claimed in claim 1, lines 2-3, from which this claim depends.

New grounds of rejection necessitated by Applicant's amendment

Claim Rejections - 35 USC § 103

6. 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.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 1-20 and 37 are rejected under 35 U.S.C. 103(a) as being obvious over Ding et al. (US 5,474,979 cited in the IDS of 11/14/07) in view of Secchi et al. (Amer Journal of Ophthalmology, 1990).

The Ding patent teaches that cyclosporins are immunosuppressant and enhance or restore lacrimal gland tearing (col. 1, lines 35-40) and minimizing the problems related to unpleasant sensation and syndrome exacerbation by reducing the oil content and dispersing the oil phase in water into an emulsion (col. 2, lines 55-67). The

emulsions of Ding utilize higher fatty acid glycerides but in combination with polysorbate 80 which results in an emulsion with a high comfort level and low irritation potential suitable for delivery of medications to sensitive areas such as ocular tissues (col. 3, lines 1-5). Ding teaches nonirritating pharmaceutical compositions with high comfort level and low irritation potential suitable for delivery to sensitive areas such as ocular tissues comprises cyclosporin in admixture with an emulsifying amount of a higher fatty acid glycerol and polysorbate 80. More particularly, the composition comprises cyclosporin A and the higher fatty acid glyceride may comprise castor oil. (e.g., cols. 1-3) for treating dry eye disease.

The Ding reference goes on to teach, preferably, the weight ratio of the castor oil to the polysorbate 80 is between about 0.3 to about 30, and a weight ratio of the cyclosporin to castor oil is below 0.16. More preferably, the weight ratio of castor oil to polysorbate 80 is between 0.5 and 12.5, and the weight ratio of cyclosporin to castor oil is between 0.12 and .02 (e.g., column 3). Additionally, Ding provides Examples 1-4 which further illustrate their invention (columns 4-5) which include treating keratoconjuctivitis sicca (dry eye) syndrome and Examples 1A-1D were also tested for ocular bioavailability in rabbits, and the therapeutic level of cyclosporin was found in the tissues of interest after dosage (e,g., col. 5). Moreover, at column 5, at lines 10-15, Ding teaches that "[t]he formulations set forth in Examples 1-4 were made for treatment of keratoconjunctivitis sicca (dry eye syndrome)…". Therefore it is clear that such compositions, including Examples 1A thru 1E (having as low as 0.05% of cyclosporin) were all intended as therapeutic compositions. Please note that Example 1D

encompasses 0.10 % of cyclosporin and shows ocular bioavailability at a therapeutic level. (e.g., column 5, lines 15-25). Therefore, one skilled in the art at the time the invention was made would have concluded that there would be a reasonable expectation of success that a composition having slightly less than 0.10% cyclosporin (e.g., 0.05%) and slightly less than 0.08 cyclosporin/castor oil (e.g., 0.07) would still maintain therapeutic activity when topically applied to the eye, especially in light of the teachings of Ding describing preferred embodiments for nonirritating pharmaceutical compositions with high comfort level and low irritation potential suitable for delivery to sensitive areas such as ocular tissues with weight ratios of cyclosporin/castor oil more preferably between 0.12 and 0.02 (e.g., column 3, lines 15-20) and the teachings of claim 8 that encompass pharmaceutical emulsions for topical application encompassing 0.05% cyclosporin or more (which reads upon the instantly claimed “equal to or less than 0.05% of cyclosporin”) and as low as 0.02 ratio of cyclosporin to castor oil (which reads upon the instantly claimed "less than 0.08" weight ratio of cyclosporin/castor oil).

Ding et al. do not expressly teach treating the diseases “vernal conjunctivitis or atopic keratoconjunctivitis”.

However, at the time the invention was made, it was known to use cyclosporin to treat vernal conjunctivitis. For example, Secchi et al. teach that cyclosporine was effective in the treatment of both corticosteroid-dependent and corticosteroid-resistant vernal keratoconjunctivitis. Secchi et al. teach that several investigations have demonstrated that the modulation of the helper/suppressor interaction and the inhibition of the interleukin production (mainly interleukin-2), both phenomena induced by the

systemic use of cyclosporine were highly effective in the treatment of severe ocular disease of immunologic origin. The experiments were made by using topical cyclosporine (2% in castor oil) in the long-term treatment of 11 patients with vernal keratoconjunctivitis. (e.g., page 641) Additionally, Secchi et al. taught that cyclosporine 2% solution in castor oil seemed to be better tolerated than 1% suspension in balanced salt solution. A few patients treated with the balanced salt solution suspension showed severe lesions in the corneal epithelium within the first week of treatment. Conversely, the patients treated with the castor oil solution alone had only mild and transient discomfort, and minor epithelial changes (e.g., page 644).

Secchi et al. disclosed that the topical use of cyclosporine would permit the use of lower concentration with less frequent daily administrations and shorter treatment time.

With respect to the limitations claimed: Ding et al. teach 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 cyclosporin component in a therapeutically effective amount equal to or less than 0.05% by weight, the weight ratio of the cyclosporin component (cyclosporin A, e.g., Example 1D and column 3, lines 30-37) to the hydrophobic component (castor oil, a vegetable oil) is 0.08 (see, e.g., Example 1D). Ding et al. also teach embodiment 1B which has 0.2% of cyclosporin and a 0.04 ratio of cyclosporin/castor oil. Additionally, embodiment 1E has 0.05% of cyclosporin A and 0.08 ratio cyclosporin/castor oil. Ding et al. do teach that an embodiment having both less than 0.1 % of cyclosporin and

wherein the weight ratio of the cyclosporin component to the hydrophobic component can be less than 0.08 (0.12 to 0.02). In addition, Ding et al. teach in claim 8 a pharmaceutical emulsion consisting of between about 0.05% and about 0.40% by weight cyclosporin A (which reads upon the limitation “less than 0.1 % by weight cyclosporin A” of instant claim 1) and between 0.625 and about 5.0 % castor oil. The corresponding lower and upper rations for the range is 0.05%/5.0% = 0.01 weight ratio of cyclosporin A/castor oil, which reads upon the limitation in claim 1 “the weight ratio of he cyclosporin A to the castor oil being less than 0.08”. The limitations of claim 2: “dry eye syndrome” and of claim 3: “effective in treating dry eye syndrome” are taught, e.g., in column 5, lines 10-14. The limitation of claim 4: “wherein the blood of the human or animal has substantially no detectable concentration of cyclosporin component” and of claim 5: ”wherein the blood of the human or animal has substantially no detectable concentration of the cyclosporin component as measure using a validated liquid chromatography/mass spectrometry-mass spectrometry analytical method" and the limitation of claim 6: “0.1 ng/mL or less” necessarily read upon the method of Ding et al. since it teaches overlapping steps/concentrations. The limitation of claims 7-8: “cyclosporin A" is taught, e.g., in Example 1. The limitation of claim 9: “wherein the cyclosporin component is solubilized in the hydrophobic component present in the composition" is taught in column 3, lines 21-23. The limitations of claim 10: “wherein the hydrophobic component is present in the composition in an amount greater than 0.625% by weight“, of claim 11: "oily material", of claim 12: "vegetable oils" and of claim 13: "castor oil" are taught, e.g., in Examples 1A-D which teach 5.00%, 2.5% and 1.25%

of hydrophobic component (castor oil). The limitation of claim 14: “topically administering the composition to the eye" is taught, e.g., in column 5, lines 15-18 and claim 8 of Ding et al. The limitation of claim 15: “wherein the composition comprises an effective amount of an emulsifier component” is taught in column 3, lines 38-4 and 50-56. The limitations of claim 16-17: “tonicity" and "organic tonicity component" are taught in column 4, lines 12-19. The limitation of claim 18: “polyelectrolyte component in an amount effective in stabilizing the composition” is taught in column 3, lines 64-67 and column 4, lines 1-12. The limitation of claims 19-20 drawn to pH ranges of "of about 7.0 to about 8.0" and “of about 7.2 to about 7.6” are taught, e.g., in Example 1A-1E and in claim 8 of Ding et al.

Ding et al. do not expressly teach an embodiment comprising both (at the same time) equal to or less than 0.05% of cyclosporin A and less than 0.08 cyclosporin A/castor oil ratio. The closest embodiments are 1D comprising 0.10% of cyclosporin A and 0.08 cyclosporin A/castor oil ratio; **1E comprising equal to 0.05% of cyclosporin A and 0.08 cyclosporin A/castor oil ratio** and 1B comprising 0.20% cyclosporin A and 0.04 cyclosporin A/castor oil ratio. It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the compositions of Ding et al. (such as 1E) by increasing the amount of castor oil or decreasing the cyclosporin concentration in order to reduce the ratio of the cyclosporin component to hydrophobic component from 0.08 to, e.g., 0.04 as taught by the ranges described in Ding et al. (see, e.g., column 3, lines 18-20) and exemplified in embodiment 1B. Further, it would have been obvious to one skilled in the art to use the beneficial compositions of Ding et al.,

which had low irritation level and were effective in treating dryness in vernal conjunctivitis, which was known to be treatable with cyclosporine as taught by Secchi et al. With respect to the ranges, the skilled artisan would have been motivated to do so because such proportions were encompassed by the Ding et al. patent. There would have been a reasonable expectation of success, because Secchi et al. disclosed that the topical use of cyclosporine would permit the use of lower concentration with less frequent daily administrations and shorter treatment time and, with respect to the ratios, given that compositions with a higher amount of castor oil are encompassed by the Ding et al. claims (e.g., claim 8, embodiment 1B) optimizing the ratio of cyclosporin/hydrophobic components to below 0.08 was taught by Ding et al. in the range 0.02 to 0.12 (e.g., column 3, lines 18-20) and in embodiment 1B (which has 0.04). The adjustment of particular conventional working conditions (e.g., using all the ratios and proportions taught by Ding. et al.) is deemed merely a matter of judicious selection and routine optimization that is well within the purview of the skilled artisan. There is no evidence of criticality of these ranges (see MPEP 2144.05). As such, it would have been obvious to one skilled in the art at the time of invention to determine all optimum and operable conditions [e.g., formulation ranges and proportions such as the proportion of castor oil], because such conditions are art-recognized result-effective variables that are routinely determined and optimized in the art through routine experimentation. One would have had a reasonable expectation for success because such modifications are routinely determined and optimized in the art through routine experimentation.

From the teaching of the references, 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.

Response to Applicant's arguments

8. With respect to Applicant's arguments of 6/5/09, these have been carefully considered by the Examiner, however, they are not deemed persuasive for the reasons set forth below, for the reasons of record, and because Applicant has not disclosed the criticality of the ranges for castor oil (or hydrophobic component in general). Effectively, the Ding et al. invention does disclose a composition having 0.05% cyclosporine and 0.08 cyclosporin/castor oil which is very close to the instantly claimed range and also discloses ranges which overlap the instantly claimed concentrations. The statement cited by Applicants that Ding discloses in the Specification, at ¶ 0005: "Another drawback of [prior art] formulations is that they contain a high concentration of oils, and oils exacerbate the symptoms of certain ocular surface diseases such as dry eyes, indicated by cyclosporine. Therefore, these oily formulations may not be clinically acceptable" clearly refers to the prior art, i.e., art before Ding and not to the formulations encompassed by Ding, which are intended to remediate this prior art drawbacks. Clearly there is no critical undisclosed advantage, Applicants have not demonstrated the criticality of the specific limitations. Applicants can rebut a prima facie case of obviousness based on overlapping ranges by showing the criticality of the claimed

range. In this situation, the applicant has not shown that the particular range is critical, e.g., by showing that the particular range achieves unexpected results relative to the prior art range, which in this case is the Ding patent (see, e.g., MPEP 2144.04 and MPEP 716.02 -716.02(g)).

Examiner acknowledges that Applicant has provided a summary (6/15/09) regarding their arguments in copending application 10/927,857 (of which the instant application is a continuation), however, it is noted that the claims in that application are drawn to the products and not to a method as instantly claimed in this application.

8. Claims 1-20 and 37 are rejected under 35 U.S.C. 103(a) as being obvious over Kawashima et al. (US 5,951,971 cited in the IDS of 11/14/07) in view of Ding et al. (US 5,474,979 cited in the IDS of 11/14/07).

Kawashima et al. teach an oil free ophthalmic composition comprising a cyclosporine, a surfactant, purified water and the cyclosporine being in solution at a concentration of from about 0.01 to about 0.075% (w/v) [e.g., claim 1 of Kawashima] in a method of treating vernal conjunctivitis (col. 7). Kawashima et al. do not teach the presence of oil or hydrophobic component or an emulsion. Oil is not used because oily eye drops tend to cause a disagreeable feeling to the eyes.

Ding et al. is relied upon as above. Ding et al. discloses that cyclosporins are immunosuppressant and enhance or restore lacrimal gland tearing (col. 1, lines 35-40) and minimize the problems related to unpleasant sensation and syndrome exacerbation by reducing the oil content and dispersing the oil phase in water into an emulsion (col. 2, lines 55-67). The emulsions of Ding utilize higher fatty acid glycerides but in

combination with polysorbate 80 which results in an emulsion with a high comfort level and low irritation potential suitable for delivery of medications to sensitive areas such as ocular tissues (col. 3, lines 1-5). Ding teaches nonirritating pharmaceutical compositions with high comfort level and low irritation potential suitable for delivery to sensitive areas such as ocular tissues comprises cyclosporin in admixture with an emulsifying amount of a higher fatty acid glycerol and polysorbate 80. More particularly, the composition comprises cyclosporin A and the higher fatty acid glyceride may comprise castor oil. (e.g., cols. 1-3) for treating dry eye disease.

It would have been obvious to one of ordinary skill to utilize the method of Kawashima et al. using the emulsions of Ding et al. One of ordinary skill in the art would have been motivated to do so because Ding et al. taught emulsions which resulted in a high comfort level and low irritation potential and therefore suitable for treatment of the eye. There would have been reasonable expectation of success because Kawashima et al. teach methods of treating vernal conjunctivitis with the active agent cyclosporine at 0.01% (w/v), which is approximate to the instantly claimed equal or less than 0.05 % (w/w).

From the teaching of the references, 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

9. 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 obviousness-type double patenting rejection is appropriate where the conflicting claims 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 conflicting 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.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

10. Claims 1-20 and 37 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 (cited in the IDS of 11/14/07) in view of Secchi et al. (Amer Journal of Ophthalmology, 1990). The Ding patent claims pharmaceutical compositions of cyclosporine. The

compositions comprise the range from between about 0.05 to and about 0.40% of cyclosporine and castor oil in an amount between 0.625% to about 5.0%, which encompasses the range 0.01 to 0.64 cyclosporine/castor oil and therefore encompasses the instantly claimed range of equal or less than 0.05 and less than 0.08 (e.g., claim 7 of Ding). The pH is 7.2-7.6 as in claim 8 and are suitable for topical application to ocular tissue (claim 8 of Ding).

The Ding reference goes on to teach, preferably, the weight ratio of the castor oil to the polysorbate 80 is between about 0.3 to about 30, and a weight ratio of the cyclosporin to castor oil is below 0.16. More preferably, the weight ratio of castor oil to polysorbate 80 is between 0.5 and 12.5, and the weight ratio of cyclosporin to castor oil is between 0.12 and .02 (e.g., column 3). Additionally, Ding provides Examples 1-4 which further illustrate their invention (columns 4-5) which include treating keratoconjuctivitis sicca (dry eye) syndrome and Examples 1A-1D were also tested for ocular bioavailability in rabbits, and the therapeutic level of cyclosporin was found in the tissues of interest after dosage (e,g., col. 5). Moreover, at column 5, at lines 10-15, Ding teaches that "[t]he formulations set forth in Examples 1-4 were made for treatment of keratoconjunctivitis sicca (dry eye syndrome)…". Therefore it is clear that such compositions, including Examples 1A thru 1E (having as low as 0.05% of cyclosporin) were all intended as therapeutic compositions. Ding et al. do not expressly teach treating the diseases “vernal conjunctivitis or atopic keratoconjunctivitis”.

However, at the time the invention was made, it was known to use cyclosporin to treat vernal conjunctivitis.

For example, Secchi et al. teach that cyclosporine was effective in the treatment of both corticosteroid-dependent and corticosteroid-resistant vernal keratoconjunctivitis. Secchi et al. teach that several investigations have demonstrated that the modulation of the helper/suppressor interaction and the inhibition of the interleukin production (mainly interleukin-2), both phenomena induced by the systemic use of cyclosporine were highly effective in the treatment of severe ocular disease of immunologic origin. The experiments were made by using topical cyclosporine (2% in castor oil) in the long-term treatment of 11 patients with vernal keratoconjunctivitis. (e.g., page 641) Additionally, Secchi et al. taught that cyclosporine 2% solution in castor oil seemed to be better tolerated than 1% suspension in balanced salt solution. A few patients treated with the balanced salt solution suspension showed severe lesions in the corneal epithelium within the first week of treatment. Conversely, the patients treated with the castor oil solution alone had only mild and transient discomfort, and minor epithelial changes (e.g., page 644).

Secchi et al. disclosed that the topical use of cyclosporine would permit the use of lower concentration with less frequent daily administrations and shorter treatment time.

With respect to the limitations claimed: Ding et al. teach 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 cyclosporin component in a therapeutically effective amount equal to or less than 0.05% by weight, the weight ratio of the cyclosporin component (cyclosporin A, e.g.,

Example 1D and column 3, lines 30-37) to the hydrophobic component (castor oil, a vegetable oil) is 0.08 (see, e.g., Example 1D). Ding et al. also teach embodiment 1B which has 0.2% of cyclosporin and a 0.04 ratio of cyclosporin/castor oil. Additionally, embodiment 1E has 0.05% of cyclosporin A and 0.08 ratio cyclosporin/castor oil. Ding et al. do teach that an embodiment having both less than 0.1 % of cyclosporin and wherein the weight ratio of the cyclosporin component to the hydrophobic component can be less than 0.08 (0.12 to 0.02). In addition, Ding et al. teach in claim 8 a pharmaceutical emulsion consisting of between about 0.05% and about 0.40% by weight cyclosporin A (which reads upon the limitation “less than 0.1 % by weight cyclosporin A” of instant claim 1) and between 0.625 and about 5.0 % castor oil. The corresponding lower and upper rations for the range is 0.05%/5.0% = 0.01 weight ratio of cyclosporin A/castor oil, which reads upon the limitation in claim 1 “the weight ratio of he cyclosporin A to the castor oil being less than 0.08”. The limitations of claim 2: “dry eye syndrome” and of claim 3: “effective in treating dry eye syndrome” are taught, e.g., in column 5, lines 10-14. The limitation of claim 4: “wherein the blood of the human or animal has substantially no detectable concentration of cyclosporin component” and of claim 5: ”wherein the blood of the human or animal has substantially no detectable concentration of the cyclosporin component as measure using a validated liquid chromatography/mass spectrometry-mass spectrometry analytical method" and the limitation of claim 6: “0.1 ng/mL or less” necessarily read upon the method of Ding et al. since it teaches overlapping steps/concentrations. The limitation of claims 7-8: “cyclosporin A" is taught, e.g., in Example 1. The limitation of claim 9: “wherein the

cyclosporin component is solubilized in the hydrophobic component present in the composition" is taught in column 3, lines 21-23. The limitations of claim 10: “wherein the hydrophobic component is present in the composition in an amount greater than 0.625% by weight“, of claim 11: "oily material", of claim 12: "vegetable oils" and of claim 13: "castor oil" are taught, e.g., in Examples 1A-D which teach 5.00%, 2.5% and 1.25% of hydrophobic component (castor oil). The limitation of claim 14: “topically administering the composition to the eye" is taught, e.g., in column 5, lines 15-18 and claim 8 of Ding et al. The limitation of claim 15: “wherein the composition comprises an effective amount of an emulsifier component” is taught in column 3, lines 38-4 and 50-56. The limitations of claim 16-17: “tonicity" and "organic tonicity component" are taught in column 4, lines 12-19. The limitation of claim 18: “polyelectrolyte component in an amount effective in stabilizing the composition” is taught in column 3, lines 64-67 and column 4, lines 1-12. The limitation of claims 19-20 drawn to pH ranges of "of about 7.0 to about 8.0" and “of about 7.2 to about 7.6” are taught, e.g., in Example 1A-1E and in claim 8 of Ding et al.

Ding et al. do not expressly teach an embodiment comprising both (at the same time) equal to or less than 0.05% of cyclosporin A and less than 0.08 cyclosporin A/castor oil ratio. The closest embodiments are 1D comprising 0.10% of cyclosporin A and 0.08 cyclosporin A/castor oil ratio; **1E comprising equal to 0.05% of cyclosporin A and 0.08 cyclosporin A/castor oil ratio** and 1B comprising 0.20% cyclosporin A and 0.04 cyclosporin A/castor oil ratio. It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the compositions of Ding et al.

(such as 1E) by increasing the amount of castor oil or decreasing the cyclosporin concentration in order to reduce the ratio of the cyclosporin component to hydrophobic component from 0.08 to, e.g., 0.04 as taught by the ranges described in Ding et al. (see, e.g., column 3, lines 18-20) and exemplified in embodiment 1B. Further, it would have been obvious to one skilled in the art to use the beneficial compositions of Ding et al., which had low irritation level and were effective in treating dryness in vernal conjunctivitis, which was known to be treatable with cyclosporine as taught by Secchi et al. With respect to the ranges, the skilled artisan would have been motivated to do so because such proportions were encompassed by the Ding et al. patent. There would have been a reasonable expectation of success, because Secchi et al. disclosed that the topical use of cyclosporine would permit the use of lower concentration with less frequent daily administrations and shorter treatment time and, with respect to the ratios, given that compositions with a higher amount of castor oil are encompassed by the Ding et al. claims (e.g., claim 8, embodiment 1B) optimizing the ratio of cyclosporin/hydrophobic components to below 0.08 was taught by Ding et al. in the range 0.02 to 0.12 (e.g., column 3, lines 18-20) and in embodiment 1B (which has 0.04). The adjustment of particular conventional working conditions (e.g., using all the ratios and proportions taught by Ding. et al.) is deemed merely a matter of judicious selection and routine optimization that is well within the purview of the skilled artisan. There is no evidence of criticality of these ranges (see MPEP 2144.05). As such, it would have been obvious to one skilled in the art at the time of invention to determine all optimum and operable conditions [e.g., formulation ranges and proportions such as the proportion of

castor oil], because such conditions are art-recognized result-effective variables that are routinely determined and optimized in the art through routine experimentation. One would have had a reasonable expectation for success because such modifications are routinely determined and optimized in the art through routine experimentation.

From the teaching of the references, 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.

Conclusion

No claim is allowed.

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

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, Cecilia J. Tsang can be reached on (571) 272-0562. 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/
Examiner, Art Unit 1654

MMCG 08/09

Notice of References Cited	Application/Control No. 11/897,177	Applicant(s)/Patent Under Reexamination ACHEAMPONG ET AL.	
	Examiner MARCELA M. CORDERO	Art Unit 1654	Page 1 of 1

U.S. PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Name	Classification
	A	US-			
	B	US-			
	C	US-			
	D	US-			
	E	US-			
	F	US-			
	G	US-			
	H	US-			
	I	US-			
	J	US-			
	K	US-			
	L	US-			
	M	US-			

FOREIGN PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Country	Name	Classification
	N					
	O					
	P					
	Q					
	R					
	S					
	T					

NON-PATENT DOCUMENTS

*		Include as applicable: Author, Title Date, Publisher, Edition or Volume, Pertinent Pages)
	U	Secchi et al. Topical Use of Cyclosporine in the Treatment of Vernal Keratoconjunctivitis.American Journal of Ophthalmology, December 1990, Vol.110. pages 641-645.
	V	Bonini et al. Vernal keratoconjunctivitis. Eye. 2004. Vol. 18, pages 345-351.
	W	Restasis Increasing Tear Production. Accesed online at http://www.restasisprofessional.com/_clinical/clinical_increasing.htm on 8/14/09, pages 1-3.
	X	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. Last updated 12/04/06. 1 page.

*A copy of this reference is not being furnished with this Office action. (See MPEP § 707.05(a).)
Dates in MM-YYYY format are publication dates. Classifications may be US or foreign.

Search Notes	Application/Control No.	Applicant(s)/Patent Under Reexamination
	11897177	ACHEAMPONG ET AL.
	Examiner	Art Unit
	MARCELA M CORDERO GARCIA	1654

SEARCHED			
Class	Subclass	Date	Examiner
none	none	12/01/08	MMCG

SEARCH NOTES		
Search Notes	Date	Examiner
updated	12/01/08	MMCG
STN searched by STIC (available via SCORE / PAIR)	4/14/08	MMCG
STN searched by STIC (available via SCORE / PAIR)	6/25/09	MMCG
EAST searched (attached)	8/16/09	MMCG
internet search (google.com) terms: restasis, dry eye, vernal conjunctivitis, atopic keratoconjunctivitis, cyclosporin	8/14/09	MMCG

INTERFERENCE SEARCH			
Class	Subclass	Date	Examiner

EAST Search History

EAST Search History (Prior Art)

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	2153	vernal conjunctivitis or atopic keratoconjunctivitis	US-PGPUB; USPAT; EPO; JPO; DERWENT	ADJ	ON	2009/08/16 19:09
L2	28055	cyclosporin$2	US-PGPUB; USPAT; EPO; JPO; DERWENT	ADJ	ON	2009/08/16 19:09
L3	39	l1 same l2	US-PGPUB; USPAT; EPO; JPO; DERWENT	ADJ	ON	2009/08/16 19:09
L4	5	l1 same l2 and (oil).clm.	US-PGPUB; USPAT; EPO; JPO; DERWENT	ADJ	ON	2009/08/16 19:14
L5	252	l2 same ("dry eye")	US-PGPUB; USPAT; EPO; JPO; DERWENT	ADJ	ON	2009/08/16 19:16
L6	113	l2 same ("dry eye") and "0.05"	US-PGPUB; USPAT; EPO; JPO; DERWENT	ADJ	ON	2009/08/16 19:18
L7	0	l2 same ("dry eye") near3 "0.05"	US-PGPUB; USPAT; EPO; JPO; DERWENT	ADJ	ON	2009/08/16 19:18
L8	0	l2 same ("dry eye") near10 "0.05"	US-PGPUB; USPAT; EPO; JPO; DERWENT	ADJ	ON	2009/08/16 19:18
L9	2	l2 same ("dry eye") same "0.05"	US-PGPUB; USPAT; EPO; JPO; DERWENT	ADJ	ON	2009/08/16 19:18
S1	1	"11897177"	US-PGPUB; USPAT; EPO; JPO; DERWENT	ADJ	ON	2009/08/15 14:10
S2	52	"5474979"	US-PGPUB; USPAT; EPO; JPO; DERWENT	ADJ	ON	2009/08/15 14:11
S3	86	"4839342"	US-PGPUB; USPAT; EPO; JPO; DERWENT	ADJ	ON	2009/08/15 14:27

8/16/09 8:21:18 PM

FORM PTO-1449 U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE	ATTY. DOCKET NO.	SERIAL NO.
INFORMATION DISCLOSURE STATEMENT BY APPLICANT	17618CON1(AP)	11/897,177
(USE SEVERAL SHEETS IF NECESSARY)	APPLICANT: Andrew Acheampong	
	FILING DATE: August 28, 2007	GROUP: 1654

U.S. PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE (IF APPROPRIATE)

EIGN PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUM	COUNTRY	CLASS	SUBCLASS	TRANSLATION YES	TRANSLATION NO

EXAMINER INITIAL		**OTHER DOCUMENTS** (INCLUDING AUTHOR, TITLE, DATE, PERTINENT PAGES, ETC.)
/MMCG/		Restasis Product Information Sheet - 5 pages Last revision date: 1/09

EXAMINER /Marcela M Cordero Garcia/	DATE CONSIDERED 08/13/2009

***EXAMINER**: INITIAL IF CITATION CONSIDERED, WHETHER OR NOT CITATION IS IN CONFORMANCE WITH MPEP 609; DRAW LINE THROUGH CITATION IF NOT IN CONFORMANCE AND NOT CONSIDERED, INCLUDE COPY OF THIS FORM WITH NEXT COMMUNICATION TO APPLICANT.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Confirmation No.	:	3860
Appln. No.	:	**11/897,177**
Applicants	:	**Andrew Acheampong et al.**
Filed	:	**08/28/2007**
TC/A.U.	:	**1654**
Examiner	:	**Cordero Garcia, Marcela M.**
Docket No.	:	**17618CON (AP)**
Customer No.	:	**51957**
Title	:	**Methods of Providing Therapeutic Effects Using Cyclosporine Components**

AMENDMENT AND REMARKS

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

Dear Sir:

The Applicants submit the following Amendment and Remarks in Response to the Office Action dated August 17, 2009 in the above referenced patent application.

Concurrently, the Applicants request a 3-month extension of time to extend the time for response from November 17, 2009 to February 17, 2010 and hereby authorize that the fees for a three month extension of time be withdrawn from the deposit account identified in the "Conclusion" section of this paper.

Amendments to the Claims are reflected in the listing of claims which begins on page 2 of this paper.

Remarks/Arguments begin on page 4 of this paper.

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (Previously Presented) A method of treating or preventing ~~a condition selected from vernal conjunctivitis and atopic keratoconjunctivitis~~ corneal graft rejection, the method 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 equal to or less than 0.05% by weight of the composition, wherein the weight ratio of the cyclosporin component to the hydrophobic component is less than 0.08.

2-3. (Canceled)

4. (Previously presented) The method of claim 1 wherein the blood of the human or animal has no detectable concentration of the cyclosporin component.

5. (Previously presented) 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 chromatographylmass spectrometry analytical method.

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

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

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

10. (Original) 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. (Original) The method of claim 1 wherein the hydrophobic component comprises an oily material.

12. (Original) 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. (Original) The method of claim 1 wherein the hydrophobic component comprises castor oil.

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

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

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

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

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

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

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

21-36. (Canceled).

37. (Previously presented) The method of claim 1, where the cyclosporin component is in a therapeutically effective amount of less than 0.05% by weight of the composition.

REMARKS

Claims 1-20 and 37 are currently pending in the application. Claim 1 is currently amended. Claims 2 and 3 are canceled in the present reply. These claims have been amended or canceled without prejudice to, or disclaimer of, the subject matter thereof. Applicants reserve the right to file continuing applications directed to the subject matter of any claim amended or canceled for any reason. Applicants do not acquiesce to the propriety of the Office's rejections and do not disclaim any subject matter to which Applicants are entitled. *Cf. Warner Jenkinson Co. v. Hilton-Davis Chem. Co.*, 41 USPQ.2d 1865 (US 1997).

The amendment to claim 1 places the application in better condition for examination. It is submitted that no new matter has been introduced by these amendments with support found throughout the specification as filed and particularly in paragraphs [0011] and [0031]. By this amendment, Applicants do not acquiesce to the propriety of the Office's rejections and do not disclaim any subject matter to which Applicants are entitled. *Cf. Warner Jenkinson Co. v. Hilton-Davis Chem. Co.*, 41 USPQ.2d 1865 (US 1997).

I. 35 U.S.C. § 112 Rejections

Claims 2 and 3 stand rejected under 35 U.S.C. § 112, second paragraph, as vague and indefinite. Office Action mailed August 17, 2009 ("OA"), page 3. Applicants respectfully disagree. Nonetheless, Applicants have canceled claims 2 and 3. Accordingly, these rejections are moot.

II. 35 U.S.C. § 103 Rejections

A. Claims 1-20 and 37 over Ding in view of Secchi

Claims 1-20 and 37 stand rejected under 35 USC § 103(a) as unpatentable over USPN 5,474,979 (Ding) in view of Secchi et al., American Journal of Ophthalmology, 1990 (Secchi). OA, page 4. Applicants respectfully disagree.

To maintain a proper rejection under 35 U.S.C. § 103, the Office must meet four conditions to establish a *prima facie* case of obviousness. First, the Office must show that the prior art suggested to those of ordinary skill in the art that they should make the

claimed composition or device or carry out the claimed process. Second, the Office must show that the prior art would have provided one of ordinary skill in the art with a reasonable expectation of success. Both the suggestion and the reasonable expectation of success must be adequately founded in the prior art and not in an applicant's disclosure. Third, the prior art must teach or suggest all the claim limitations. *In re Vaeck,* 20 U.S.P.Q.2d 1438, 1442 (Fed. Cir. 1991). Fourth, if an obviousness rejection is based on some combination of prior art references, the Office must show a suggestion, teaching, or motivation to combine the prior art references ("the TSM test"). *In re Dembiczak,* 50 U.S.P.Q.2d 1614, 1617 (Fed. Cir. 1999). Following *KSR Int'l Co. v. Teleflex, Inc*., this fourth prong of the *prima facie* obviousness analysis must not be applied in a rigid or formulaic way such that it becomes inconsistent with the more flexible approach of *Graham v. John Deere*, 383 U.S. 1, 17-18 (1966); 127 S. Ct. 1727 (2007). It must still be applied, however, as the TSM test captures the important insight that "a patent composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art." *Id*. at 1741 (citing *United States v. Adams*, 383 U.S. 39, 50-52 (1966)).

As amended, the pending claims recite a method of treating or preventing corneal graft rejection 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 equal to or less than 0.05% by weight of the composition, wherein the weight ratio of the cyclosporin component to the hydrophobic component is less than 0.08. Ding and Secchi do not teach or suggest all of these limitations including the treatment or prevention of corneal graft rejections.

Accordingly, Applicants respectfully request that the Office reconsider and withdraw the pending rejections of claims 1-20 and 37 under 35 USC § 103 over Ding in view of Secchi.

B. Claims 1-20 and 37 over Kawashima in view of Ding

Claims 1-20 and 37 stand rejected under 35 USC § 103(a) as unpatentable over USPN 5,951,971 (Kawashima) in view of Ding. OA, page 12. Applicants respectfully disagree.

As amended, the pending claims recite a method of treating or preventing corneal graft rejection 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 equal to or less than 0.05% by weight of the composition, wherein the weight ratio of the cyclosporin component to the hydrophobic component is less than 0.08. Kawashima and Ding do not teach or suggest all of these limitations including the treatment or prevention of corneal graft rejections.

Accordingly, Applicants respectfully request that the Office reconsider and withdraw the pending rejections of claims 1-20 and 37 under 35 USC § 103 over Kawashima in view of Ding.

III. Obviousness-Type Double Patenting Rejections

Claims 1-20 and 37 stand rejected under the doctrine of obviousness-type double patenting based on claims 1-8 of Ding in view of Secchi. OA, page 14. Applicants respectfully disagree.

As stated, the pending claims recite a method of treating or preventing corneal graft rejection 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 equal to or less than 0.05% by weight of the composition, wherein the weight ratio of the cyclosporin component to the hydrophobic component is less than 0.08. Ding and Secchi do not teach or suggest all of these limitations including the treatment or prevention of corneal graft rejections.

Accordingly, Applicants respectfully request that the Office reconsider and withdraw the pending rejections of claims 1-20 and 37 under the doctrine of obviousness-type double patenting based on claims 1-8 of Ding in view of Secchi.

CONCLUSION

Applicants submit that the present application is now in condition for allowance. If the Examiner has any questions or believes further discussion will aid examination and advance prosecution of the application, a telephone call to the undersigned is invited. If there are any additional fees due in connection with the filing of this amendment, please charge the fees to undersigned's Deposit Account No. 50-3207. If any extensions or fees are not accounted for, such extension is requested and the associated fee should be charged to our deposit account.

Respectfully Submitted,

Date: February 15, 2010

/C. Rachal Winger/
C. Rachal Winger
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CUSTOMER NUMBER: 85943

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Electronic Patent Application Fee Transmittal

Application Number:	11897177
Filing Date:	28-Aug-2007
Title of Invention:	Methods of providing therapeutic effects using cyclosporin components
First Named Inventor/Applicant Name:	Andrew Acheampong
Filer:	Camilla Rachal Winger/Suzanne Carter
Attorney Docket Number:	17618CON (AP)

Filed as Large Entity

Utility under 35 USC 111(a) Filing Fees

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Basic Filing:				
Pages:				
Claims:				
Miscellaneous-Filing:				
Petition:				
Patent-Appeals-and-Interference:				
Post-Allowance-and-Post-Issuance:				
Extension-of-Time:				
Extension - 3 months with $0 paid	1253	1	1110	1110

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Miscellaneous:				
		Total in USD ($)		**1110**

Electronic Acknowledgement Receipt	
EFS ID:	7012519
Application Number:	11897177
International Application Number:	
Confirmation Number:	3860
Title of Invention:	Methods of providing therapeutic effects using cyclosporin components
First Named Inventor/Applicant Name:	Andrew Acheampong
Customer Number:	51957
Filer:	Camilla Rachal Winger/Suzanne Carter
Filer Authorized By:	Camilla Rachal Winger
Attorney Docket Number:	17618CON (AP)
Receipt Date:	15-FEB-2010
Filing Date:	28-AUG-2007
Time Stamp:	18:00:16
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	Deposit Account
Payment was successfully received in RAM	$1110
RAM confirmation Number	12747
Deposit Account	503207
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 1.21 (Miscellaneous fees and charges)	

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1		ROA_DATED-8-17-09.pdf	117777 954fbcd7eb1399755a6a4e35085e7608e8a969ea	yes	7

Multipart Description/PDF files in .zip description		
Document Description	**Start**	**End**
Amendment/Req. Reconsideration-After Non-Final Reject	1	1
Claims	2	3
Applicant Arguments/Remarks Made in an Amendment	4	7

Warnings:

Information:

2	Fee Worksheet (PTO-875)	fee-info.pdf	30334 8e4308e91a01fc35e4b56071bb7ce9c0091f7dda	no	2

Warnings:

Information:

Total Files Size (in bytes):	148111

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.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Confirmation No.	:	**3860**
Appln. No.	:	**11/897,177**
Applicants	:	**Andrew Acheampong et al.**
Filed	:	**08/28/2007**
TC/A.U.	:	**1654**
Examiner	:	**Cordero Garcia, Marcela M.**
Docket No.	:	**17618CON (AP)**
Customer No.	:	**51957**
Title	:	**Methods of Providing Therapeutic Effects Using Cyclosporine Components**

CORRECTED AMENDMENT AND REMARKS

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

Dear Sir:

The Applicants submit the following Amendment and Remarks in Response to the Office Action dated August 17, 2009 in the above referenced patent application. Please substitute this response for the one filed on February 15, 2010. Please replace the response filed on February 15, 2010 with this current response.

Concurrently, the Applicants request a 3-month extension of time to extend the time for response from November 17, 2009 to February 17, 2010 and hereby authorize that the fees for a three month extension of time be withdrawn from the deposit account identified in the "Conclusion" section of this paper.

Amendments to the Claims are reflected in the listing of claims which begins on page 2 of this paper.

Remarks/Arguments begin on page 4 of this paper.

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (Previously Presented) A method of treating or preventing ~~a condition selected from vernal conjunctivitis and atopic keratoconjunctivitis~~ corneal graft rejection, the method 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 equal to or less than 0.05% by weight of the composition, wherein the weight ratio of the cyclosporin component to the hydrophobic component is less than 0.08.

2-3. (Canceled)

4. (Previously presented) The method of claim 1 wherein the blood of the human or animal has no detectable concentration of the cyclosporin component.

5. (Previously presented) 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 chromatographylmass spectrometry analytical method.

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

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

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

10. (Original) 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. (Original) The method of claim 1 wherein the hydrophobic component comprises an oily material.

12. (Original) 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. (Original) The method of claim 1 wherein the hydrophobic component comprises castor oil.

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

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

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

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

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

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

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

21-36. (Canceled).

37. (Previously presented) The method of claim 1, where the cyclosporin component is in a therapeutically effective amount of less than 0.05% by weight of the composition.

REMARKS

Claims 1-20 and 37 are currently pending in the application. Claim 1 is currently amended. Claims 2 and 3 are canceled in the present reply. These claims have been amended or canceled without prejudice to, or disclaimer of, the subject matter thereof. Applicants reserve the right to file continuing applications directed to the subject matter of any claim amended or canceled for any reason. Applicants do not acquiesce to the propriety of the Office's rejections and do not disclaim any subject matter to which Applicants are entitled. *Cf. Warner Jenkinson Co. v. Hilton-Davis Chem. Co.*, 41 USPQ.2d 1865 (US 1997).

The amendment to claim 1 places the application in better condition for examination. It is submitted that no new matter has been introduced by these amendments with support found throughout the specification as filed and particularly in paragraphs [0011] and [0031]. By this amendment, Applicants do not acquiesce to the propriety of the Office's rejections and do not disclaim any subject matter to which Applicants are entitled. *Cf. Warner Jenkinson Co. v. Hilton-Davis Chem. Co.*, 41 USPQ.2d 1865 (US 1997).

I. 35 U.S.C. § 112 Rejections

Claims 2 and 3 stand rejected under 35 U.S.C. § 112, second paragraph, as vague and indefinite. Office Action mailed August 17, 2009 ("OA"), page 3. Applicants respectfully disagree. Nonetheless, Applicants have canceled claims 2 and 3. Accordingly, these rejections are moot.

II. 35 U.S.C. § 103 Rejections

A. Claims 1-20 and 37 over Ding in view of Secchi

Claims 1-20 and 37 stand rejected under 35 USC § 103(a) as unpatentable over USPN 5,474,979 (Ding) in view of Secchi et al., American Journal of Ophthalmology, 1990 (Secchi). OA, page 4. Applicants respectfully disagree.

To maintain a proper rejection under 35 U.S.C. § 103, the Office must meet four conditions to establish a *prima facie* case of obviousness. First, the Office must show that the prior art suggested to those of ordinary skill in the art that they should make the

claimed composition or device or carry out the claimed process. Second, the Office must show that the prior art would have provided one of ordinary skill in the art with a reasonable expectation of success. Both the suggestion and the reasonable expectation of success must be adequately founded in the prior art and not in an applicant's disclosure. Third, the prior art must teach or suggest all the claim limitations. *In re Vaeck,* 20 U.S.P.Q.2d 1438, 1442 (Fed. Cir. 1991). Fourth, if an obviousness rejection is based on some combination of prior art references, the Office must show a suggestion, teaching, or motivation to combine the prior art references ("the TSM test"). *In re Dembiczak,* 50 U.S.P.Q.2d 1614, 1617 (Fed. Cir. 1999). Following *KSR Int'l Co. v. Teleflex, Inc*., this fourth prong of the *prima facie* obviousness analysis must not be applied in a rigid or formulaic way such that it becomes inconsistent with the more flexible approach of *Graham v. John Deere*, 383 U.S. 1, 17-18 (1966); 127 S. Ct. 1727 (2007). It must still be applied, however, as the TSM test captures the important insight that "a patent composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art." *Id*. at 1741 (citing *United States v. Adams*, 383 U.S. 39, 50-52 (1966)).

As amended, the pending claims recite a method of treating or preventing corneal graft rejection 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 equal to or less than 0.05% by weight of the composition, wherein the weight ratio of the cyclosporin component to the hydrophobic component is less than 0.08. Ding and Secchi do not teach or suggest all of these limitations including the treatment or prevention of corneal graft rejections.

Accordingly, Applicants respectfully request that the Office reconsider and withdraw the pending rejections of claims 1-20 and 37 under 35 USC § 103 over Ding in view of Secchi.

B. Claims 1-20 and 37 over Kawashima in view of Ding

Claims 1-20 and 37 stand rejected under 35 USC § 103(a) as unpatentable over USPN 5,951,971 (Kawashima) in view of Ding. OA, page 12. Applicants respectfully disagree.

As amended, the pending claims recite a method of treating or preventing corneal graft rejection 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 equal to or less than 0.05% by weight of the composition, wherein the weight ratio of the cyclosporin component to the hydrophobic component is less than 0.08. Kawashima and Ding do not teach or suggest all of these limitations including the treatment or prevention of corneal graft rejections.

Accordingly, Applicants respectfully request that the Office reconsider and withdraw the pending rejections of claims 1-20 and 37 under 35 USC § 103 over Kawashima in view of Ding.

III. Obviousness-Type Double Patenting Rejections

Claims 1-20 and 37 stand rejected under the doctrine of obviousness-type double patenting based on claims 1-8 of Ding in view of Secchi. OA, page 14. Applicants respectfully disagree.

As stated, the pending claims recite a method of treating or preventing corneal graft rejection 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 equal to or less than 0.05% by weight of the composition, wherein the weight ratio of the cyclosporin component to the hydrophobic component is less than 0.08. Ding and Secchi do not teach or suggest all of these limitations including the treatment or prevention of corneal graft rejections.

Accordingly, Applicants respectfully request that the Office reconsider and withdraw the pending rejections of claims 1-20 and 37 under the doctrine of obviousness-type double patenting based on claims 1-8 of Ding in view of Secchi.

CONCLUSION

Applicants submit that the present application is now in condition for allowance. If the Examiner has any questions or believes further discussion will aid examination and advance prosecution of the application, a telephone call to the undersigned is invited. If there are any additional fees due in connection with the filing of this amendment, please charge the fees to undersigned's Deposit Account No. 50-3207. If any extensions or fees are not accounted for, such extension is requested and the associated fee should be charged to our deposit account.

Respectfully Submitted,

Date: February 22, 2010

/C. Rachal Winger/
C. Rachal Winger
Registration No. 55,815
CUSTOMER NUMBER: 85943

K&L GATES
925 4th Avenue
Suite 2900
Seattle, WA 98104
Telephone: 206-370-6641
email: seattle.patents@klgates.com

Electronic Acknowledgement Receipt

EFS ID:	7056769
Application Number:	11897177
International Application Number:	
Confirmation Number:	3860
Title of Invention:	Methods of providing therapeutic effects using cyclosporin components
First Named Inventor/Applicant Name:	Andrew Acheampong
Customer Number:	51957
Filer:	Camilla Rachal Winger/Suzanne Carter
Filer Authorized By:	Camilla Rachal Winger
Attorney Docket Number:	17618CON (AP)
Receipt Date:	22-FEB-2010
Filing Date:	28-AUG-2007
Time Stamp:	14:03:41
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	Amendment/Req. Reconsideration-After Non-Final Reject	ROA_corrected.pdf	85514 40176a912d84e4b0b90ca874a75b2503635deab5	no	7

Warnings:	
Information:	

Total Files Size (in bytes):	85514

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.

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PTO/SB/06 (07-06)
Approved for use through 1/31/2007. 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	Filing Date	☐ To be Mailed
11/897,177	08/28/2007	

APPLICATION AS FILED – PART I

	(Column 1)	(Column 2)	SMALL ENTITY ☐		OR	OTHER THAN SMALL ENTITY	
FOR	NUMBER FILED	NUMBER EXTRA	RATE ($)	FEE ($)		RATE ($)	FEE ($)
☐ BASIC FEE (37 CFR 1.16(a), (b), or (c))	N/A	N/A	N/A			N/A	
☐ SEARCH FEE (37 CFR 1.16(k), (i), or (m))	N/A	N/A	N/A			N/A	
☐ EXAMINATION FEE (37 CFR 1.16(o), (p), or (q))	N/A	N/A	N/A			N/A	
TOTAL CLAIMS (37 CFR 1.16(i))	minus 20 =	*	X $ =		OR	X $ =	
INDEPENDENT CLAIMS (37 CFR 1.16(h))	minus 3 =	*	X $ =			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 $250 ($125 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			TOTAL	

APPLICATION AS AMENDED – PART II

		(Column 1)		(Column 2)	(Column 3)	SMALL ENTITY		OR	OTHER THAN SMALL ENTITY	
AMENDMENT	02/22/2010	CLAIMS REMAINING AFTER AMENDMENT		HIGHEST NUMBER PREVIOUSLY PAID FOR	PRESENT EXTRA	RATE ($)	ADDITIONAL FEE ($)		RATE ($)	ADDITIONAL FEE ($)
	Total (37 CFR 1.16(i))	* 19	Minus	** 37	= 0	X $ =		OR	X $52=	0
	Independent (37 CFR 1.16(h))	* 1	Minus	***3	= 0	X $ =		OR	X $220=	0
	☐ 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	0

		(Column 1)		(Column 2)	(Column 3)					
AMENDMENT		CLAIMS REMAINING AFTER AMENDMENT		HIGHEST NUMBER PREVIOUSLY PAID FOR	PRESENT EXTRA	RATE ($)	ADDITIONAL FEE ($)		RATE ($)	ADDITIONAL FEE ($)
	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 number found in the appropriate box in column 1.

Legal Instrument Examiner:
/TAMMY ACREE/

This collection of information is required by 37 CFR 1.16. 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 12 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.

UNITED STATES PATENT AND TRADEMARK OFFICE

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51957 e 03/17/2010

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

Paper No.

Application No.:	**11/897,177**	**Date Mailed:**	**03/17/2010**
First Named Inventor:	Acheampong, Andrew,	Examiner:	CORDERO GARCIA, MARCELA M
Attorney Docket No.:	17618CON (AP)	Art Unit:	1654
Confirmation No.:	3860	Filing Date:	08/28/2007

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

Commissioner for Patents

PTO-90c (Rev.08-06)

Notice of Non-Compliant Amendment (37 CFR 1.121)	Application No. 11/897,177	Applicant(s) ACHEAMPONG ET AL.	
		Art Unit 3998	

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

The amendment document filed on *22 February, 2010* is considered non-compliant because it has failed to meet the requirements of 37 CFR 1.121 or 1.4. In order for the amendment document to be compliant, correction of the following item(s) is required.

THE FOLLOWING MARKED (X) ITEM(S) CAUSE THE AMENDMENT DOCUMENT TO BE NON-COMPLIANT:

- ☐ 1. Amendments to the specification:
  - ☐ A. Amended paragraph(s) do not include markings.
  - ☐ B. New paragraph(s) should not be underlined.
  - ☐ C. Other _____.
- ☐ 2. Abstract:
  - ☐ A. Not presented on a separate sheet. 37 CFR 1.72.
  - ☐ B. Other _____.
- ☐ 3. Amendments to the drawings:
  - ☐ A. The drawings are not properly identified in the top margin as "Replacement Sheet," "New Sheet," or "Annotated Sheet" as required by 37 CFR 1.121(d).
  - ☐ B. The practice of submitting proposed drawing correction has been eliminated. Replacement drawings showing amended figures, without markings, in compliance with 37 CFR 1.84 are required.
  - ☐ C. Other _____.
- ☒ 4. Amendments to the claims:
  - ☐ A. A complete listing of all of the claims is not present.
  - ☐ B. The listing of claims does not include the text of all pending claims (including withdrawn claims)
  - ☒ C. Each claim has not been provided with the proper status identifier, and as such, the individual status of each claim cannot be identified. Note: the status of every claim must be indicated after its claim number by using one of the following status identifiers: (Original), (Currently amended), (Canceled), (Previously presented), (New), (Not entered), (Withdrawn) and (Withdrawn-currently amended).
  - ☐ D. The claims of this amendment paper have not been presented in ascending numerical order.
  - ☒ E. Other: *See Continuation Sheet*.
- ☐ 5. Other (e.g., the amendment is unsigned or not signed in accordance with 37 CFR 1.4): For further explanation of the amendment format required by 37 CFR 1.121, see MPEP § 714.

TIME PERIODS FOR FILING A REPLY TO THIS NOTICE:

1. Applicant is given **no new time period** if the non-compliant amendment is an after-final amendment or an amendment filed after allowance, or a drawing submission (only) If applicant wishes to resubmit the non-compliant after-final amendment with corrections, the **entire corrected amendment** must be resubmitted.

2. Applicant is given **one month**, or thirty (30) days, whichever is longer, from the mail date of this notice to supply the correction, if the non-compliant amendment is one of the following: a preliminary amendment, a non-final amendment (including a submission for a request for continued examination (RCE) under 37 CFR 1.114), a supplemental amendment filed within a suspension period under 37 CFR 1.103(a) or (c), and an amendment filed in response to a Quayle action. If any of above boxes 1 to 4 are checked, the correction required is only the corrected section of the non-compliant amendment in compliance with 37 CFR 1.121.

   Extensions of time are available under 37 CFR 1.136(a) only if the non-compliant amendment is a non-final amendment or an amendment filed in response to a *Quayle* action.
   Failure to timely respond to this notice will result in:
   Abandonment of the application if the non-compliant amendment is a non-final amendment or an amendment filed in response to a *Quayle* action; or
   Non-entry of the amendment if the non-compliant amendment is a preliminary amendment or supplemental amendment.

Legal Instruments Examiner (LIE), if applicable /TAMMY ACREE/ Telephone No: (571)272-7017

Continuation of 4. Other: Claim 1 has not been provided with a proper status identifier.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Confirmation No.	:	**3860**
Appln. No.	:	**11/897,177**
Applicants	:	**Andrew Acheampong et al.**
Filed	:	**08/28/2007**
TC/A.U.	:	**1654**
Examiner	:	**Cordero Garcia, Marcela M.**
Docket No.	:	**17618CON (AP)**
Customer No.	:	**51957**
Title	:	**Methods of Providing Therapeutic Effects Using Cyclosporine Components**

RESPONSE TO NOTICE OF NON-COMPLIANT AMENDMENT

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

Dear Sir:

The Applicants submit the following Amendment and Remarks in Response to the Notice of Non-Compliant Amendment dated March 17, 2010 in the above referenced patent application. Please substitute this response for the one filed on February 22, 2010.

Amendments to the Claims are reflected in the listing of claims which begins on page 2 of this paper.

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Claims 1-20 and 37 stand rejected under 35 USC § 103(a) as unpatentable over USPN 5,474,979 (Ding) in view of Secchi et al., American Journal of Ophthalmology, 1990 (Secchi). OA, page 4. Applicants respectfully disagree.

To maintain a proper rejection under 35 U.S.C. § 103, the Office must meet four conditions to establish a *prima facie* case of obviousness. First, the Office must show that the prior art suggested to those of ordinary skill in the art that they should make the

claimed composition or device or carry out the claimed process. Second, the Office must show that the prior art would have provided one of ordinary skill in the art with a reasonable expectation of success. Both the suggestion and the reasonable expectation of success must be adequately founded in the prior art and not in an applicant's disclosure. Third, the prior art must teach or suggest all the claim limitations. *In re Vaeck,* 20 U.S.P.Q.2d 1438, 1442 (Fed. Cir. 1991). Fourth, if an obviousness rejection is based on some combination of prior art references, the Office must show a suggestion, teaching, or motivation to combine the prior art references ("the TSM test"). *In re Dembiczak,* 50 U.S.P.Q.2d 1614, 1617 (Fed. Cir. 1999). Following *KSR Int'l Co. v. Teleflex, Inc*., this fourth prong of the *prima facie* obviousness analysis must not be applied in a rigid or formulaic way such that it becomes inconsistent with the more flexible approach of *Graham v. John Deere*, 383 U.S. 1, 17-18 (1966); 127 S. Ct. 1727 (2007). It must still be applied, however, as the TSM test captures the important insight that "a patent composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art." *Id*. at 1741 (citing *United States v. Adams*, 383 U.S. 39, 50-52 (1966)).

As amended, the pending claims recite a method of treating or preventing corneal graft rejection 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 equal to or less than 0.05% by weight of the composition, wherein the weight ratio of the cyclosporin component to the hydrophobic component is less than 0.08. Ding and Secchi do not teach or suggest all of these limitations including the treatment or prevention of corneal graft rejections.

Accordingly, Applicants respectfully request that the Office reconsider and withdraw the pending rejections of claims 1-20 and 37 under 35 USC § 103 over Ding in view of Secchi.

B. Claims 1-20 and 37 over Kawashima in view of Ding

Claims 1-20 and 37 stand rejected under 35 USC § 103(a) as unpatentable over USPN 5,951,971 (Kawashima) in view of Ding. OA, page 12. Applicants respectfully disagree.

As amended, the pending claims recite a method of treating or preventing corneal graft rejection 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 equal to or less than 0.05% by weight of the composition, wherein the weight ratio of the cyclosporin component to the hydrophobic component is less than 0.08. Kawashima and Ding do not teach or suggest all of these limitations including the treatment or prevention of corneal graft rejections.

Accordingly, Applicants respectfully request that the Office reconsider and withdraw the pending rejections of claims 1-20 and 37 under 35 USC § 103 over Kawashima in view of Ding.

III. Obviousness-Type Double Patenting Rejections

Claims 1-20 and 37 stand rejected under the doctrine of obviousness-type double patenting based on claims 1-8 of Ding in view of Secchi. OA, page 14. Applicants respectfully disagree.

As stated, the pending claims recite a method of treating or preventing corneal graft rejection 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 equal to or less than 0.05% by weight of the composition, wherein the weight ratio of the cyclosporin component to the hydrophobic component is less than 0.08. Ding and Secchi do not teach or suggest all of these limitations including the treatment or prevention of corneal graft rejections.

Accordingly, Applicants respectfully request that the Office reconsider and withdraw the pending rejections of claims 1-20 and 37 under the doctrine of obviousness-type double patenting based on claims 1-8 of Ding in view of Secchi.

CONCLUSION

Applicants submit that the present application is now in condition for allowance. If the Examiner has any questions or believes further discussion will aid examination and advance prosecution of the application, a telephone call to the undersigned is invited. If there are any additional fees due in connection with the filing of this amendment, please charge the fees to undersigned's Deposit Account No. 01-0885. If any extensions or fees are not accounted for, such extension is requested and the associated fee should be charged to our deposit account.

Respectfully submitted,

/Joel B. German/
Joel B. German

Dated: April 8, 2010

Registration No. 48,676
CUSTOMER NUMBER: 51957

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Facsimile: 714-246-4249

Electronic Acknowledgement Receipt

EFS ID:	7380589
Application Number:	11897177
International Application Number:	
Confirmation Number:	3860
Title of Invention:	Methods of providing therapeutic effects using cyclosporin components
First Named Inventor/Applicant Name:	Andrew Acheampong
Customer Number:	51957
Filer:	Joel B. German/Bonnie Ferguson
Filer Authorized By:	Joel B. German
Attorney Docket Number:	17618CON (AP)
Receipt Date:	08-APR-2010
Filing Date:	28-AUG-2007
Time Stamp:	18:12:44
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		NCA_3-17-10-17618CON-4-8-10.pdf	93203 73f565db4b614f0d62f3fe1bb7b13ec340386c1d	yes	7

	Multipart Description/PDF files in .zip description		
	Document Description	**Start**	**End**
	Supplemental Response or Supplemental Amendment	1	1
	Amendment Copy Claims/Response to Suggested Claims	2	3
	Amendment/Req. Reconsideration-After Non-Final Reject	4	7
Warnings:			
Information:			
	Total Files Size (in bytes):	93203	

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.

PTO/SB/06 (07-06)
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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	Filing Date	☐ To be Mailed
11/897,177	08/28/2007	

APPLICATION AS FILED – PART I

	(Column 1)	(Column 2)	SMALL ENTITY ☐		OR	OTHER THAN SMALL ENTITY	
FOR	NUMBER FILED	NUMBER EXTRA	RATE ($)	FEE ($)		RATE ($)	FEE ($)
☐ BASIC FEE (37 CFR 1.16(a), (b), or (c))	N/A	N/A	N/A			N/A	
☐ SEARCH FEE (37 CFR 1.16(k), (i), or (m))	N/A	N/A	N/A			N/A	
☐ EXAMINATION FEE (37 CFR 1.16(o), (p), or (q))	N/A	N/A	N/A			N/A	
TOTAL CLAIMS (37 CFR 1.16(i))	minus 20 =	*	X $ =		OR	X $ =	
INDEPENDENT CLAIMS (37 CFR 1.16(h))	minus 3 =	*	X $ =			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 $250 ($125 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			TOTAL	

APPLICATION AS AMENDED – PART II

AMENDMENT	04/08/2010	(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA	SMALL ENTITY RATE ($)	ADDITIONAL FEE ($)	OR	OTHER THAN SMALL ENTITY RATE ($)	ADDITIONAL FEE ($)
	Total (37 CFR 1.16(i))	* 19	Minus	** 37	=	X $ =		OR	X $ =	
	Independent (37 CFR 1.16(h))	* 1	Minus	***3	=	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	

AMENDMENT		(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA	RATE ($)	ADDITIONAL FEE ($)		RATE ($)	ADDITIONAL FEE ($)
	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 number found in the appropriate box in column 1.

Legal Instrument Examiner:
/KATRINA S. TURNER/

PTO/SB/06 (07-06)
Approved for use through 1/31/2007. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
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PATENT APPLICATION FEE DETERMINATION RECORD

Substitute for Form PTO-875

Application or Docket Number	Filing Date	☐ To be Mailed
11/897,177	08/28/2007	

APPLICATION AS FILED – PART I

	(Column 1)	(Column 2)	SMALL ENTITY ☐		OR	OTHER THAN SMALL ENTITY	
FOR	NUMBER FILED	NUMBER EXTRA	RATE ($)	FEE ($)		RATE ($)	FEE ($)
☐ BASIC FEE (37 CFR 1.16(a), (b), or (c))	N/A	N/A	N/A			N/A	
☐ SEARCH FEE (37 CFR 1.16(k), (i), or (m))	N/A	N/A	N/A			N/A	
☐ EXAMINATION FEE (37 CFR 1.16(o), (p), or (q))	N/A	N/A	N/A			N/A	
TOTAL CLAIMS (37 CFR 1.16(i))	minus 20 =	*	X $ =		OR	X $ =	
INDEPENDENT CLAIMS (37 CFR 1.16(h))	minus 3 =	*	X $ =			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 $250 ($125 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			TOTAL	

APPLICATION AS AMENDED – PART II

AMENDMENT 04/08/2010	(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA	SMALL ENTITY RATE ($)	ADDITIONAL FEE ($)	OR	OTHER THAN SMALL ENTITY RATE ($)	ADDITIONAL FEE ($)
Total (37 CFR 1.16(i))	* 19	Minus	** 37	=	X $ =		OR	X $ =	
Independent (37 CFR 1.16(h))	* 1	Minus	***3	=	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	

AMENDMENT	(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA	RATE ($)	ADDITIONAL FEE ($)		RATE ($)	ADDITIONAL FEE ($)
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 number found in the appropriate box in column 1.

Legal Instrument Examiner:
/KATRINA S. TURNER/

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
11/897,177	08/28/2007	Andrew Acheampong	17618CON (AP)	3860

51957 7590 06/23/2010

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

EXAMINER	
CORDERO GARCIA, MARCELA M	
ART UNIT	PAPER NUMBER
1654	

MAIL DATE	DELIVERY MODE
06/23/2010	PAPER

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.

Office Action Summary	Application No.	Applicant(s)	
	11/897,177	ACHEAMPONG ET AL.	
	Examiner	Art Unit	
	MARCELA M. CORDERO GARCIA	1654	

-- 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 *2/15/2010, 2/22/2010 and 4/8/2010*.

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

3)☐ 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

4)☒ Claim(s) *1, 4-20, 37* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 4-20 and 37* is/are rejected.

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

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

Application Papers

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

10)☐ 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).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

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).

a)☐ All b)☐ Some * c)☐ None of:

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) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

U.S. Patent and Trademark Office

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed previously (on 6/5/2009) and an Office Action on the merits was previously sent to Applicants (8/17/2009). Responses to this Office Action on 2/15/2010 and 2/22/2010 were not in compliance with respect to the claims (see Notice of non-compliant amendment mailed out on 3/17/2010). Applicants provided a compliant amendment on 4/8/2010.

2. Claims 1-20 and 37 were pending in the application. The claims have been amended as shown below. Claims 2-3 have now been cancelled. Claims 1, 4-20 and 37 are currently pending.

Amendment of 6/5/09:

1. (Currently amended) 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~~ hydrophobic

component, and a cyclosporin component in a therapeutically effective amount ~~of~~

~~less than 0.1%~~ equal to or less than 0.05% by weight of the composition, wherein

the weight ratio of the cyclosporin component to the hydrophobic

component is

less than 0.08.

Subsequently a second amendment was filed (6/15/09) as follows:

1. (Currently amended) A method of treating ~~an eye of a human or animal comprising:~~ a condition selected from vernal conjunctivitis and atopic keratoconjunctivitis, the method 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 equal to or less than 0.05% by weight of the composition, wherein the weight ratio of the cyclosporin component to the hydrophobic component is less than 0.08.

Current amendment of 4/8/2010:

1. (Currently amended) A method of treating ~~a condition selected from vernal conjunctivitis and atopic keratoconjunctivitis,~~ corneal graft rejection, the method 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 equal to or less than 0.05% by weight of the composition, wherein the weight ratio of the cyclosporin component to the hydrophobic component is less than 0.08.

3. Any rejection from the previous office action, which is not restated here, is withdrawn.

4. Applicant's arguments with respect to the previous rejections (drawn to vernal conjunctivitis and atopic conjunctivitis) have been considered but are moot in view of the new ground(s) of rejection which address the newly amended claims now drawn to corneal graft rejection instead of vernal conjunctivitis and atopic conjunctivitis.

New grounds of rejection necessitated by Applicant's amendment

Claim Rejections - 35 USC § 103

5. 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.

6. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 1, 4-20 and 37 are rejected under 35 U.S.C. 103(a) as being obvious over Ding et al. (US 5,474,979 cited in the IDS of 11/14/07) in view of Kaswan (US 5,411,952).

The Ding patent teaches that cyclosporins are immunosuppressant and enhance or restore lacrimal gland tearing (col. 1, lines 35-40) and minimizing the problems related to unpleasant sensation and syndrome exacerbation by reducing the oil content and dispersing the oil phase in water into an emulsion (col. 2, lines 55-67). In addition, the composition has stability for up to 9 months without crystallization of cyclosporin (e.g., abstract). The emulsions of Ding utilize higher fatty acid glycerides but in combination with polysorbate 80 which results in an emulsion with a high comfort level and low irritation potential suitable for delivery of medications to sensitive areas such as ocular tissues (col. 3, lines 1-5). Ding teaches nonirritating pharmaceutical compositions with high comfort level and low irritation potential suitable for delivery to sensitive areas such as ocular tissues comprises cyclosporin in admixture with an emulsifying amount of a higher fatty acid glycerol and polysorbate 80. More particularly, the composition comprises cyclosporin A and the higher fatty acid glyceride may comprise castor oil. (e.g., cols. 1-3) for treating dry eye disease.

The Ding reference goes on to teach, preferably, the weight ratio of the castor oil to the polysorbate 80 is between about 0.3 to about 30, and a weight ratio of the cyclosporin to castor oil is below 0.16. More preferably, the weight ratio of castor oil to polysorbate 80 is between 0.5 and 12.5, and the weight ratio of cyclosporin to castor oil is between 0.12 and .02 (e.g., column 3). Additionally,

Ding provides Examples 1-4 which further illustrate their invention (columns 4-5) which include treating keratoconjuctivitis sicca (dry eye) syndrome and Examples 1A-1D were also tested for ocular bioavailability in rabbits, and the therapeutic level of cyclosporin was found in the tissues of interest after dosage (e,g., col. 5). Moreover, at column 5, at lines 10-15, Ding teaches that "[t]he formulations set forth in Examples 1-4 were made for treatment of keratoconjunctivitis sicca (dry eye syndrome)…". Therefore it is clear that such compositions, including Examples 1A thru 1E (having as low as 0.05% of cyclosporin) were all intended as therapeutic compositions. Please note that Example 1D encompasses 0.10 % of cyclosporin and shows ocular bioavailability at a therapeutic level. (e.g., column 5, lines 15-25). Therefore, one skilled in the art at the time the invention was made would have concluded that there would be a reasonable expectation of success that a composition having slightly less than 0.10% cyclosporin (e.g., 0.05%) and slightly less than 0.08 cyclosporin/castor oil (e.g., 0.07) would still maintain therapeutic activity when topically applied to the eye, especially in light of the teachings of Ding describing preferred embodiments for nonirritating pharmaceutical compositions with high comfort level and low irritation potential suitable for delivery to sensitive areas such as ocular tissues with weight ratios of cyclosporin/castor oil more preferably between 0.12 and 0.02 (e.g., column 3, lines 15-20) and the teachings of claim 8 that encompass pharmaceutical emulsions for topical application encompassing 0.05% cyclosporin or more (which reads upon the instantly claimed “equal to or less than 0.05% of

cyclosporin") and as low as 0.02 ratio of cyclosporin to castor oil (which reads upon the instantly claimed "less than 0.08" weight ratio of cyclosporin/castor oil).

Ding et al. do not expressly teach treating or preventing "corneal graft rejection". However, at the time the invention was made, it was known to use cyclosporin to treat corneal transplantation. For example, Kaswan discloses that cyclosporine was effective in the treatment of corneal graft transplantation. Kaswan teaches cyclosporine A compositions in corn oil comprising between 0.01% cyclosporine and saturation for topical ophthalmic use for treatment of immune disorders, to enhance or restore tear production and to enhance the normal healing of the surface of the eye in e.g., corneal transplantation (e.g., claims, cols. 1-2) Kaswan discloses several Examples, e.g., stimulation of tearing in humans suffering Sjogren's syndrome (cols. 4-5), stimulation of tearing in normal dogs (col. 5) and topically applied cyclosporine effect in the reduction of corneal scars in dogs with keratoconjunctivis sicca (cols. 5-7), and promotion of normal healing of the eye surface without restoration of normal tearing in a dog (col. 7). Further, olive oil was also used and compared, and it was observed that the corn oil was favorable. The preferred topical ophthalmic formulation consisted of 2% cyclosporine, 1 mole % alpha tocopherol and 0.005% methyl paraben. However, Karwan discloses that cyclosporine solutions can be prepared of between approximately 0.01% by weight of cyclosporine and saturation.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to utilize, e.g., the compositions of Karwan or of Ding et al. to treat or prevent corneal transplantation rejection. One of ordinary skill in the art

at the time the invention was made would have been motivated to do so in order to decrease irritation in the eyes and decrease systemic side effects. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success since cyclosporine A was known to be an active agent with immunosuppressive activity in the healing of cornea including allografts. With respect to the limitations claimed: Ding et al. teach 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 cyclosporin component in a therapeutically effective amount equal to or less than 0.05% by weight, the weight ratio of the cyclosporin component (cyclosporin A, e.g., Example 1D and column 3, lines 30-37) to the hydrophobic component (castor oil, a vegetable oil) is 0.08 (see, e.g., Example 1D). Ding et al. also teach embodiment 1B which has 0.2% of cyclosporin and a 0.04 ratio of cyclosporin/castor oil. Additionally, embodiment 1E has 0.05% of cyclosporin A and 0.08 ratio cyclosporin/castor oil. Ding et al. do teach that an embodiment having both less than 0.1 % of cyclosporin and wherein the weight ratio of the cyclosporin component to the hydrophobic component can be less than 0.08 (0.12 to 0.02). In addition, Ding et al. teach in claim 8 a pharmaceutical emulsion consisting of between about 0.05% and about 0.40% by weight cyclosporin A (which reads upon the limitation “less than 0.1 % by weight cyclosporin A” of instant claim 1) and between 0.625 and about 5.0 % castor oil. The corresponding lower and upper rations for the range is 0.05%/5.0% = 0.01 weight ratio of cyclosporin A/castor oil, which reads upon the

limitation in claim 1 “the weight ratio of he cyclosporin A to the castor oil being less than 0.08”. The limitation of claim 4: “wherein the blood of the human or animal has substantially no detectable concentration of cyclosporin component” and of claim 5: ”wherein the blood of the human or animal has substantially no detectable concentration of the cyclosporin component as measure using a validated liquid chromatography/mass spectrometry-mass spectrometry analytical method" and the limitation of claim 6: “0.1 ng/mL or less” necessarily read upon the method of Ding et al. since it teaches overlapping steps/concentrations. The limitation of claims 7-8: “cyclosporin A" is taught, e.g., in Example 1. The limitation of claim 9: “wherein the cyclosporin component is solubilized in the hydrophobic component present in the composition" is taught in column 3, lines 21-23. The limitations of claim 10: “wherein the hydrophobic component is present in the composition in an amount greater than 0.625% by weight“, of claim 11: "oily material", of claim 12: "vegetable oils" and of claim 13: "castor oil" are taught, e.g., in Examples 1A-D which teach 5.00%, 2.5% and 1.25% of hydrophobic component (castor oil). The limitation of claim 14: “topically administering the composition to the eye" is taught, e.g., in column 5, lines 15-18 and claim 8 of Ding et al. The limitation of claim 15: “wherein the composition comprises an effective amount of an emulsifier component” is taught in column 3, lines 38-4 and 50-56. The limitations of claim 16-17: “tonicity" and "organic tonicity component" are taught in column 4, lines 12-19. The limitation of claim 18: “polyelectrolyte component in an amount effective in stabilizing the composition” is taught in column 3, lines 64-67 and column 4, lines 1-12. The

limitation of claims 19-20 drawn to pH ranges of "of about 7.0 to about 8.0" and “of about 7.2 to about 7.6” are taught, e.g., in Example 1A-1E and in claim 8 of Ding et al.

Ding et al. do not expressly teach an embodiment comprising both (at the same time) equal to or less than 0.05% of cyclosporin A and less than 0.08 cyclosporin A/castor oil ratio. The closest embodiments are 1D comprising 0.10% of cyclosporin A and 0.08 cyclosporin A/castor oil ratio; **1E comprising equal to 0.05% of cyclosporin A and 0.08 cyclosporin A/castor oil ratio** and 1B comprising 0.20% cyclosporin A and 0.04 cyclosporin A/castor oil ratio. It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the compositions of Ding et al. (such as 1E) by increasing the amount of castor oil or decreasing the cyclosporin concentration in order to reduce the ratio of the cyclosporin component to hydrophobic component from 0.08 to, e.g., 0.04 as taught by the ranges described in Ding et al. (see, e.g., column 3, lines 18-20) and exemplified in embodiment 1B. Further, it would have been obvious to one skilled in the art to use the beneficial compositions of Ding et al., which had low irritation level and contained the active agent for corneal allograft rejection prevention as taught by Kaswan. Further, Kaswan teach that the preferred topical ophthalmic formulation consisted of 2% cyclosporine, 1 mole % alpha tocopherol and 0.005% methyl paraben. However, Karwan discloses that treating corneal allografts can be done with cyclosporine solutions having 0.01% by weight of cyclosporine.

With respect to the ranges, the skilled artisan would have been motivated to do so because such proportions were encompassed by the Ding et al. patent. Further, the active agent proportion was taught expressly for allograft corneal rejection in Kaswan There would have been a reasonable expectation of success, because such ranges were disclosed to be effective in corneal allograft rejection as evidenced by Kaswan Please note that compositions with a higher amount of castor oil are encompassed by the Ding et al. claims (e.g., claim 8, embodiment 1B) optimizing the ratio of cyclosporin/hydrophobic components to below 0.08 was taught by Ding et al. in the range 0.02 to 0.12 (e.g., column 3, lines 18-20) and in embodiment 1B (which has 0.04). The adjustment of particular conventional working conditions (e.g., using all the ratios and proportions taught by Ding. et al. and Kaswan) is deemed merely a matter of judicious selection and routine optimization that is well within the purview of the skilled artisan. There is no evidence of criticality of these ranges. “Generally, 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). As such, it would have been obvious to one skilled in the art at the time of invention to determine all optimum and operable conditions [e.g., formulation ranges and proportions such as the proportion of castor oil and corn oil], because such conditions are art-recognized result-effective variables that are routinely determined and optimized in the art through routine experimentation. One would

have had a reasonable expectation for success because such modifications are routinely determined and optimized in the art through routine experimentation.

From the teaching of the references, 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.

New ground of rejection necessitated by Applicants' amendment

Double Patenting

8. 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 obviousness-type double patenting rejection is appropriate where the conflicting claims 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 conflicting 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.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

9. Claims 1, 4-20 and 37 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 (cited in the IDS of 11/14/07) in view of Kaswan (US 5,411,952). The Ding patent claims pharmaceutical compositions of cyclosporine. The compositions comprise the range from between about 0.05 to and about 0.40% of cyclosporine and castor oil in an amount between 0.625% to about 5.0%, which encompasses the range 0.01 to 0.64 cyclosporine/castor oil and therefore encompasses the instantly claimed range of equal or less than 0.05 and less than 0.08 (e.g., claim 7 of Ding). The pH is 7.2-7.6 as in claim 8 and are suitable for topical application to ocular tissue (claim 8 of Ding).

The Ding reference goes on to teach, preferably, the weight ratio of the castor oil to the polysorbate 80 is between about 0.3 to about 30, and a weight ratio of the cyclosporin to castor oil is below 0.16. More preferably, the weight ratio of castor oil to polysorbate 80 is between 0.5 and 12.5, and the weight ratio of cyclosporin to castor oil is between 0.12 and .02 (e.g., column 3).

Ding et al. do not expressly teach treating or preventing “corneal graft rejection”. However, at the time the invention was made, it was known to use cyclosporin to treat corneal transplantation. For example, Kaswan discloses that

cyclosporine was effective in the treatment of corneal graft transplantation. Kaswan teaches cyclosporine A compositions in corn oil comprising between 0.01% cyclosporine and saturation for topical ophthalmic use for treatment of immune disorders, to enhance or restore tear production and to enhance the normal healing of the surface of the eye in e.g., corneal transplantation (e.g., claims, cols. 1-2) Kaswan discloses several Examples, e.g., stimulation of tearing in humans suffering Sjogren's syndrome (cols. 4-5), stimulation of tearing in normal dogs (col. 5) and topically applied cyclosporine effect in the reduction of corneal scars in dogs with keratoconjunctivis sicca (cols. 5-7), and promotion of normal healing of the eye surface without restoration of normal tearing in a dog (col. 7). Further, olive oil was also used and compared, and it was observed that the corn oil was favorable. The preferred topical ophthalmic formulation consisted of 2% cyclosporine, 1 mole % alpha tocopherol and 0.005% methyl paraben. However, Karwan discloses that cyclosporine solutions can be prepared of between approximately 0.01% by weight of cyclosporine and saturation.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to utilize, e.g., the compositions of Karwan or of Ding et al. to treat or prevent corneal transplantation rejection. One of ordinary skill in the art at the time the invention was made would have been motivated to do so in order to decrease irritation in the eyes and decrease systemic side effects. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success since cyclosporine A was known to be an active agent with immunosuppressive activity in the healing of cornea including

allografts. With respect to the limitations claimed: Ding et al. teach 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 cyclosporin component in a therapeutically effective amount equal to or less than 0.05% by weight, the weight ratio of the cyclosporin component (cyclosporin A, e.g., Example 1D and column 3, lines 30-37) to the hydrophobic component (castor oil, a vegetable oil) is 0.08 (see, e.g., Example 1D). Ding et al. also teach embodiment 1B which has 0.2% of cyclosporin and a 0.04 ratio of cyclosporin/castor oil. Additionally, embodiment 1E has 0.05% of cyclosporin A and 0.08 ratio cyclosporin/castor oil. Ding et al. do teach that an embodiment having both less than 0.1 % of cyclosporin and wherein the weight ratio of the cyclosporin component to the hydrophobic component can be less than 0.08 (0.12 to 0.02). In addition, Ding et al. teach in claim 8 a pharmaceutical emulsion consisting of between about 0.05% and about 0.40% by weight cyclosporin A (which reads upon the limitation “less than 0.1 % by weight cyclosporin A” of instant claim 1) and between 0.625 and about 5.0 % castor oil. The corresponding lower and upper rations for the range is 0.05%/5.0% = 0.01 weight ratio of cyclosporin A/castor oil, which reads upon the limitation in claim 1 “the weight ratio of he cyclosporin A to the castor oil being less than 0.08”. The limitation of claim 4: “wherein the blood of the human or animal has substantially no detectable concentration of cyclosporin component” and of claim 5: ”wherein the blood of the human or animal has substantially no detectable concentration of the cyclosporin component as measure using a

validated liquid chromatography/mass spectrometry-mass spectrometry analytical method" and the limitation of claim 6: “0.1 ng/mL or less” necessarily read upon the method of Ding et al. since it teaches overlapping steps/concentrations. The limitation of claims 7-8: “cyclosporin A" is taught, e.g., in Example 1. The limitation of claim 9: “wherein the cyclosporin component is solubilized in the hydrophobic component present in the composition" is taught in column 3, lines 21-23. The limitations of claim 10: “wherein the hydrophobic component is present in the composition in an amount greater than 0.625% by weight“, of claim 11: "oily material", of claim 12: "vegetable oils" and of claim 13: "castor oil" are taught, e.g., in Examples 1A-D which teach 5.00%, 2.5% and 1.25% of hydrophobic component (castor oil). The limitation of claim 14: “topically administering the composition to the eye" is taught, e.g., in column 5, lines 15-18 and claim 8 of Ding et al. The limitation of claim 15: “wherein the composition comprises an effective amount of an emulsifier component” is taught in column 3, lines 38-4 and 50-56. The limitations of claim 16-17: “tonicity" and "organic tonicity component" are taught in column 4, lines 12-19. The limitation of claim 18: “polyelectrolyte component in an amount effective in stabilizing the composition” is taught in column 3, lines 64-67 and column 4, lines 1-12. The limitation of claims 19-20 drawn to pH ranges of "of about 7.0 to about 8.0" and “of about 7.2 to about 7.6” are taught, e.g., in Example 1A-1E and in claim 8 of Ding et al.

Ding et al. do not expressly teach an embodiment comprising both (at the same time) equal to or less than 0.05% of cyclosporin A and less than 0.08

cyclosporin A/castor oil ratio. The closest embodiments are 1D comprising 0.10% of cyclosporin A and 0.08 cyclosporin A/castor oil ratio; **1E comprising equal to 0.05% of cyclosporin A and 0.08 cyclosporin A/castor oil ratio** and 1B comprising 0.20% cyclosporin A and 0.04 cyclosporin A/castor oil ratio. It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the compositions of Ding et al. (such as 1E) by increasing the amount of castor oil or decreasing the cyclosporin concentration in order to reduce the ratio of the cyclosporin component to hydrophobic component from 0.08 to, e.g., 0.04 as taught by the ranges described in Ding et al. (see, e.g., column 3, lines 18-20) and exemplified in embodiment 1B. Further, it would have been obvious to one skilled in the art to use the beneficial compositions of Ding et al., which had low irritation level and contained the active agent for corneal allograft rejection prevention as taught by Kaswan Further, Kaswan teach that the preferred topical ophthalmic formulation consisted of 2% cyclosporine, 1 mole % alpha tocopherol and 0.005% methyl paraben. However, Karwan discloses that treating corneal allografts can be done with cyclosporine solutions having 0.01% by weight of cyclosporine.

With respect to the ranges, the skilled artisan would have been motivated to select them because such proportions were encompassed by the Ding et al. patent. Further, the active agent proportion was taught expressly for allograft corneal rejection in Kaswan. There would have been a reasonable expectation of success, because such ranges were disclosed to be effective in corneal allograft rejection as evidenced by Kaswan. Please note that compositions with

a higher amount of castor oil are encompassed by the Ding et al. claims (e.g., claim 8, embodiment 1B) optimizing the ratio of cyclosporin/hydrophobic components to below 0.08 was taught by Ding et al. in the range 0.02 to 0.12 (e.g., column 3, lines 18-20) and in embodiment 1B (which has 0.04). The adjustment of particular conventional working conditions (e.g., using all the ratios and proportions taught by Ding. et al. and Kaswan) is deemed merely a matter of judicious selection and routine optimization that is well within the purview of the skilled artisan. There is no evidence of criticality of these ranges. “Generally, 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). As such, it would have been obvious to one skilled in the art at the time of invention to determine all optimum and operable conditions [e.g., formulation ranges and proportions such as the proportion of castor oil and corn oil], because such conditions are art-recognized result-effective variables that are routinely determined and optimized in the art through routine experimentation. One would have had a reasonable expectation for success because such modifications are routinely determined and optimized in the art through routine experimentation.

From the teaching of the references, 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.

Conclusion

10. No claim is allowed.

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

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

11. A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

12. 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, Cecilia J. Tsang can be reached on (571) 272-0562. 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/
Examiner, Art Unit 1654

MMCG 06/2010

Notice of References Cited	Application/Control No. 11/897,177	Applicant(s)/Patent Under Reexamination ACHEAMPONG ET AL.	
	Examiner MARCELA M. CORDERO	Art Unit 1654	Page 1 of 1

U.S. PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Name	Classification
*	A	US-5,411,952	05-1995	Kaswan, Renee	514/11
*	B	US-4,764,503	08-1988	Wenger, Roland	514/11
*	C	US-4,996,193	02-1991	Hewitt et al.	514/11
	D	US-			
	E	US-			
	F	US-			
	G	US-			
	H	US-			
	I	US-			
	J	US-			
	K	US-			
	L	US-			
	M	US-			

FOREIGN PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Country	Name	Classification
	N					
	O					
	P					
	Q					
	R					
	S					
	T					

NON-PATENT DOCUMENTS

*		Include as applicable: Author, Title Date, Publisher, Edition or Volume, Pertinent Pages)
	U	Xie et al. Effect of a cyclosporine A delivery system in corneal transplantation. Chinese Medical Journal 2002. Vol. 115, No.1, pages 110-113.
	V	Stephenson. The Latest Uses of Restasis. Review of Ophthalmology. Accessed online on 6/18/2010 at http://www.revophth.com/index.asp?page=1_829.htm. 7 pages.
	W	Donnenfeld. The Economics of Using Restasis. October 2003. Ophthalomology Management. Accessed online on 6/18/2010 at http://www.ophmanagement.com/article.aspx?article=85896. 3 pages.
	X	

*A copy of this reference is not being furnished with this Office action. (See MPEP § 707.05(a).)
Dates in MM-YYYY format are publication dates. Classifications may be US or foreign.

Search Notes	Application/Control No.	Applicant(s)/Patent Under Reexamination
	11897177	ACHEAMPONG ET AL.
	Examiner	Art Unit
	MARCELA M CORDERO GARCIA	1654

SEARCHED

Class	Subclass	Date	Examiner
none	none	12/01/08	MMCG

SEARCH NOTES

Search Notes	Date	Examiner
updated	12/01/08	MMCG
STN searched by STIC (available via SCORE / PAIR)	4/14/08	MMCG
STN searched by STIC (available via SCORE / PAIR)	6/25/09	MMCG
EAST searched (attached)	8/16/09	MMCG
internet search (google.com) terms: restasis, dry eye, vernal conjunctivitis, atopic keratoconjunctivitis, cyclosporin	8/14/09	MMCG
STN searched by STIC (available via SCORE / PAIR)	4/26/10	MMCG
EAST searched (attached)	6/18/10	MMCG
also updated PALM Inventor search	6/18/10	MMCG
internet search (google.com) terms: restasis, corneal or cornea, graft, allograft, transplant, rejection	6/18/10	MMCG

INTERFERENCE SEARCH

Class	Subclass	Date	Examiner

EAST Search History

EAST Search History (Prior Art)

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	34547	corneal	US-PGPUB; USPAT; EPO; JPO; DERWENT	ADJ	ON	2010/06/19 08:29
L2	50	corneal same rejection same cyclosporin	US-PGPUB; USPAT; EPO; JPO; DERWENT	ADJ	ON	2010/06/19 08:30
L3	17	corneal same rejection same cyclosporine	US-PGPUB; USPAT; EPO; JPO; DERWENT	ADJ	ON	2010/06/19 08:32
L4	22	ding.inv. and allograft	US-PGPUB; USPAT; EPO; JPO; DERWENT	ADJ	ON	2010/06/19 09:34
L5	341	ding.inv. and graft	US-PGPUB; USPAT; EPO; JPO; DERWENT	ADJ	ON	2010/06/19 09:34
L6	29	ding.inv. and graft.clm.	US-PGPUB; USPAT; EPO; JPO; DERWENT	ADJ	ON	2010/06/19 09:34
L7	188	corneal.clm. and (transplant or graft or allograft) and cyclosporin	US-PGPUB; USPAT; EPO; JPO; DERWENT	ADJ	ON	2010/06/19 09:56
L8	33	corneal.clm. and (transplant or graft or allograft) and cyclosporin.clm.	US-PGPUB; USPAT; EPO; JPO; DERWENT	ADJ	ON	2010/06/19 09:56
L9	2225	cornea same transplant	US-PGPUB; USPAT; EPO; JPO; DERWENT	ADJ	ON	2010/06/19 10:10
L10	58	l9 same cyclosporin$	US-PGPUB; USPAT; EPO; JPO; DERWENT	ADJ	ON	2010/06/19 10:10
L11	142142	acheampong.inv. or tang-liu.inv. or chang. inv. or power.inv.	US-PGPUB; USPAT; EPO; JPO; DERWENT	ADJ	ON	2010/06/19 10:22
L12	26	l11 and cyclosporin and cornea	US-PGPUB; USPAT; EPO; JPO; DERWENT	ADJ	ON	2010/06/19 10:22
S1	3	"20040254225"	US-PGPUB; USPAT; EPO; JPO; DERWENT	ADJ	ON	2010/06/18 07:01

S2	103	endomorphin same analog	US-PGPUB; USPAT; EPO; JPO; DERWENT	ADJ	ON	2010/06/18 07:13
S3	59	S2 and (topical or cosmetic)	US-PGPUB; USPAT; EPO; JPO; DERWENT	ADJ	ON	2010/06/18 07:13
S4	59	endomorphin and S3	US-PGPUB; USPAT; EPO; JPO; DERWENT	ADJ	ON	2010/06/18 07:15
S5	1	"9842732"	US-PGPUB; USPAT; EPO; JPO; DERWENT	ADJ	ON	2010/06/18 07:34
S6	11	endomorphin same acetyl	US-PGPUB; USPAT; EPO; JPO; DERWENT	ADJ	ON	2010/06/18 17:11
S7	153	endomorphin and acetyl	US-PGPUB; USPAT; EPO; JPO; DERWENT	ADJ	ON	2010/06/18 17:12
S8	2	tyr-pro-phe-phe	US-PGPUB; USPAT; EPO; JPO; DERWENT	ADJ	ON	2010/06/18 17:13
S9	4	tyr-pro-trp-phe	US-PGPUB; USPAT; EPO; JPO; DERWENT	ADJ	ON	2010/06/18 17:13
S10	0	tyr adj pro adj phe adj phe	US-PGPUB; USPAT; EPO; JPO; DERWENT	ADJ	ON	2010/06/18 17:14
S11	3	"7259234"	US-PGPUB; USPAT; EPO; JPO; DERWENT	ADJ	ON	2010/06/18 17:19
S12	0	n-acetylation of peptides	US-PGPUB; USPAT; EPO; JPO; DERWENT	ADJ	ON	2010/06/18 17:21
S13	235	n-acetylation same peptide	US-PGPUB; USPAT; EPO; JPO; DERWENT	ADJ	ON	2010/06/18 17:21
S14	0	n-acetylation same peptide and endomorphin	US-PGPUB; USPAT; EPO; JPO; DERWENT	ADJ	ON	2010/06/18 17:21
S15	235	n-acetylation same peptide	US-PGPUB; USPAT; EPO; JPO; DERWENT	ADJ	ON	2010/06/18 17:21
S16	0	n-acetylation.ttl. same peptide	US-PGPUB; USPAT; EPO; JPO; DERWENT	ADJ	ON	2010/06/18 17:22
S17	235	n-acetylation same peptide	US-PGPUB; USPAT; EPO; JPO; DERWENT	ADJ	ON	2010/06/18 17:22

S18	16668	acetyl same peptide	US-PGPUB; USPAT; EPO; JPO; DERWENT	ADJ	ON	2010/06/18 17:33
S19	10	acetyl same peptide same endomorphin	US-PGPUB; USPAT; EPO; JPO; DERWENT	ADJ	ON	2010/06/18 17:33
S20	1113	retinoid same carrier	US-PGPUB; USPAT; EPO; JPO; DERWENT	ADJ	ON	2010/06/18 18:20
S21	88	retinoid same carrier same external	US-PGPUB; USPAT; EPO; JPO; DERWENT	ADJ	ON	2010/06/18 18:20
S22	4	retinoid same carrier same external same peptide	US-PGPUB; USPAT; EPO; JPO; DERWENT	ADJ	ON	2010/06/18 18:21
S23	8	retinoid same carrier same pain	US-PGPUB; USPAT; EPO; JPO; DERWENT	ADJ	ON	2010/06/18 18:21
S24	135	retinoid same carrier same analgesic	US-PGPUB; USPAT; EPO; JPO; DERWENT	ADJ	ON	2010/06/18 18:23
S25	2	retinoid same carrier same analgesic and (alpha or beta) same hydroxyacid	US-PGPUB; USPAT; EPO; JPO; DERWENT	ADJ	ON	2010/06/18 18:24
S26	186	retinoid same analgesic and (alpha or beta) same hydroxyacid	US-PGPUB; USPAT; EPO; JPO; DERWENT	ADJ	ON	2010/06/18 18:24
S27	280	retinoid and analgesic and (alpha or beta) same hydroxyacid	US-PGPUB; USPAT; EPO; JPO; DERWENT	ADJ	ON	2010/06/18 18:31
S28	1512	retinoid and analgesic and (alpha or beta) same hydroxy	US-PGPUB; USPAT; EPO; JPO; DERWENT	ADJ	ON	2010/06/18 18:31
S29	1342	retinoid and analgesic and (alpha or beta) same hydroxy same acid	US-PGPUB; USPAT; EPO; JPO; DERWENT	ADJ	ON	2010/06/18 18:31
S30	504	retinoid same analgesic and (alpha or beta) same hydroxy same acid	US-PGPUB; USPAT; EPO; JPO; DERWENT	ADJ	ON	2010/06/18 18:31
S31	154	retinoid same analgesic same (alpha or beta) same hydroxy same acid	US-PGPUB; USPAT; EPO; JPO; DERWENT	ADJ	ON	2010/06/18 18:31
S32	1032	retinoid same analgesic	US-PGPUB; USPAT; EPO; JPO; DERWENT	ADJ	ON	2010/06/18 18:48

S33	149	retinoid same analgesic. clm.	US-PGPUB; USPAT; EPO; JPO; DERWENT	ADJ	ON	2010/06/18 18:48
S34	14	retinoid near3 analgesic. clm.	US-PGPUB; USPAT; EPO; JPO; DERWENT	ADJ	ON	2010/06/18 19:17
S35	37	retinoid near3 peptide. clm.	US-PGPUB; USPAT; EPO; JPO; DERWENT	ADJ	ON	2010/06/18 19:19
S36	62	retinoid near3 analgesic	US-PGPUB; USPAT; EPO; JPO; DERWENT	ADJ	ON	2010/06/18 19:24
S37	69	External Skin Composition	US-PGPUB; USPAT; EPO; JPO; DERWENT	ADJ	ON	2010/06/18 19:27
S38	2	External Skin Composition and analgesic	US-PGPUB; USPAT; EPO; JPO; DERWENT	ADJ	ON	2010/06/18 19:27
S39	4	"2003020463"	US-PGPUB; USPAT; EPO; JPO; DERWENT	ADJ	ON	2010/06/18 20:09
S40	2	"20030020463"	US-PGPUB; USPAT; EPO; JPO; DERWENT	ADJ	ON	2010/06/18 20:09
S41	1684	psoriasis same retinoid	US-PGPUB; USPAT; EPO; JPO; DERWENT	ADJ	ON	2010/06/18 20:12
S42	37	psoriasis.clm. same retinoid	US-PGPUB; USPAT; EPO; JPO; DERWENT	ADJ	ON	2010/06/18 20:12
S43	20	"5763576"	US-PGPUB; USPAT; EPO; JPO; DERWENT	ADJ	ON	2010/06/18 20:35
S44	2	"5763576".pn.	US-PGPUB; USPAT; EPO; JPO; DERWENT	ADJ	ON	2010/06/18 20:35
S45	5837	corneal same graft	US-PGPUB; USPAT; EPO; JPO; DERWENT	ADJ	ON	2010/06/18 22:33
S46	7343	corneal same (graft or transplantation)	US-PGPUB; USPAT; EPO; JPO; DERWENT	ADJ	ON	2010/06/18 22:33
S47	31123	cyclosporin or cyclosporine	US-PGPUB; USPAT; EPO; JPO; DERWENT	ADJ	ON	2010/06/18 22:34
S48	58	S46 same S47	US-PGPUB; USPAT; EPO; JPO; DERWENT	ADJ	ON	2010/06/18 22:34

S49	491	corneal same (graft or transplantation).clm.	US-PGPUB; USPAT; EPO; JPO; DERWENT	ADJ	ON	2010/06/18 22:36
S50	99	corneal same (graft or transplantation).clm. and S47	US-PGPUB; USPAT; EPO; JPO; DERWENT	ADJ	ON	2010/06/18 22:36
S51	0	ding.inv. same corneal	US-PGPUB; USPAT; EPO; JPO; DERWENT	ADJ	ON	2010/06/18 23:02
S52	0	ding.inv. same cornea	US-PGPUB; USPAT; EPO; JPO; DERWENT	ADJ	ON	2010/06/18 23:02
S53	49	ding.inv. and corneal	US-PGPUB; USPAT; EPO; JPO; DERWENT	ADJ	ON	2010/06/18 23:03
S54	17	ding.inv. and corneal same (transplant or transplantation or graft or allograft)	US-PGPUB; USPAT; EPO; JPO; DERWENT	ADJ	ON	2010/06/18 23:03
S55	1674	cyclosporin and corneal same (transplant or transplantation or graft or allograft)	US-PGPUB; USPAT; EPO; JPO; DERWENT	ADJ	ON	2010/06/18 23:03
S56	97	S47 same corneal same (transplant or transplantation or graft or allograft)	US-PGPUB; USPAT; EPO; JPO; DERWENT	ADJ	ON	2010/06/18 23:04
S57	56	"5474979"	US-PGPUB; USPAT; EPO; JPO; DERWENT	ADJ	ON	2010/06/18 23:14
S58	2	"5474979".pn.	US-PGPUB; USPAT; EPO; JPO; DERWENT	ADJ	ON	2010/06/18 23:17

6/19/10 10:26:04 AM

PTO/SB/30 (07-09)
Approved for use through 07/31/2012. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Request for Continued Examination (RCE) Transmittal

Address to:
Mail Stop RCE
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Application Number	11/897,177
Filing Date	August 28, 2007
First Named Inventor	Andrew Acheampong
Art Unit	1654
Examiner Name	Marcela M. Cordero Garcia
Attorney Docket Number	17618CON1(AP)

This is a Request for Continued Examination (RCE) under 37 CFR 1.114 of the above-identified application.
Request for Continued Examination (RCE) practice under 37 CFR 1.114 does not apply to any utility or plant application filed prior to June 8, 1995, or to any design application. See Instruction Sheet for RCEs (not to be submitted to the USPTO) on page 2.

1. Submission required under 37 CFR 1.114 Note: If the RCE is proper, any previously filed unentered amendments and amendments enclosed with the RCE will be entered in the order in which they were filed unless applicant instructs otherwise. If applicant does not wish to have any previously filed unentered amendment(s) entered, applicant must request non-entry of such amendment(s).

   a. ☐ Previously submitted. If a final Office action is outstanding, any amendments filed after the final Office action may be considered as a submission even if this box is not checked.

      i. ☐ Consider the arguments in the Appeal Brief or Reply Brief previously filed on _____

      ii. ☐ Other _____

   b. ☑ Enclosed

      i. ☑ Amendment/Reply

      ii. ☐ Affidavit(s)/ Declaration(s)

      iii. ☑ Information Disclosure Statement (IDS)

      iv. ☐ Other _____

2. Miscellaneous

   a. ☐ Suspension of action on the above-identified application is requested under 37 CFR 1.103(c) for a period of _____ months. (Period of suspension shall not exceed 3 months; Fee under 37 CFR 1.17(i) required)

   b. ☐ Other _____

3. Fees The RCE fee under 37 CFR 1.17(e) is required by 37 CFR 1.114 when the RCE is filed.

   a. ☑ The Director is hereby authorized to charge the following fees, any underpayment of fees, or credit any overpayments, to Deposit Account No. 01-0885.

      i. ☑ RCE fee required under 37 CFR 1.17(e)

      ii. ☑ Extension of time fee (37 CFR 1.136 and 1.17)

      iii. ☐ Other _____

   b. ☐ Check in the amount of $ _____ enclosed

   c. ☐ Payment by credit card (Form PTO-2038 enclosed)

WARNING: Information on this form may become public. Credit card information should not be included on this form. Provide credit card information and authorization on PTO-2038.

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT REQUIRED

Signature	/Joel B. German/	Date	November 17, 2010
Name (Print/Type)	Joel B. German	Registration No.	48,676

CERTIFICATE OF MAILING OR TRANSMISSION

I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Mail Stop RCE, Commissioner for Patents, P. O. Box 1450, Alexandria, VA 22313-1450 or facsimile transmitted to the U.S. Patent and Trademark Office on the date shown below.

Signature			
Name (Print/Type)		Date	

PTO/SB/30 (07-09)
Approved for use through 07/31/2012. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Instruction Sheet for RCEs

(not to be submitted to the USPTO)

NOTES:

An RCE is not a new application, and filing an RCE will not result in an application being accorded a new filing date.

Filing Qualifications:

The application must be a utility or plant application filed on or after June 8, 1995. The application cannot be a provisional application, a utility or plant application filed before June 8, 1995, a design application, or a patent under reexamination. See 37 CFR 1.114(e).

Filing Requirements:

Prosecution in the application must be closed. Prosecution is closed if the application is under appeal, or the last Office action is a final action, a notice of allowance, or an action that otherwise closes prosecution in the application (e.g., an Office action under *Ex parte Quayle*). See 37 CFR 1.114(b).

A submission and a fee are required at the time the RCE is filed. If reply to an Office action under 35 U.S.C. 132 is outstanding (e.g., the application is under final rejection), the submission must meet the reply requirements of 37 CFR 1.111. If there is no outstanding Office action, the submission can be an information disclosure statement, an amendment, new arguments, or new evidence. See 37 CFR 1.114(c). The submission may be a previously filed amendment (e.g., an amendment after final rejection).

WARNINGS:

Request for Suspension of Action:

All RCE filing requirements must be met before suspension of action is granted. A request for a suspension of action under 37 CFR 1.103(c) does not satisfy the submission requirement and does not permit the filing of the required submission to be suspended.

Improper RCE will NOT toll Any Time Period:

Before Appeal **-** If the RCE is improper (e.g., prosecution in the application is not closed or the submission or fee has not been filed) and the application is not under appeal, the time period set forth in the last Office action will continue to run and the application will be abandoned after the statutory time period has expired if a reply to the Office action is not timely filed. No additional time will be given to correct the improper RCE.

Under Appeal **-** If the RCE is improper (e.g., the submission or the fee has not been filed) and the application is under appeal, the improper RCE is effective to withdraw the appeal. Withdrawal of the appeal results in the allowance or abandonment of the application depending on the status of the claims. If there are no allowed claims, the application is abandoned. If there is at least one allowed claim, the application will be passed to issue on the allowed claim(s). See MPEP 1215.01.

See MPEP 706.07(h) for further information on the RCE practice.

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.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Acheampong et al	Examiner: Marcela M. Cordero Garcia
Serial No.: 11/897,177	Group Art Unit: 1654
Filed: August 28, 2007	Confirmation No.: 3860
For: METHODS OF PROVIDING THERAPEUTIC EFFECTS USING CYCLOSPORIN COMPONENTS	Customer No.: 051957

Response

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

Dear Sir:

The Applicants respond to the Office action of June 23, 2010 (the "Office action") with the claim amendments beginning at page 2, and the remarks that follow at page 5.

CLAIMS

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

1. (Currently amended) A method of treating or preventing corneal graft rejection, the method comprising administering to an eye of a human or animal, at a frequency selected from the group consisting of once, twice, or three times a day, a composition in the form of an emulsion comprising water, a hydrophobic component, and a cyclosporin component in a therapeutically effective amount equal to or less than 0.05% by weight of the composition, wherein the weight ratio of the cyclosporin component to the hydrophobic component is less than 0.08.

2. – 3. (Canceled)

4. (Previously presented) The method of claim 1 wherein the blood of the human or animal has no detectable concentration of the cyclosporin component.

5. (Previously presented) 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 chromatographylmass spectrometry analytical method.

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

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

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

10. (Original) 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. (Original) The method of claim 1 wherein the hydrophobic component comprises an oily material.

12. (Original) 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. (Original) The method of claim 1 wherein the hydrophobic component comprises castor oil.

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

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

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

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

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

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

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

21. – 36. (Canceled).

37. (Previously presented) The method of claim 1, where the cyclosporin component is in a therapeutically effective amount of less than 0.05% by weight of the composition.

38. (New) The method of claim 1, wherein the cyclosporin component is in a therapeutically effective amount of 0.05% by weight of the composition.

39. (New) The method of claim 1, wherein the composition is administered once per day.

40. (New) The method of claim 1, wherein the composition is administered twice per day.

41. (New) The method of claim 1, wherein the composition is administered three times per day.

REMARKS

The applicants have amended claim 1 and added claims 38-41. Support for the dosing frequency recited in claims 1 and 39-41 may be found at paragraph 32; support for the concentration of cyclosporin recited in claim 38 may be found at Example 1.

The § 103 rejection

The Office rejected claims 1, 4-20, and 37 under 35 U.S.C. § 103(a) arguing that the claims are obvious in view of the Ding reference (US 5,474,979) when combined with the Kaswan reference (US 5,411,952). The applicants respectfully disagree that the rejection is proper.

The Office states that "Kaswan discloses that cyclosporine was effective in the treatment of corneal graft transplantation." The Kaswan reference states as follows:

> As disclosed in pending applications U.S. Ser. No. 092,466 entitled "Method of Increasing Tear Production by Topical Administration of Cyclosporin" filed Sep. 3, 1987, now U.S. Pat. No. 4,839,342 issued Jun. 13, 1989, by Renee Kaswan, U.S. Ser. No. 117,218 entitled "Method of Treating a Specific Antigen Mediated Immune Response by Local Administration of Cyclosporin" filed Nov. 4, 1987, now abandoned, by Renee Kaswan and U.S. Pat. No. 4,649,047 issued Mar. 10, 1987 to Kaswan, cyclosporine can be topically applied to the surface of the eye to treat both immune mediated eye disease and eye disease of unknown etiology. It can also be used to inhibit corneal graft rejection.

Renee Kaswan thus cites her earlier publications to support her claim that cyclosporin "can also be used to inhibit corneal graft rejection." Those earlier publications state only the following:

> Hunter *et al., Clin. Exp. Immunol.* 45, 173-177 (1981) describe the topical administration of cyclosporine in a rabbit model of corneal graft rejection with positive results. These effects were found to be

> attributable to T-cell suppression within the eye or within systemic compartments such as blood or lymph.

US 4,649,047, at col. 1, ln. 65 – col. 2, ln. 2, and US 4,839,342, at col. 3, lns. 35-40 (the 07/117,218 application was never published, but the Kaswan reference claims priority directly from it, so the disclosure of that application is no broader than that of the Kaswan reference).

The Hunter reference discloses an experiment in which the authors explored the effect of cyclosporin on corneal graft survival in rabbits (the applicants attach the Hunter reference to this paper as Exhibit 1). The authors used cyclosporin at a concentration of 1% – twenty times that provided in the claims – at a frequency of five times a day. The total dose of cyclosporin thus delivered is one hundred times that of claim 39 (1% x 5 / 0.05% x 1), fifty times that of claim 40 (1% x 5 / 0.05% x 2), and thirty three times that of claim 41 (1% x 5 / 0.05% x 3), the upper bound of the dosing specified in claim 1.

Hence, Kaswan discloses no more than Hunter *et al.'s* observation that cyclosporin was used in rabbits to prevent corneal graft rejection at a dose that is thirty three to one hundred times greater than those specified in the claims. It gives one of ordinary skill in the art no reason to expect that cyclosporin could successfully prevent corneal graft rejection at the significantly lower doses the applicants have claimed.

The Office seems to regard as significant the fact that the Kaswan reference discloses that ophthalmic compositions may contain cyclosporin in amounts that are as low as 0.01% by weight. Office action, at 6 ("Kaswan discloses that cyclosporin solutions can be prepared of between approximately 0.01% by weight of cyclosporin and saturation.") (emphasis in original). The reference states as follows:

> The preferred formulation for topical ophthalmic use consists of 2% cyclosporine, 1 mole % alpha tocopherol and 0.005% methyl paraben. However, cyclosporine solutions can be prepared of between approximately 0.01% by weight and saturation, approximately 20% by weight.

US 5,411,952, col. 4, lns. 1-7. But this does not make the claimed invention obvious for two at least three reasons. First, the breadth of the range itself – spanning one value to another that is 2,000 times higher – permits a vast number of possible concentrations. Second, the reference gives no reason to favor the lower end of this range for preventing corneal graft rejection. The reference speaks only to the suitability of the formulation. For example, it alleges that corn oil, when substituted for olive oil, reduces redness and burning. At col. 3, lns. 20-42. But it does not say that any value within this range would be effective for the treatment of any particular condition. Third, the reference provides evidence of the effect of cyclosporin only at a 2% dose, and for the treatment of keratoconjunctivitis sicca. It provides no guidance for the doses that might be effective in preventing corneal graft rejection. It discloses no experiments concerning the prevention of that condition or provide any information concerning the doses that one could use to prevent it – with the exception, of course, of the information that one can use doses that are thirty-three to one hundred times higher.

For the foregoing reasons, the Kaswan reference gives one of skill in the art no reason to believe that one could use cyclosporin, administered in the doses claimed here, to effectively prevent corneal graft rejection. The applicants respectfully submit, therefore, that the Kaswan reference, even when combined with the Ding reference, does not render the claims obvious. They respectfully request that the Office withdraw the § 103 rejection.

The double patenting rejection

The Office rejected claims 1, 4-20, and 37 for nonstatutory obviousness-type double patenting, arguing that the claims are obvious over claims 1-8 of the Ding reference in view of the Kaswan reference. For the reasons the applicants state above, the Kaswan reference gives one of skill in the art no reason to believe that one could use cyclosporin, administered in the doses claimed here, to effectively prevent corneal graft rejection. The applicants respectfully request, therefore, that the Office withdraw the double patenting rejection.

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,

/JOEL B. GERMAN/

Date: November 17, 2010

JOEL B. GERMAN
Attorney of Record
Registration Number 48,676

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17618CON1(AP)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Acheampong et al	Examiner: Marcela M. Cordero Garcia
Serial No.: 11/897,177	Group Art Unit: 1654
Filed: August 28, 2007	Confirmation No.: 3860
For: METHODS OF PROVIDING THERAPEUTIC EFFECTS USING CYCLOSPORIN COMPONENTS	Customer No.: 051957

INFORMATION DISCLOSURE STATEMENT

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

Dear Sir:

In accordance with the provisions of 37 C.F.R. 1.56, 1.97, and 1.98, the attention of the Patent and Trademark Office is hereby directed to the documents listed on the attached form PTO-SB/08b (formerly 1449). It is respectfully requested that the documents be expressly considered during the prosecution of this application, and that the documents be made of record therein and appear among the "References Cited" on any patent to issue therefrom.

While these documents may be material pursuant to 37 C.F.R. §1.56, their disclosure is not intended to constitute an admission that the documents are prior art in regard to this invention. The filing of this Statement should not be construed to mean that a search has been conducted or that no other material documents or information exists. Please do not hesitate to contact the undersigned should any questions arise regarding this Statement.

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,

/JOEL B. GERMAN/

Date: November 17, 2010

JOEL B. GERMAN
Attorney of Record
Registration Number 48,676

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FORM PTO-1449 U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE	ATTY. DOCKET NO.	SERIAL NO.
INFORMATION DISCLOSURE STATEMENT BY APPLICANT	17618CON1(AP)	11/897,177
(USE SEVERAL SHEETS IF NECESSARY)	APPLICANT: Andrew Acheampong	
	FILING DATE: August 28, 2007	GROUP: 1654

U.S. PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE (IF APPROPRIATE)

FOREIGN PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION	
							YES	NO

EXAMINER INITIAL		**OTHER DOCUMENTS** (INCLUDING AUTHOR, TITLE, DATE, PERTINENT PAGES, ETC.)
		Hunter et al, "Cyclosporin A applied topically to the recipient eye inhibits corneal graft rejection", Clin. Exp. Immunol, 45, pages 173-177, 1981

EXAMINER	DATE CONSIDERED

***EXAMINER**: INITIAL IF CITATION CONSIDERED, WHETHER OR NOT CITATION IS IN CONFORMANCE WITH MPEP 609; DRAW LINE THROUGH CITATION IF NOT IN CONFORMANCE AND NOT CONSIDERED, INCLUDE COPY OF THIS FORM WITH NEXT COMMUNICATION TO APPLICANT.

Electronic Patent Application Fee Transmittal

Application Number:	11897177
Filing Date:	28-Aug-2007
Title of Invention:	Methods of providing therapeutic effects using cyclosporin components
First Named Inventor/Applicant Name:	Andrew Acheampong
Filer:	Joel B. German/Bonnie Ferguson
Attorney Docket Number:	17618CON (AP)

Filed as Large Entity

Utility under 35 USC 111(a) Filing Fees

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Basic Filing:				
Pages:				
Claims:				
Miscellaneous-Filing:				
Petition:				
Patent-Appeals-and-Interference:				
Post-Allowance-and-Post-Issuance:				
Extension-of-Time:				
Extension - 2 months with $0 paid	1252	1	490	490

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Miscellaneous:				
Request for continued examination	1801	1	810	810
		Total in USD ($)		**1300**

Electronic Acknowledgement Receipt

EFS ID:	8859619
Application Number:	11897177
International Application Number:	
Confirmation Number:	3860
Title of Invention:	Methods of providing therapeutic effects using cyclosporin components
First Named Inventor/Applicant Name:	Andrew Acheampong
Customer Number:	51957
Filer:	Joel B. German/Bonnie Ferguson
Filer Authorized By:	Joel B. German
Attorney Docket Number:	17618CON (AP)
Receipt Date:	17-NOV-2010
Filing Date:	28-AUG-2007
Time Stamp:	16:57:26
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	Deposit Account
Payment was successfully received in RAM	$1300
RAM confirmation Number	3700
Deposit Account	010885
Authorized User	

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)

1	Request for Continued Examination (RCE)	RCE-form-17618CON1-11-17-10b.pdf	58433 e7f5f710418df59f506845f9cd2f09ef87dc4ba5	no	3
Warnings:					
This is not a USPTO supplied RCE SB30 form.					
Information:					
2		17618Response111710toOfficeactionb.pdf	32249 6ee3c92ae77f51860da6b7cb567a0e2031c5d181	yes	8
	Multipart Description/PDF files in .zip description				
	Document Description		**Start**	**End**	
	Amendment After Final		1	1	
	Amendment Copy Claims/Response to Suggested Claims		2	4	
	Applicant Arguments/Remarks Made in an Amendment		5	8	
Warnings:					
Information:					
3	Information Disclosure Statement (IDS) Filed (SB/08)	17618CON-IDS-Trans11-17-10b.pdf	36012 95ced9331a1162fcccc52404cf195f3037a1dff9	no	3
Warnings:					
Information:					
This is not an USPTO supplied IDS fillable form					
4	NPL Documents	clinexpimmunol00178-0182.pdf	546000 dcd3b686bd87c171a4f71a96683e3ba1a92f3bd9	no	5
Warnings:					
Information:					
5	Fee Worksheet (PTO-875)	fee-info.pdf	32020 6d6268d8ca16d9c7a42080362dbca8b3dc22d052	no	2
Warnings:					
Information:					
		Total Files Size (in bytes):	704714		

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New Applications Under 35 U.S.C. 111
If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

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

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

PTO/SB/06 (07-06)
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U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
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PATENT APPLICATION FEE DETERMINATION RECORD

Substitute for Form PTO-875

Application or Docket Number	Filing Date	☐ To be Mailed
11/897,177	08/28/2007	

APPLICATION AS FILED – PART I

	(Column 1)	(Column 2)	SMALL ENTITY ☐		OR	OTHER THAN SMALL ENTITY	
FOR	NUMBER FILED	NUMBER EXTRA	RATE ($)	FEE ($)		RATE ($)	FEE ($)
☐ BASIC FEE (37 CFR 1.16(a), (b), or (c))	N/A	N/A	N/A			N/A	
☐ SEARCH FEE (37 CFR 1.16(k), (i), or (m))	N/A	N/A	N/A			N/A	
☐ EXAMINATION FEE (37 CFR 1.16(o), (p), or (q))	N/A	N/A	N/A			N/A	
TOTAL CLAIMS (37 CFR 1.16(i))	minus 20 =	*	X $ =		OR	X $ =	
INDEPENDENT CLAIMS (37 CFR 1.16(h))	minus 3 =	*	X $ =			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 $250 ($125 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			TOTAL	

APPLICATION AS AMENDED – PART II

		(Column 1)		(Column 2)	(Column 3)	SMALL ENTITY		OR	OTHER THAN SMALL ENTITY	
	11/17/2010	CLAIMS REMAINING AFTER AMENDMENT		HIGHEST NUMBER PREVIOUSLY PAID FOR	PRESENT EXTRA	RATE ($)	ADDITIONAL FEE ($)		RATE ($)	ADDITIONAL FEE ($)
AMENDMENT	Total (37 CFR 1.16(i))	* 23	Minus	** 37	=	X $ =		OR	X $ =	
	Independent (37 CFR 1.16(h))	* 1	Minus	***3	=	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)		(Column 2)	(Column 3)					
		CLAIMS REMAINING AFTER AMENDMENT		HIGHEST NUMBER PREVIOUSLY PAID FOR	PRESENT EXTRA	RATE ($)	ADDITIONAL FEE ($)		RATE ($)	ADDITIONAL FEE ($)
AMENDMENT	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 number found in the appropriate box in column 1.

Legal Instrument Examiner:
/KATRINA S. TURNER/

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
11/897,177	08/28/2007	Andrew Acheampong	17618CON (AP)	3860

51957 7590 02/17/2012

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

EXAMINER	
CORDERO GARCIA, MARCELA M	
ART UNIT	PAPER NUMBER
1654	

NOTIFICATION DATE	DELIVERY MODE
02/17/2012	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

Office Action Summary	Application No.	Applicant(s)	
	11/897,177	ACHEAMPONG ET AL.	
	Examiner	Art Unit	
	MARCELA M. CORDERO GARCIA	1654	

-- 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 *17 November 2010*.

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) *1,4-20 and 37-41* 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) *1,4-20 and 37-41* is/are rejected.

8)☒ Claim(s) *5* is/are objected to.

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

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).

12)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

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

a)☐ All b)☐ Some * c)☐ None of:

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) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/17/2011*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *Revised Notice to Comply*.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 11/17/2010 has been entered.

Status of the claims

2. Claims 1, 4-20, 37-41 are pending in the application. Claim 1 has been amended. Claims 38-41 are new claims. Claims 1, 4-20, 37-41 are presented for examination on the merits.

Claim Rejections - 35 USC § 103

3. 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.

4. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation

under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

5. Claims 1, 4-20 and 37-41 are rejected under 35 U.S.C. 103(a) as being obvious over Ding et al. (US 5,474,979 cited in the IDS of 11/14/07) in view of Kaswan (US 5,411,952) and Hunter et al. (Clin. Exp. Immunol., 1981, cited in the IDS dated 11/17/2010).

The Ding patent teaches nonirritating pharmaceutical compositions of cyclosporin with high comfort level and low irritation potential suitable for delivery to sensitive areas such as ocular tissues comprising cyclosporin in admixture with an emulsifying amount of a higher fatty acid glycerol and polysorbate 80. More particularly, the composition may comprise cyclosporin A and the higher fatty acid glyceride may comprise castor oil (e.g., col. 3) The compositions minimize the problems related to unpleasant sensation and syndrome exacerbation by reducing the oil content and dispersing the oil phase in water into an emulsion (col. 2, lines 55-67). In addition, the composition has stability for up to 9 months without crystallization of cyclosporin (e.g., abstract). The emulsions of Ding utilize higher fatty acid glycerides but in combination with polysorbate 80 which results in an emulsion with a high comfort level and low irritation potential suitable for delivery of medications to sensitive areas such as ocular tissues (col. 3, lines 1-5).

The Ding reference goes on to teach, preferably, the weight ratio of the castor oil to the polysorbate 80 is between about 0.3 to about 30, and a weight ratio of the

cyclosporin to castor oil is below 0.16. More preferably, the weight ratio of castor oil to polysorbate 80 is between 0.5 and 12.5, and the weight ratio of cyclosporin to castor oil is between 0.12 and .02 (e.g., column 3). Additionally, Ding provides Examples 1-4 which further illustrate their invention (columns 4-5). It is clear that such compositions, including Examples 1A thru 1E (having as low as 0.05% of cyclosporin) were all intended as therapeutic compositions. Please note that Example 1D encompasses 0.10 % of cyclosporin and shows ocular bioavailability at a therapeutic level. (e.g., column 5, lines 15-25). Therefore, one skilled in the art at the time the invention was made would have concluded that there would be a reasonable expectation of success that a composition having slightly less than 0.10% cyclosporin (e.g., 0.05%) and slightly less than 0.08 cyclosporin/castor oil (e.g., 0.07) would still maintain therapeutic activity when topically applied to the eye, especially in light of the teachings of Ding describing preferred embodiments for nonirritating pharmaceutical compositions with high comfort level and low irritation potential suitable for delivery to sensitive areas such as ocular tissues with weight ratios of cyclosporin/castor oil more preferably between 0.12 and 0.02 (e.g., column 3, lines 15-20) and the teachings of claim 8 of Ding et all. which encompass pharmaceutical emulsions for topical application encompassing 0.05% cyclosporin or more (which reads upon the instantly claimed “equal to or less than 0.05% of cyclosporin”) and as low as 0.02 ratio of cyclosporin to castor oil (which reads upon the instantly claimed "less than 0.08" weight ratio of cyclosporin/castor oil).

Ding et al. do not expressly teach treating or preventing “corneal graft rejection” with their cyclosporin compositions. However, at the time the invention was made, it

was known to use cyclosporin to treat corneal transplantation. For example, Kaswan discloses that cyclosporin was effective in the treatment of corneal graft transplantation. Kaswan teaches cyclosporin A compositions in corn oil comprising between 0.01% cyclosporin and saturation for topical ophthalmic use for treatment of immune disorders, to enhance or restore tear production and to enhance the normal healing of the surface of the eye in e.g., corneal transplantation (e.g., claims, cols. 1-2) Kaswan discloses several Examples and further, olive oil was also used and compared, and it was observed that the corn oil was favorable. The preferred topical ophthalmic formulation consisted of 2% cyclosporin, 1 mole % alpha tocopherol and 0.005% methyl paraben. However, Kaswan discloses that cyclosporin solutions can be prepared of between approximately 0.01% by weight of cyclosporin and saturation.

Furthermore, Hunter et al. also disclose that corneal graft survival in rabbits was significantly ($P<0.001$) prolonged by topical treatment to the recipient eye with cyclosporin A 1% in arachis oil applied five times daily for 4 weeks. No graft was rejected whilst treatment was maintained but all grafts subsequently underwent rejection by the 64th postoperative day. All animals in a simultaneous control group in this fully masked study developed allograft reactions by the 23rd day. No local or systemic side-effects attributable to cyclosporin A were observed (e.g., abstract, pages 174-175).

Hunter et al. go on to teach that corneal graft rejection still remains the main limitation to the application of corneal grafting, and is a leading cause of failure of corneal grafts. A safe method of ocular immunosuppression that is more effective than the current very prolonged topical administration of corticosteroids could thus provide a

major advance in the treatment of blindness from corneal disease. This is especially the case in those parts of the world where lack of skilled postoperative supervision makes such operations of little use because of the problems of monitoring and treating patients for subsequent rejection. The ability of topically applied CyA to inhibit corneal graft rejection in a rabbit model, which is a much closer analogue of the clinical situation in man than previous models, means that there may be an important role for topically administered CyA. Furthermore, these observations indicate that at least a substantial proportion of the events in sensitization induced by corneal transplantation that can be inhibited by CyA occur locally in the ocular tissue. This strengthens the concept of the eye as an immunologically competent organ (e.g., page 176).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to utilize, e.g., the pharmaceutical compositions of Ding et al. to treat or prevent corneal transplantation rejection. One of ordinary skill in the art at the time the invention was made would have been motivated to do so in order to decrease irritation in the eyes and decrease systemic side effects. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success since cyclosporin A was known to be an active agent with immunosuppressive activity in the healing of cornea including allografts as taught by Kaswan and by Hunter et al. With respect to the limitations claimed: Ding et al. teach 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 cyclosporin component in a therapeutically effective amount equal to or less than

0.05% by weight, the weight ratio of the cyclosporin component (cyclosporin A, e.g., Example 1D and column 3, lines 30-37) to the hydrophobic component (castor oil, a vegetable oil) is 0.08 (see, e.g., Example 1D). Ding et al. also teach embodiment 1B which has 0.2% of cyclosporin and a 0.04 ratio of cyclosporin/castor oil. Additionally, embodiment 1E has 0.05% of cyclosporin A and 0.08 ratio cyclosporin/castor oil. Ding et al. do teach that an embodiment having both less than 0.1 % of cyclosporin and wherein the weight ratio of the cyclosporin component to the hydrophobic component can be less than 0.08 (0.12 to 0.02). In addition, Ding et al. teach in claim 8 a pharmaceutical emulsion consisting of between about 0.05% and about 0.40% by weight cyclosporin A (which reads upon the limitation “less than 0.1 % by weight cyclosporin A” of instant claim 1) and between 0.625 and about 5.0 % castor oil. The corresponding lower and upper rations for the range is 0.05%/5.0% = 0.01 weight ratio of cyclosporin A/castor oil, which reads upon the limitation in claim 1 “the weight ratio of the cyclosporin A to the castor oil being less than 0.08”. The limitation of claim 4: “wherein the blood of the human or animal has substantially no detectable concentration of cyclosporin component” and of claim 5: ”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" and the limitation of claim 6: “0.1 ng/mL or less” necessarily read upon the method of Ding et al. since it teaches overlapping steps/concentrations. The limitation of claims 7-8: “cyclosporin A" is taught, e.g., in Example 1. The limitation of claim 9: “wherein the cyclosporin component is solubilized

in the hydrophobic component present in the composition" is taught in column 3, lines 21-23. The limitations of claim 10: “wherein the hydrophobic component is present in the composition in an amount greater than 0.625% by weight“, of claim 11: "oily material", of claim 12: "vegetable oils" and of claim 13: "castor oil" are taught, e.g., in Examples 1A-D which teach 5.00%, 2.5% and 1.25% of hydrophobic component (castor oil). The limitation of claim 14: “topically administering the composition to the eye" is taught, e.g., in column 5, lines 15-18 and claim 8 of Ding et al. The limitation of claim 15: “wherein the composition comprises an effective amount of an emulsifier component” is taught in column 3, lines 38-4 and 50-56. The limitations of claim 16-17: “tonicity" and "organic tonicity component" are taught in column 4, lines 12-19. The limitation of claim 18: “polyelectrolyte component in an amount effective in stabilizing the composition” is taught in column 3, lines 64-67 and column 4, lines 1-12. The limitation of claims 19-20 drawn to pH ranges of "of about 7.0 to about 8.0" and “of about 7.2 to about 7.6” are taught, e.g., in Example 1A-1E and in claim 8 of Ding et al. Furthermore, one of ordinary skill in the art would have been motivated to optimize the dosage and specifically the number of times the dosage is provided on a daily basis (e.g., once, twice or thrice a day).

Ding et al. do not expressly teach an embodiment comprising both (at the same time) equal to or less than 0.05% of cyclosporin A and less than 0.08 cyclosporin A/castor oil ratio. The closest embodiments are 1D comprising 0.10% of cyclosporin A and 0.08 cyclosporin A/castor oil ratio; **1E comprising equal to 0.05% of cyclosporin A and 0.08 cyclosporin A/castor oil ratio** and 1B comprising 0.20% cyclosporin A and

0.04 cyclosporin A/castor oil ratio. However, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the compositions of Ding et al. (such as 1E) by increasing the amount of castor oil or decreasing the cyclosporin concentration in order to reduce the ratio of the cyclosporin component to hydrophobic component from 0.08 to, e.g., 0.04 as taught by the ranges described in Ding et al. (see, e.g., column 3, lines 18-20) and exemplified in embodiment 1B. Further, it would have been obvious to one skilled in the art to use the beneficial compositions of Ding et al., which had low irritation level and contained the active agent for corneal allograft rejection prevention as taught by Kaswan and Hunter et al..

With respect to the ranges, the skilled artisan would have been motivated to do so because such proportions were encompassed by the Ding et al. patent. Please note that compositions with a higher amount of castor oil are encompassed by the Ding et al. claims (e.g., claim 8, embodiment 1B) optimizing the ratio of cyclosporin to hydrophobic components to below 0.08 was taught by Ding et al. in the range 0.02 to 0.12 (e.g., column 3, lines 18-20) and in embodiment 1B (which has 0.04). The adjustment of particular conventional working conditions (e.g., using all the ratios and proportions taught by Ding. et al. and Kaswan) is deemed merely a matter of judicious selection and routine optimization that is well within the purview of the skilled artisan. There is no evidence of criticality of these ranges: “[g]enerally, 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). As such, it would have been obvious to one skilled in the

art at the time of invention to determine all optimum and operable conditions [e.g., formulation ranges and proportions such as the proportion of oils], because such conditions are art-recognized result-effective variables that are routinely determined and optimized in the art through routine experimentation. One would have had a reasonable expectation for success because such modifications are routinely determined and optimized in the art through routine experimentation and because of the guidance provided by Kaswan which spans the instantly claimed range of cyclosporin concentrations (see claims of Kaswan).

From the teaching of the references, 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.

Applicant's arguments

6. The Office states that "Kaswan discloses that cyclosporin was effective in the treatment of corneal graft transplantation." The Kaswan reference states as follows: As disclosed in pending applications U.S. Ser. No. 092,466 entitled "Method of Increasing Tear Production by Topical Administration of Cyclosporin" filed Sep. 3, 1987, now U.S. Pat. No. 4,839,342 issued Jun. 13, 1989, by Renee Kaswan, U.S. Ser. No. 117,218 entitled "Method of Treating a Specific Antigen Mediated Immune Response by Local Administration of Cyclosporin" filed Nov. 4, 1987, now abandoned, by Renee Kaswan and U.S. Pat. No. 4,649,047 issued Mar. 10, 1987 to Kaswan, cyclosporin can be

topically applied to the surface of the eye to treat both immune mediated eye disease and eye disease of unknown etiology. It can also be used to inhibit corneal graft rejection. Renee Kaswan thus cites her earlier publications to support her claim that cyclosporin "can also be used to inhibit corneal graft rejection". Those earlier publications state only the following: Hunter et al., Clin. Exp. Immunol 45~ 173-177 (1981) describe the topical administration of cyclosporin in a rabbit model of corneal graft rejection with positive results. These effects were found to be attributable to T-cell suppression within the eye or within systemic compartments such as blood or lymph. US 4,649,047, at col. 1, ln. 65 - col. 2, ln. 2, and US 4,839,342, at col. 3, lns. 35-40 (the 071117,218 application was never published, but the Kaswan reference claims priority directly from it, so the disclosure of that application is no broader than that of the Kaswan reference).

The Hunter reference discloses an experiment in which the authors explored the effect of cyclosporin on corneal graft survival in rabbits (the applicants attach the Hunter reference to this paper as Exhibit 1). The authors used cyclosporin at a concentration oil 1% - twenty times that provided in the claims - at a frequency of five times a day. The total dose of cyclosporin thus delivered is one hundred times that of claim 39 (1% x 5 / 0.05% x 1), fifty times that of claim 40 (1% x 5 / 0.05% x 2), and thirty three times that of claim 41 (1% x 5 / 0.05% x 3), the upper bound of the dosing specified in claim I.

Hence, Kaswan discloses no more than Hunter et al.'s observation that cyclosporin was used in rabbits to prevent corneal graft rejection at a dose that is thirty three to one hundred times greater than those specified in the claims. It gives one of

ordinary skill in the art no reason to expect that cyclosporin could successfully prevent corneal graft rejection at the significantly lower doses the applicants have claimed.

The Office seems to regard as significant the fact that the Kaswan reference discloses that ophthalmic compositions may contain cyclosporin in amounts that are as low as 0.01% by weight. Office action, at 6 ("Kaswan discloses that cyclosporin solutions can be prepared of between approximately 0.01% by weight of cyclosporin and saturation."). The reference states as follows:

The preferred formulation for topical ophthalmic use consists of 2% cyclosporin, 1 mole % alpha tocopherol and 0.005% methyl paraben. However, cyclosporin solutions can be prepared of between approximately 0.01% by weight and saturation, approximately 20% by weight. US 5,411,952, col. 4, lns. 1-7. But this does not make the claimed invention obvious for two at least three reasons° First, the breadth of the range itself- spanning one value to another that is 2,000 times higher - permits a vast number of possible concentrations. Second, the reference gives no reason to favor the lower end of this range for preventing corneal graft rejection. The reference speaks only to the suitability of the formulation. For example, it alleges that corn oil, when substituted for olive oil, reduces redness and burning. At col. 3, lns. 20-42. But it does not say that any value within this range would be effective for the treatment of any particular condition. Third, the reference provides evidence of the effect of cyclosporin only at a 2% dose, and for the treatment of keratoconjunctivitis sicca. It provides no guidance for the doses that might be effective in preventing corneal graft rejection, it discloses no experiments concerning the prevention of that condition or provide any information concerning the

doses that one could use to prevent it - with the exception, of course, of the information that one can use doses that are thirty-three to one hundred times higher.

For the foregoing reasons, the Kaswan reference gives one of skill in the art no reason to believe that one could use cyclosporin, administered in the doses claimed here, to effectively prevent corneal graft rejection° The applicants respectfully submit, therefore, that the Kaswan reference, even when combined with the Ding reference, does not render the claims obvious. They respectfully request that the Office withdraw the § 103 rejection.

Response to arguments

7. Applicant's arguments have been carefully considered but not deemed persuasive for the reasons of record, for the reasons set forth above, and for the following reasons: The Ding patent teaches nonirritating pharmaceutical compositions of cyclosporin with high comfort level and low irritation potential suitable for delivery to sensitive areas such as ocular tissues comprising cyclosporin in admixture with an emulsifying amount of a higher fatty acid glycerol and polysorbate 80. More particularly, the composition may comprise cyclosporin A and the higher fatty acid glyceride may comprise castor oil (e.g., col. 3) The compositions minimize the problems related to unpleasant sensation and syndrome exacerbation by reducing the oil content and dispersing the oil phase in water into an emulsion (col. 2, lines 55-67). In addition, the composition has stability for up to 9 months without crystallization of cyclosporin (e.g., abstract). The emulsions of Ding utilize higher fatty acid glycerides but in combination with polysorbate 80 which results in an emulsion with a high comfort level and low

irritation potential suitable for delivery of medications to sensitive areas such as ocular tissues (col. 3, lines 1-5). The pharmaceutical compositions are not limited to a specific use (e.g., claims of Ding). The prior art (Kaswan and Hunter et al.) teach that cyclosporin is an active agent for the prevention and treatment of corneal graft rejection and thus one of ordinary skill in the art would have been motivated to find an effective range for the nonirritating pharmaceutical compositions of Ding in the treatment of corneal graft rejection. It is noted again that “[g]enerally, 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. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation."” (See MPEP 2144.05). Further, even though Kaswan does not expressly teach using the compositions expressly for treating corneal graft rejection, it is also noted that Kaswan also teaches that the cyclosporin compositions may contain as low as 0.01 % of cyclosporin and that such compositions may be used for suppressing an immune disorder of the eye (e.g., claims of Kaswan) and that one of these disorders is treatment of corneal graft rejection (col.1). With regards to the examples presented in both Ding and Kaswan, it is noted that both references are drawn to pharmaceutical compositions and not limited to a specific application (beyond suppressing an immune disorder of the eye) and thus one of ordinary skill in the art at the time the invention was made would have been motivated to use such compositions for treating immune disorders of the eyes which were known in the art such as treating corneal graft rejections as taught

both in Kaswan and in Hunter et al. Furthermore Applicant has not provided evidence of the criticality of the claimed ranges of molar proportions beyond the statement that the range of Kaswan spanned a vast number of concentrations and that no reason was provided for the use of the lower range. However, it is noted that Kaswan and Ding teach ranges and thus provide the motivation to use the proportions within the whole taught ranges. Further, as set forth above, one of ordinary skill in the art would have been motivated to use the compositions of Ding et al. which were nonirritating pharmaceutical compositions of cyclosporin with high comfort level and low irritation potential suitable for delivery to sensitive areas such as ocular tissues comprising cyclosporin in admixture with an emulsifying amount of a higher fatty acid glycerol and polysorbate 80. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success given that Kaswan discloses ranges from 0.01 % to saturation of the active agent (cyclosporin A) in compositions for suppressing immune disorders in the eye (which encompass inhibition of corneal graft rejection as evidence by Kaswan and Hunter et al.).

From the teaching of the references, 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

8. 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 obviousness-type double patenting rejection is appropriate where the conflicting claims 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 conflicting 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.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

9. Claims 1, 4-20 and 37-41 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 (cited in the IDS of 11/14/07) in view of Kaswan (US 5,411,952) and Hunter et al. (Clin. Exp. Immunol., 1981, cited in the IDS dated 11/17/2010).

The Ding patent claims pharmaceutical compositions of cyclosporin. The compositions comprise the range from between about 0.05 to and about 0.40% of cyclosporin and castor oil in an amount between 0.625% to about 5.0%, which encompasses the range 0.01 to 0.64 cyclosporin/castor oil and therefore encompasses the instantly claimed range of equal or less than 0.05 and less than 0.08 (e.g., claim 7 of Ding). The pH is 7.2-7.6 as in claim 8 and are suitable for topical application to ocular tissue (claim 8 of Ding).

The Ding reference goes on to teach, preferably, the weight ratio of the castor oil to the polysorbate 80 is between about 0.3 to about 30, and a weight ratio of the cyclosporin to castor oil is below 0.16. More preferably, the weight ratio of castor oil to polysorbate 80 is between 0.5 and 12.5, and the weight ratio of cyclosporin to castor oil is between 0.12 and .02 (e.g., column 3).

Ding et al. do not expressly teach treating or preventing “corneal graft rejection” with their cyclosporin compositions. However, at the time the invention was made, it was known to use cyclosporin to treat corneal transplantation. For example, Kaswan discloses that cyclosporin was effective in the treatment of corneal graft transplantation. Kaswan teaches cyclosporin A compositions in corn oil comprising between 0.01% cyclosporin and saturation for topical ophthalmic use for treatment of immune disorders, to enhance or restore tear production and to enhance the normal healing of the surface of the eye in e.g., corneal transplantation (e.g., claims, cols. 1-2) Kaswan discloses several Examples and further, olive oil was also used and compared, and it was observed that the corn oil was favorable. The preferred topical ophthalmic formulation

consisted of 2% cyclosporin, 1 mole % alpha tocopherol and 0.005% methyl paraben. However, Kaswan discloses that cyclosporin solutions can be prepared of between approximately 0.01% by weight of cyclosporin and saturation.

Furthermore, Hunter et al. also disclose that corneal graft survival in rabbits was significantly ($P<0.001$) prolonged by topical treatment to the recipient eye with cyclosporin A 1% in arachis oil applied five times daily for 4 weeks. No graft was rejected whilst treatment was maintained but all grafts subsequently underwent rejection by the 64th postoperative day. All animals in a simultaneous control group in this fully masked study developed allograft reactions by the 23rd day. No local or systemic side-effects attributable to cyclosporin A were observed (e.g., abstract, pages 174-175).

Hunter et al. go on to teach that corneal graft rejection still remains the main limitation to the application of corneal grafting, and is a leading cause of failure of corneal grafts. A safe method of ocular immunosuppression that is more effective than the current very prolonged topical administration of corticosteroids could thus provide a major advance in the treatment of blindness from corneal disease. This is especially the case in those parts of the world where lack of skilled postoperative supervision makes such operations of little use because of the problems of monitoring and treating patients for subsequent rejection. The ability of topically applied CyA to inhibit corneal graft rejection in a rabbit model, which is a much closer analogue of the clinical situation in man than previous models, means that there may be an important role for topically administered CyA. Furthermore, these observations indicate that at least a substantial proportion of the events in sensitization induced by corneal transplantation that can be

inhibited by CyA occur locally in the ocular tissue. This strengthens the concept of the eye as an immunologically competent organ (e.g., page 176).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to utilize, e.g., the pharmaceutical compositions of Ding et al. to treat or prevent corneal transplantation rejection. One of ordinary skill in the art at the time the invention was made would have been motivated to do so in order to decrease irritation in the eyes and decrease systemic side effects. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success since cyclosporin A was known to be an active agent with immunosuppressive activity in the healing of cornea including allografts as taught by Kaswan and by Hunter et al. With respect to the limitations claimed: Ding et al. teach 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 cyclosporin component in a therapeutically effective amount equal to or less than 0.05% by weight, the weight ratio of the cyclosporin component (cyclosporin A, e.g., Example 1D and column 3, lines 30-37) to the hydrophobic component (castor oil, a vegetable oil) is 0.08 (see, e.g., Example 1D). Ding et al. also teach embodiment 1B which has 0.2% of cyclosporin and a 0.04 ratio of cyclosporin/castor oil. Additionally, embodiment 1E has 0.05% of cyclosporin A and 0.08 ratio cyclosporin/castor oil. Ding et al. do teach that an embodiment having both less than 0.1 % of cyclosporin and wherein the weight ratio of the cyclosporin component to the hydrophobic component can be less than 0.08 (0.12 to 0.02). In addition, Ding et al. teach in claim 8 a

pharmaceutical emulsion consisting of between about 0.05% and about 0.40% by weight cyclosporin A (which reads upon the limitation “less than 0.1 % by weight cyclosporin A” of instant claim 1) and between 0.625 and about 5.0 % castor oil. The corresponding lower and upper rations for the range is 0.05%/5.0% = 0.01 weight ratio of cyclosporin A/castor oil, which reads upon the limitation in claim 1 “the weight ratio of the cyclosporin A to the castor oil being less than 0.08”. The limitation of claim 4: “wherein the blood of the human or animal has substantially no detectable concentration of cyclosporin component” and of claim 5: ”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" and the limitation of claim 6: “0.1 mg/mL or less” necessarily read upon the method of Ding et al. since it teaches overlapping steps/concentrations. The limitation of claims 7-8: “cyclosporin A" is taught, e.g., in Example 1. The limitation of claim 9: “wherein the cyclosporin component is solubilized in the hydrophobic component present in the composition" is taught in column 3, lines 21-23. The limitations of claim 10: “wherein the hydrophobic component is present in the composition in an amount greater than 0.625% by weight“, of claim 11: "oily material", of claim 12: "vegetable oils" and of claim 13: "castor oil" are taught, e.g., in Examples 1A-D which teach 5.00%, 2.5% and 1.25% of hydrophobic component (castor oil). The limitation of claim 14: “topically administering the composition to the eye" is taught, e.g., in column 5, lines 15-18 and claim 8 of Ding et al. The limitation of claim 15: “wherein the composition comprises an effective amount of an emulsifier

component" is taught in column 3, lines 38-4 and 50-56. The limitations of claim 16-17: "tonicity" and "organic tonicity component" are taught in column 4, lines 12-19. The limitation of claim 18: "polyelectrolyte component in an amount effective in stabilizing the composition" is taught in column 3, lines 64-67 and column 4, lines 1-12. The limitation of claims 19-20 drawn to pH ranges of "of about 7.0 to about 8.0" and "of about 7.2 to about 7.6" are taught, e.g., in Example 1A-1E and in claim 8 of Ding et al. Furthermore, one of ordinary skill in the art would have been motivated to optimize the dosage and specifically the number of times the dosage is provided on a daily basis (e.g., once, twice or thrice a day).

Ding et al. do not expressly teach an embodiment comprising both (at the same time) equal to or less than 0.05% of cyclosporin A and less than 0.08 cyclosporin A/castor oil ratio. The closest embodiments are 1D comprising 0.10% of cyclosporin A and 0.08 cyclosporin A/castor oil ratio; **1E comprising equal to 0.05% of cyclosporin A and 0.08 cyclosporin A/castor oil ratio** and 1B comprising 0.20% cyclosporin A and 0.04 cyclosporin A/castor oil ratio. However, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the compositions of Ding et al. (such as 1E) by increasing the amount of castor oil or decreasing the cyclosporin concentration in order to reduce the ratio of the cyclosporin component to hydrophobic component from 0.08 to, e.g., 0.04 as taught by the ranges described in Ding et al. (see, e.g., column 3, lines 18-20) and exemplified in embodiment 1B. Further, it would have been obvious to one skilled in the art to use the beneficial

compositions of Ding et al., which had low irritation level and contained the active agent for corneal allograft rejection prevention as taught by Kaswan and Hunter et al..

With respect to the range of cyclosporin to hydrophobic component, the skilled artisan would have been motivated to do so because such proportions were encompassed by the Ding et al. patent. Please note that compositions with a higher amount of castor oil are encompassed by the Ding et al. claims (e.g., claim 8, embodiment 1B) optimizing the ratio of cyclosporin to hydrophobic components to below 0.08 was taught by Ding et al. in the range 0.02 to 0.12 (e.g., column 3, lines 18-20) and in embodiment 1B (which has 0.04). The adjustment of particular conventional working conditions (e.g., using all the ratios and proportions taught by Ding. et al. and Kaswan) is deemed merely a matter of judicious selection and routine optimization that is well within the purview of the skilled artisan. There is no evidence of criticality of these ranges: “[g]enerally, 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). As such, it would have been obvious to one skilled in the art at the time of invention to determine all optimum and operable conditions [e.g., formulation ranges and proportions such as the proportion of oils], because such conditions are art-recognized result-effective variables that are routinely determined and optimized in the art through routine experimentation. One would have had a reasonable expectation for success because such modifications are routinely determined and optimized in the art through routine

experimentation and because of the guidance provided by Kaswan which spans the instantly claimed range of cyclosporin concentrations (see claims of Kaswan et al.).

From the teaching of the references, 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.

Applicant's arguments

10. The Office rejected claims 1, 4-20, and 37 for nonstatutory obviousness-type double patenting, arguing that the claims are obvious over claims 1-8 of the Ding reference in view of the Kaswan reference. For the reasons the applicants state above, the Kaswan reference gives one of skill in the art no reason to believe that one could use cyclosporin, administered in the doses claimed here, to effectively prevent corneal graft rejection° The applicants respectfully request, therefore, that the Office withdraw the double patenting rejection.

Response to arguments

11. Please see arguments above in paragraph 7.

Claim objections

12. Claim 5 is objected to because of the phrase "liquid chromatography|mass spectrometry". It appears that Applicant intends to claim "liquid chromatograph/mass spectrometry". Appropriate correction is required.

Specification / Trademarks

13. The use of the trademarks, e.g., Pemulen® (page 20) Purite®, Bio-Cide®, Anthium Dioxide® (page 24) Premulen® (page 26) has been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Specification / Sequence Compliance

14. Applicant is advised that the application is not in compliance with 37 CFR §§ 1.821-1.825.

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR § 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR §§ 1.821-1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. Applicant must comply with the requirements of the sequence rules (37 CFR §§ 1.821- 1.825) in order to completely respond to this office action.

15. Specifically, the amino acid sequences presented in, e.g., pages 12-13 (Formulas I-III) require sequence identifiers. In order to satisfy the sequence rules requirements, Applicant needs to provide an amendment to the instant claims, specification and drawings to include reference to the appropriate sequence identifier “SEQ ID NO:” in parenthesis next to each of the sequences having 4 or more amino acids. Please confirm that all peptides having 4 or more than 4 amino acid residues have sequence identifiers and are included in the sequence listing.

In case of any new sequences not properly identified in the instant specification, Applicant is required to provide a substitute computer readable form (CRF) copy of a "Sequence Listing" which includes all of the sequences that are present in the instant application and encompassed by these rules, a new or substitute paper copy of that "Sequence Listing", an amendment directing the entry of that paper copy into the specification, and a statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. § 1.821(e) or 1.821(f) or 1.821(g) or 1.825(d). The instant specification will also need to be amended so that it complies with 37 C.F.R. § 1.821(d) which requires a reference to a particular sequence identifier (SEQ ID NO:) be made in the specification and claims wherever a reference is made to that sequence. For rules interpretation Applicant may call (571) 272-2533. See M.P.E.P. 2422.04.

Please direct all replies to the United States Patent and Trademark Office via one (1) of the following:

1. Electronically submitted through EFS-Bio (<http://www.uspto.gov/ebc/efs/downloads/documents.htm>, EFS Submission User Manual - ePave)

2. US Postal Service:
Commissioner for Patents
PO Box 22313-1450
Alexandria, VA 22313-1450

3. Hand carry, Federal Express, United Parcel Service, or other delivery service:
U.S. Patent and Trademark Office
Mail Stop Sequence
Customer Window, Randolph Building
401 Dulany Street
Alexandria, VA 22314

Conclusion

16. No claim is 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, Cecilia J. Tsang can be reached on (571) 272-0562. 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 1654

MMCG 02/2012

FORM PTO-1449 U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE	ATTY. DOCKET NO.	SERIAL NO.
INFORMATION DISCLOSURE STATEMENT BY APPLICANT (USE SEVERAL SHEETS IF NECESSARY)	17618CON1(AP)	11/897,177
	APPLICANT: Andrew Acheampong	
	FILING DATE: August 28, 2007	GROUP: 1654

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

U.S. PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE (IF APPROPRIATE)

FOREIGN PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION	
							YES	NO

EXAMINER INITIAL		**OTHER DOCUMENTS** (INCLUDING AUTHOR, TITLE, DATE, PERTINENT PAGES, ETC.)
		Hunter et al, "Cyclosporin A applied topically to the recipient eye inhibits corneal graft rejection", Clin. Exp. Immunol, 45, pages 173-177, 1981

EXAMINER	/Marcela Cordero Garcia/	DATE CONSIDERED	02/13/2012

*EXAMINER: INITIAL IF CITATION CONSIDERED, WHETHER OR NOT CITATION IS IN CONFORMANCE WITH MPEP 609; DRAW LINE THROUGH CITATION IF NOT IN CONFORMANCE AND NOT CONSIDERED, INCLUDE COPY OF THIS FORM WITH NEXT COMMUNICATION TO APPLICANT.

Search Notes	Application/Control No.	Applicant(s)/Patent Under Reexamination
	11897177	ACHEAMPONG ET AL.
	Examiner	Art Unit
	MARCELA M CORDERO GARCIA	1654

SEARCHED

Class	Subclass	Date	Examiner
none	none	12/01/08	MMCG

SEARCH NOTES

Search Notes	Date	Examiner
updated	12/01/08	MMCG
STN searched by STIC (available via SCORE / PAIR)	4/14/08	MMCG
STN searched by STIC (available via SCORE / PAIR)	6/25/09	MMCG
EAST searched (attached)	8/16/09	MMCG
internet search (google.com) terms: restasis, dry eye, vernal conjunctivitis, atopic keratoconjunctivitis, cyclosporin	8/14/09	MMCG
STN searched by STIC (available via SCORE / PAIR)	4/26/10	MMCG
EAST searched (attached)	6/18/10	MMCG
also updated PALM Inventor search	6/18/10	MMCG
internet search (google.com) terms: restasis, corneal or cornea, graft, allograft, transplant, rejection	6/18/10	MMCG
EAST updated (attached)	02/13/2012	MMCG
also updated PALM Inventor search	02/13/2012	MMCG

INTERFERENCE SEARCH

Class	Subclass	Date	Examiner
EAST search			

EAST Search History

EAST Search History (Prior Art)

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	36663	cyclosporin or cyclosporine	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2012/02/13 19:28
L2	445	l1 same (corneal or cornea)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2012/02/13 19:29
L3	85	l2 same graft	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2012/02/13 19:29
L4	27	l2 same graft same (eye or ocular)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2012/02/13 19:30

EAST Search History (Interference)

<This search history is empty>

2/ 13/ 2012 7:52:08 PM
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Notice to Comply	Application No. 11/897,177	Applicant(s) ACHEAMPONG et al.	
	Examiner M.M. Cordero Garcia	Art Unit 1654	

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

Applicant must file the items indicated below within the time period set the Office action to which the Notice is attached to avoid abandonment under 35 U.S.C. § 133 (extensions of time may be obtained under the provisions of 37 CFR 1.136(a)).

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

☒ 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). If the effective filing date is on or after July 1, 1998, see the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998).

☐ 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).

☐ 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).

☐ 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."

☐ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).

☐ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable from of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).

☒ 7. Other: Specifically, the amino acid sequences presented in the specification, e.g., pages 12-13 (Formulas I-III) require sequence identifiers.

Applicant Must Provide:

☒ An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".

☒ An initial or substitute paper copy of the "Sequence Listing".

☒ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (571) 272-0731 or (571) 272-0951
For CRF Submission Help, call (571) 272-2510
PatentIn Software Program Support
Technical Assistance.1-866-217-9197 or 703-305-3028 or 571-272-6845
PatentIn Software is Available At www.USPTO.gov

PLEASE RETURN A COPY OF THIS NOTICE WITH YOUR REPLY

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Acheampong et al	Examiner: Marcela M. Cordero Garcia
Serial No.: 11/897,177	Group Art Unit: 1654
Filed: August 28, 2007	Confirmation No.: 3860
For: METHODS OF PROVIDING THERAPEUTIC EFFECTS USING CYCLOSPORIN COMPONENTS	Customer No.: 051957

Response

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

Dear Sir:

The Applicants respond to the Office action of February 17, 2012 (the "Office action") with the claim amendments beginning at page 2, and the remarks that follow at page 5.

CLAIMS

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

1. (Currently amended) A method of treating or preventing corneal graft rejection, the method comprising administering to an eye of a human or animal, at a frequency ~~selected from the group consisting of once, twice, or three times a day~~ of once per day, a composition in the form of an emulsion comprising water, a hydrophobic component, and a cyclosporin component in a therapeutically effective amount equal to or less than 0.05% by weight of the composition, wherein the weight ratio of the cyclosporin component to the hydrophobic component is less than 0.08.

2. – 3. (Canceled)

4. (Previously presented) The method of claim 1 wherein the blood of the human or animal has no detectable concentration of the cyclosporin component.

5. (Previously presented) 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 chromatographylmass spectrometry analytical method.

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

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

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

10. (Original) 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. (Original) The method of claim 1 wherein the hydrophobic component comprises an oily material.

12. (Original) 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. (Original) The method of claim 1 wherein the hydrophobic component comprises castor oil.

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

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

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

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

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

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

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

21. – 36. (Canceled).

37. (Previously presented) The method of claim 1, where the cyclosporin component is in a therapeutically effective amount of less than 0.05% by weight of the composition.

38. (New) The method of claim 1, wherein the cyclosporin component is in a therapeutically effective amount of 0.05% by weight of the composition.

39. – 41. (Canceled).

REMARKS

The applicants have amended claim 1 by deleting claim limitations; hence, no new matter has been added.

The Office rejected claims 1, 4-20, and 37 under 35 U.S.C. § 103(a) arguing that the claims are obvious in view of the Ding reference (US 5,474,979) when combined with the Kaswan reference (US 5,411,952) and the Hunter reference. The claims, as amended, are directed to a method of treating or preventing corneal graft rejection, the method comprising administering to an eye of a human or animal, at a frequency of once per day, a composition in the form of an emulsion comprising water, a hydrophobic component, and a cyclosporin component in a therapeutically effective amount equal to or less than 0.05% by weight of the composition, wherein the weight ratio of the cyclosporin component to the hydrophobic component is less than 0.08. The applicants respectfully submit that the cited references do not teach or suggest such a method. They respectfully request that the Office therefore withdraw the § 103 rejection.

The double patenting rejection

The Office rejected claims 1, 4-20, and 37 for nonstatutory obviousness-type double patenting, arguing that the claims are obvious over claims 1-8 of the Ding reference in view of the Kaswan reference. For the reasons the applicants state above, the Kaswan reference gives one of skill in the art no reason to believe that one could use cyclosporin, administered in the doses claimed here, to effectively prevent corneal graft rejection. The applicants respectfully request, therefore, that the Office withdraw the double patenting rejection.

Sequence compliance

The Office states that the specification recites one or more amino acid sequences, and therefore requires that the applicants amend the claims and specification to comply with the sequence rules of 37 C.F.R. §§ 1.821 – 1.825. The applicants respectfully submit that the Office is in error: the specification does not

recite any amino acid sequences. The compounds of formulas 1-3 are not amino acid sequences within the meaning of those rules. They are cyclic peptides – it is not possible to represent such compounds as a linear sequence of amino acids (indeed, the Office has never treated cyclosporin as a amino acid subject to the sequence rules). For this reason, the applicants respectfully request that the Office withdraw the requirement.

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,

/JOEL B. GERMAN/

Date: August 17, 2012

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Electronic Patent Application Fee Transmittal

Application Number:	11897177
Filing Date:	28-Aug-2007
Title of Invention:	Methods of providing therapeutic effects using cyclosporin components
First Named Inventor/Applicant Name:	Andrew Acheampong
Filer:	Joel B. German/Bonnie Ferguson
Attorney Docket Number:	17618CON (AP)

Filed as Large Entity

Utility under 35 USC 111(a) Filing Fees

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Basic Filing:				
Pages:				
Claims:				
Miscellaneous-Filing:				
Petition:				
Patent-Appeals-and-Interference:				
Post-Allowance-and-Post-Issuance:				
Extension-of-Time:				
Extension - 3 months with $0 paid	1253	1	1270	1270

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Miscellaneous:				
		Total in USD ($)		**1270**

Electronic Acknowledgement Receipt

EFS ID:	13522130
Application Number:	11897177
International Application Number:	
Confirmation Number:	3860
Title of Invention:	Methods of providing therapeutic effects using cyclosporin components
First Named Inventor/Applicant Name:	Andrew Acheampong
Customer Number:	51957
Filer:	Joel B. German/Bonnie Ferguson
Filer Authorized By:	Joel B. German
Attorney Docket Number:	17618CON (AP)
Receipt Date:	17-AUG-2012
Filing Date:	28-AUG-2007
Time Stamp:	12:49:33
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	Deposit Account
Payment was successfully received in RAM	$1270
RAM confirmation Number	9291
Deposit Account	010885
Authorized User	

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)

1	Amendment/Req. Reconsideration-After Non-Final Reject	17618Response081712toOfficeaction.pdf	56107 20e2254292c60e036374222c0e944bb88eec839c	no	6
Warnings:					
Information:					
2	Fee Worksheet (SB06)	fee-info.pdf	30370 7bca6e6ef96af9b9a4776575b6ba2b4129f78300	no	2
Warnings:					
Information:					
		Total Files Size (in bytes):	86477		

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.

<u>New Applications Under 35 U.S.C. 111</u>
If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

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

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

PTO/SB/06 (07-06)
Approved for use through 1/31/2007. 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	Filing Date	☐ To be Mailed
11/897,177	08/28/2007	

APPLICATION AS FILED – PART I

	(Column 1)	(Column 2)	SMALL ENTITY ☐		OR	OTHER THAN SMALL ENTITY	
FOR	NUMBER FILED	NUMBER EXTRA	RATE ($)	FEE ($)		RATE ($)	FEE ($)
☐ BASIC FEE (37 CFR 1.16(a), (b), or (c))	N/A	N/A	N/A			N/A	
☐ SEARCH FEE (37 CFR 1.16(k), (i), or (m))	N/A	N/A	N/A			N/A	
☐ EXAMINATION FEE (37 CFR 1.16(o), (p), or (q))	N/A	N/A	N/A			N/A	
TOTAL CLAIMS (37 CFR 1.16(i))	minus 20 =	*	X $ =		OR	X $ =	
INDEPENDENT CLAIMS (37 CFR 1.16(h))	minus 3 =	*	X $ =			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 $250 ($125 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			TOTAL	

APPLICATION AS AMENDED – PART II

AMENDMENT	08/17/2012	(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA	SMALL ENTITY RATE ($)	ADDITIONAL FEE ($)	OR	OTHER THAN SMALL ENTITY RATE ($)	ADDITIONAL FEE ($)
	Total (37 CFR 1.16(i))	* 20	Minus	** 37	= 0	X $ =		OR	X $60=	0
	Independent (37 CFR 1.16(h))	* 1	Minus	***3	= 0	X $ =		OR	X $250=	0
	☐ 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	0

AMENDMENT		(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA	RATE ($)	ADDITIONAL FEE ($)	OR	RATE ($)	ADDITIONAL FEE ($)
	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 number found in the appropriate box in column 1.

Legal Instrument Examiner:
/STELLA LITTLE/

UNITED STATES PATENT AND TRADEMARK OFFICE

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
11/897,177	08/28/2007	Andrew Acheampong	17618CON (AP)	3860

51957 7590 10/30/2012

ALLERGAN, INC.
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EXAMINER	
CORDERO GARCIA, MARCELA M	
ART UNIT	PAPER NUMBER
1654	

NOTIFICATION DATE	DELIVERY MODE
10/30/2012	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

Office Action Summary	Application No.	Applicant(s)	
	11/897,177	ACHEAMPONG ET AL.	
	Examiner	Art Unit	
	MARCELA M. CORDERO GARCIA	1654	

-- 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 *17 August 2012*.

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) *1,4-20,37 and 38* 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) *1,4-20,37 and 38* is/are rejected.

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

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

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).

12)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

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

a)☐ All b)☐ Some * c)☐ None of:

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) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. This Office Action is in response to the reply received on 8/17/2012.

Any objection and/or rejection from the previous office action, which is not restated here, is withdrawn. Examiner contacted Applicant's representative, Joel B. German, on 10/18/2012 to attempt to advance prosecution in this Application, however no follow up call was received in a timely manner, and therefore an Office Action is herein provided.

Status of the claims

2. Claims 1, 4-20, 37-38 are pending in the application. In the amendment dated 8/17/2012 claim 1 has been amended. Further, please note that claim 38 is identified as "new", however the claim was previously presented (11/17/2010). Appropriate correction is required. Claims 1, 4-20, 37-38 are presented for examination on the merits.

Claim Rejections - 35 USC § 103

3. 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.

4. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein

were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

5. Claims 1, 4-20 and 37-38 are rejected under 35 U.S.C. 103(a) as being obvious over Ding et al. (US 5,474,979 cited in the IDS of 11/14/07) in view of Kaswan (US 5,411,952) and Hunter et al. (Clin. Exp. Immunol., 1981, cited in the IDS dated 11/17/2010).

The Ding patent teaches nonirritating pharmaceutical compositions of cyclosporin with high comfort level and low irritation potential suitable for delivery to sensitive areas such as ocular tissues comprising cyclosporin in admixture with an emulsifying amount of a higher fatty acid glycerol and polysorbate 80. More particularly, the composition may comprise cyclosporin A and the higher fatty acid glyceride may comprise castor oil (e.g., col. 3) The compositions minimize the problems related to unpleasant sensation and syndrome exacerbation by reducing the oil content and dispersing the oil phase in water into an emulsion (col. 2, lines 55-67). In addition, the composition has stability for up to 9 months without crystallization of cyclosporin (e.g., abstract). The emulsions of Ding utilize higher fatty acid glycerides but in combination with polysorbate 80 which results in an emulsion with a high comfort level and low irritation potential suitable for delivery of medications to sensitive areas such as ocular tissues (col. 3, lines 1-5).

The Ding reference goes on to teach, preferably, the weight ratio of the castor oil to the polysorbate 80 is between about 0.3 to about 30, and a weight ratio of the cyclosporin to castor oil is below 0.16. More preferably, the weight ratio of castor oil to polysorbate 80 is between 0.5 and 12.5, and the weight ratio of cyclosporin to castor oil is between 0.12 and .02 (e.g., column 3). Additionally, Ding provides Examples 1-4 which further illustrate their invention (columns 4-5). It is clear that such compositions, including Examples 1A thru 1E (having as low as 0.05% of cyclosporin) were all intended as therapeutic compositions. Please note that Example 1D encompasses 0.10 % of cyclosporin and shows ocular bioavailability at a therapeutic level. (e.g., column 5, lines 15-25). Therefore, one skilled in the art at the time the invention was made would have concluded that there would be a reasonable expectation of success that a composition having slightly less than 0.10% cyclosporin (e.g., 0.05%) and slightly less than 0.08 cyclosporin/castor oil (e.g., 0.07) would still maintain therapeutic activity when topically applied to the eye, especially in light of the teachings of Ding describing preferred embodiments for nonirritating pharmaceutical compositions with high comfort level and low irritation potential suitable for delivery to sensitive areas such as ocular tissues with weight ratios of cyclosporin/castor oil more preferably between 0.12 and 0.02 (e.g., column 3, lines 15-20) and the teachings of claim 8 of Ding et all. which encompass pharmaceutical emulsions for topical application encompassing 0.05% cyclosporin or more (which reads upon the instantly claimed “equal to or less than 0.05% of cyclosporin”) and as low as 0.02 ratio of cyclosporin to castor oil (which reads upon the instantly claimed "less than 0.08" weight ratio of cyclosporin/castor oil).

Ding et al. do not expressly teach treating or preventing "corneal graft rejection" with their cyclosporin compositions. However, at the time the invention was made, it was known to use cyclosporin to treat corneal transplantation. For example, Kaswan discloses that cyclosporin was effective in the treatment of corneal graft transplantation. Kaswan teaches cyclosporin A compositions in corn oil comprising between 0.01% cyclosporin and saturation for topical ophthalmic use for treatment of immune disorders, to enhance or restore tear production and to enhance the normal healing of the surface of the eye in e.g., corneal transplantation (e.g., claims, cols. 1-2) Kaswan discloses several Examples and further, olive oil was also used and compared, and it was observed that the corn oil was favorable. The preferred topical ophthalmic formulation consisted of 2% cyclosporin, 1 mole % alpha tocopherol and 0.005% methyl paraben. However, Kaswan discloses that cyclosporin solutions can be prepared of between approximately 0.01% by weight of cyclosporin and saturation.

Furthermore, Hunter et al. also disclose that corneal graft survival in rabbits was significantly ($P<0.001$) prolonged by topical treatment to the recipient eye with cyclosporin A 1% in arachis oil applied five times daily for 4 weeks. No graft was rejected whilst treatment was maintained but all grafts subsequently underwent rejection by the 64th postoperative day. All animals in a simultaneous control group in this fully masked study developed allograft reactions by the 23rd day. No local or systemic side-effects attributable to cyclosporin A were observed (e.g., abstract, pages 174-175).

Hunter et al. go on to teach that corneal graft rejection still remains the main limitation to the application of corneal grafting, and is a leading cause of failure of

corneal grafts. A safe method of ocular immunosuppression that is more effective than the current very prolonged topical administration of corticosteroids could thus provide a major advance in the treatment of blindness from corneal disease. This is especially the case in those parts of the world where lack of skilled postoperative supervision makes such operations of little use because of the problems of monitoring and treating patients for subsequent rejection. The ability of topically applied CyA to inhibit corneal graft rejection in a rabbit model, which is a much closer analogue of the clinical situation in man than previous models, means that there may be an important role for topically administered CyA. Furthermore, these observations indicate that at least a substantial proportion of the events in sensitization induced by corneal transplantation that can be inhibited by CyA occur locally in the ocular tissue. This strengthens the concept of the eye as an immunologically competent organ (e.g., page 176).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to utilize, e.g., the pharmaceutical compositions of Ding et al. to treat or prevent corneal transplantation rejection. One of ordinary skill in the art at the time the invention was made would have been motivated to do so in order to decrease irritation in the eyes and decrease systemic side effects. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success since cyclosporin A was known to be an active agent with immunosuppressive activity in the healing of cornea including allografts as taught by Kaswan and by Hunter et al. With respect to the limitations claimed: Ding et al. teach 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 cyclosporin component in a therapeutically effective amount equal to or less than 0.05% by weight, the weight ratio of the cyclosporin component (cyclosporin A, e.g., Example 1D and column 3, lines 30-37) to the hydrophobic component (castor oil, a vegetable oil) is 0.08 (see, e.g., Example 1D). Ding et al. also teach embodiment 1B which has 0.2% of cyclosporin and a 0.04 ratio of cyclosporin/castor oil. Additionally, embodiment 1E has 0.05% of cyclosporin A and 0.08 ratio cyclosporin/castor oil. Ding et al. do teach that an embodiment having both less than 0.1 % of cyclosporin and wherein the weight ratio of the cyclosporin component to the hydrophobic component can be less than 0.08 (0.12 to 0.02). In addition, Ding et al. teach in claim 8 a pharmaceutical emulsion consisting of between about 0.05% and about 0.40% by weight cyclosporin A (which reads upon the limitation “less than 0.1 % by weight cyclosporin A” of instant claim 1) and between 0.625 and about 5.0 % castor oil. The corresponding lower and upper rations for the range is 0.05%/5.0% = 0.01 weight ratio of cyclosporin A/castor oil, which reads upon the limitation in claim 1 “the weight ratio of the cyclosporin A to the castor oil being less than 0.08”. The limitation of claim 4: “wherein the blood of the human or animal has substantially no detectable concentration of cyclosporin component” and of claim 5: ”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" and the limitation of claim 6: “0.1 ng/mL or less” necessarily read upon the method of Ding et al. since it teaches overlapping

steps/concentrations. The limitation of claims 7-8: “cyclosporin A" is taught, e.g., in Example 1. The limitation of claim 9: “wherein the cyclosporin component is solubilized in the hydrophobic component present in the composition" is taught in column 3, lines 21-23. The limitations of claim 10: “wherein the hydrophobic component is present in the composition in an amount greater than 0.625% by weight“, of claim 11: "oily material", of claim 12: "vegetable oils" and of claim 13: "castor oil" are taught, e.g., in Examples 1A-D which teach 5.00%, 2.5% and 1.25% of hydrophobic component (castor oil). The limitation of claim 14: “topically administering the composition to the eye" is taught, e.g., in column 5, lines 15-18 and claim 8 of Ding et al. The limitation of claim 15: “wherein the composition comprises an effective amount of an emulsifier component” is taught in column 3, lines 38-4 and 50-56. The limitations of claim 16-17: “tonicity" and "organic tonicity component" are taught in column 4, lines 12-19. The limitation of claim 18: “polyelectrolyte component in an amount effective in stabilizing the composition” is taught in column 3, lines 64-67 and column 4, lines 1-12. The limitation of claims 19-20 drawn to pH ranges of "of about 7.0 to about 8.0" and “of about 7.2 to about 7.6” are taught, e.g., in Example 1A-1E and in claim 8 of Ding et al. Furthermore, one of ordinary skill in the art would have been motivated to optimize the dosage and specifically the number of times the dosage is provided on a daily basis (e.g., once daily).

Ding et al. do not expressly teach an embodiment comprising both (at the same time) equal to or less than 0.05% of cyclosporin A and less than 0.08 cyclosporin A/castor oil ratio. The closest embodiments are 1D comprising 0.10% of cyclosporin A

and 0.08 cyclosporin A/castor oil ratio; **1E comprising equal to 0.05% of cyclosporin A and 0.08 cyclosporin A/castor oil ratio** and 1B comprising 0.20% cyclosporin A and 0.04 cyclosporin A/castor oil ratio. However, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the compositions of Ding et al. (such as 1E) by increasing the amount of castor oil or decreasing the cyclosporin concentration in order to reduce the ratio of the cyclosporin component to hydrophobic component from 0.08 to, e.g., 0.04 as taught by the ranges described in Ding et al. (see, e.g., column 3, lines 18-20) and exemplified in embodiment 1B. Further, it would have been obvious to one skilled in the art to use the beneficial compositions of Ding et al., which had low irritation level and contained the active agent for corneal allograft rejection prevention as taught by Kaswan and Hunter et al..

With respect to the ranges, the skilled artisan would have been motivated to do so because such proportions were encompassed by the Ding et al. patent. Please note that compositions with a higher amount of castor oil are encompassed by the Ding et al. claims (e.g., claim 8, embodiment 1B) optimizing the ratio of cyclosporin to hydrophobic components to below 0.08 was taught by Ding et al. in the range 0.02 to 0.12 (e.g., column 3, lines 18-20) and in embodiment 1B (which has 0.04). The adjustment of particular conventional working conditions (e.g., using all the ratios and proportions taught by Ding. et al. and Kaswan) is deemed merely a matter of judicious selection and routine optimization that is well within the purview of the skilled artisan. There is no evidence of criticality of these ranges: “[g]enerally, 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). As such, it would have been obvious to one skilled in the art at the time of invention to determine all optimum and operable conditions [e.g., formulation ranges and proportions such as the proportion of oils], because such conditions are art-recognized result-effective variables that are routinely determined and optimized in the art through routine experimentation. One would have had a reasonable expectation for success because such modifications are routinely determined and optimized in the art through routine experimentation and because of the guidance provided by Kaswan which spans the instantly claimed range of cyclosporin concentrations (see claims of Kaswan).

From the teaching of the references, 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.

Applicant's arguments

6. The Office rejected claims 1,4-20, and 37-38 under 35 U.S.C. § 103(a) arguing that the claims are obvious in view of the Ding reference (US 5,474,979) when combined with the Kaswan reference (US 5,411,952) and the Hunter reference. The claims, as amended, are directed to a method of treating or preventing corneal graft rejection, the method comprising administering to an eye of a human or animal, at a frequency of once per day, a composition in the form of an emulsion comprising water,

a hydrophobic component, and a cyclosporin component in a therapeutically effective amount equal to or less than 0.05% by weight of the composition, wherein the weight ratio of the cyclosporin component to the hydrophobic component is less than 0.08. The applicants respectfully submit that the cited references do not teach or suggest such a method. They respectfully request that the Office therefore withdraw the § 103 rejection.

Response to arguments

7. Applicant's arguments have been carefully considered but not deemed persuasive for the reasons of record and for the following reasons:

The Ding patent teaches nonirritating pharmaceutical compositions of cyclosporin with high comfort level and low irritation potential suitable for delivery to sensitive areas such as ocular tissues comprising cyclosporin in admixture with an emulsifying amount of a higher fatty acid glycerol and polysorbate 80. More particularly, the composition may comprise cyclosporin A and the higher fatty acid glyceride may comprise castor oil (e.g., col. 3) The compositions minimize the problems related to unpleasant sensation and syndrome exacerbation by reducing the oil content and dispersing the oil phase in water into an emulsion (col. 2, lines 55-67). In addition, the composition has stability for up to 9 months without crystallization of cyclosporin (e.g., abstract). The emulsions of Ding utilize higher fatty acid glycerides but in combination with polysorbate 80 which results in an emulsion with a high comfort level and low irritation potential suitable for delivery of medications to sensitive areas such as ocular tissues (col. 3, lines 1-5). The pharmaceutical compositions are not limited to a specific use (e.g., claims of Ding). The prior art (Kaswan and Hunter et al.) teach that cyclosporin is an active agent for the

prevention and treatment of corneal graft rejection and thus one of ordinary skill in the art would have been motivated to find an effective range for the nonirritating pharmaceutical compositions of Ding in the treatment of corneal graft rejection. It is noted again that “[g]enerally, 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. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation."” (See MPEP 2144.05). Further, even though Kaswan does not expressly teach using the compositions expressly for treating corneal graft rejection, it is also noted that Kaswan also teaches that the cyclosporin compositions may contain as low as 0.01 % of cyclosporin and that such compositions may be used for suppressing an immune disorder of the eye (e.g., claims of Kaswan) and that one of these disorders is treatment of corneal graft rejection (col.1). With regards to the examples presented in both Ding and Kaswan, it is noted that both references are drawn to pharmaceutical compositions and not limited to a specific application (beyond suppressing an immune disorder of the eye) and thus one of ordinary skill in the art at the time the invention was made would have been motivated to use such compositions for treating immune disorders of the eyes which were known in the art such as treating corneal graft rejections as taught both in Kaswan and in Hunter et al. Furthermore Applicant has not provided evidence of the criticality of the claimed ranges of molar proportions beyond the statement that the range of Kaswan spanned a vast number of concentrations and that no reason was provided for the use

of the lower range. However, it is noted that Kaswan and Ding teach ranges and thus provide the motivation to use the proportions within the whole taught ranges. Further, as set forth above, one of ordinary skill in the art would have been motivated to use the compositions of Ding et al. which were nonirritating pharmaceutical compositions of cyclosporin with high comfort level and low irritation potential suitable for delivery to sensitive areas such as ocular tissues comprising cyclosporin in admixture with an emulsifying amount of a higher fatty acid glycerol and polysorbate 80. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success given that Kaswan discloses ranges from 0.01 % to saturation of the active agent (cyclosporin A) in compositions for suppressing immune disorders in the eye (which encompass inhibition of corneal graft rejection as evidence by Kaswan and Hunter et al.).

From the teaching of the references, 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

8. 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

obviousness-type double patenting rejection is appropriate where the conflicting claims 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 conflicting 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.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

9. Claims 1, 4-20 and 37-38 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 (cited in the IDS of 11/14/07) in view of Kaswan (US 5,411,952) and Hunter et al. (Clin. Exp. Immunol., 1981, cited in the IDS dated 11/17/2010).

The Ding patent claims pharmaceutical compositions of cyclosporin. The compositions comprise the range from between about 0.05 to and about 0.40% of cyclosporin and castor oil in an amount between 0.625% to about 5.0%, which encompasses the range 0.01 to 0.64 cyclosporin/castor oil and therefore encompasses the instantly claimed range of equal or less than 0.05 and less than 0.08 (e.g., claim 7 of Ding). The pH is 7.2-7.6 as in claim 8 and are suitable for topical application to ocular tissue (claim 8 of Ding).

The Ding reference goes on to teach, preferably, the weight ratio of the castor oil to the polysorbate 80 is between about 0.3 to about 30, and a weight ratio of the cyclosporin to castor oil is below 0.16. More preferably, the weight ratio of castor oil to polysorbate 80 is between 0.5 and 12.5, and the weight ratio of cyclosporin to castor oil is between 0.12 and .02 (e.g., column 3).

Ding et al. do not expressly teach treating or preventing “corneal graft rejection” with their cyclosporin compositions. However, at the time the invention was made, it was known to use cyclosporin to treat corneal transplantation. For example, Kaswan discloses that cyclosporin was effective in the treatment of corneal graft transplantation. Kaswan teaches cyclosporin A compositions in corn oil comprising between 0.01% cyclosporin and saturation for topical ophthalmic use for treatment of immune disorders, to enhance or restore tear production and to enhance the normal healing of the surface of the eye in e.g., corneal transplantation (e.g., claims, cols. 1-2) Kaswan discloses several Examples and further, olive oil was also used and compared, and it was observed that the corn oil was favorable. The preferred topical ophthalmic formulation

consisted of 2% cyclosporin, 1 mole % alpha tocopherol and 0.005% methyl paraben. However, Kaswan discloses that cyclosporin solutions can be prepared of between approximately 0.01% by weight of cyclosporin and saturation.

Furthermore, Hunter et al. also disclose that corneal graft survival in rabbits was significantly ($P<0.001$) prolonged by topical treatment to the recipient eye with cyclosporin A 1% in arachis oil applied five times daily for 4 weeks. No graft was rejected whilst treatment was maintained but all grafts subsequently underwent rejection by the 64th postoperative day. All animals in a simultaneous control group in this fully masked study developed allograft reactions by the 23rd day. No local or systemic side-effects attributable to cyclosporin A were observed (e.g., abstract, pages 174-175).

Hunter et al. go on to teach that corneal graft rejection still remains the main limitation to the application of corneal grafting, and is a leading cause of failure of corneal grafts. A safe method of ocular immunosuppression that is more effective than the current very prolonged topical administration of corticosteroids could thus provide a major advance in the treatment of blindness from corneal disease. This is especially the case in those parts of the world where lack of skilled postoperative supervision makes such operations of little use because of the problems of monitoring and treating patients for subsequent rejection. The ability of topically applied CyA to inhibit corneal graft rejection in a rabbit model, which is a much closer analogue of the clinical situation in man than previous models, means that there may be an important role for topically administered CyA. Furthermore, these observations indicate that at least a substantial proportion of the events in sensitization induced by corneal transplantation that can be

inhibited by CyA occur locally in the ocular tissue. This strengthens the concept of the eye as an immunologically competent organ (e.g., page 176).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to utilize, e.g., the pharmaceutical compositions of Ding et al. to treat or prevent corneal transplantation rejection. One of ordinary skill in the art at the time the invention was made would have been motivated to do so in order to decrease irritation in the eyes and decrease systemic side effects. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success since cyclosporin A was known to be an active agent with immunosuppressive activity in the healing of cornea including allografts as taught by Kaswan and by Hunter et al. With respect to the limitations claimed: Ding et al. teach 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 cyclosporin component in a therapeutically effective amount equal to or less than 0.05% by weight, the weight ratio of the cyclosporin component (cyclosporin A, e.g., Example 1D and column 3, lines 30-37) to the hydrophobic component (castor oil, a vegetable oil) is 0.08 (see, e.g., Example 1D). Ding et al. also teach embodiment 1B which has 0.2% of cyclosporin and a 0.04 ratio of cyclosporin/castor oil. Additionally, embodiment 1E has 0.05% of cyclosporin A and 0.08 ratio cyclosporin/castor oil. Ding et al. do teach that an embodiment having both less than 0.1 % of cyclosporin and wherein the weight ratio of the cyclosporin component to the hydrophobic component can be less than 0.08 (0.12 to 0.02). In addition, Ding et al. teach in claim 8 a

pharmaceutical emulsion consisting of between about 0.05% and about 0.40% by weight cyclosporin A (which reads upon the limitation “less than 0.1 % by weight cyclosporin A” of instant claim 1) and between 0.625 and about 5.0 % castor oil. The corresponding lower and upper rations for the range is 0.05%/5.0% = 0.01 weight ratio of cyclosporin A/castor oil, which reads upon the limitation in claim 1 “the weight ratio of the cyclosporin A to the castor oil being less than 0.08”. The limitation of claim 4: “wherein the blood of the human or animal has substantially no detectable concentration of cyclosporin component” and of claim 5: ”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" and the limitation of claim 6: “0.1 mg/mL or less” necessarily read upon the method of Ding et al. since it teaches overlapping steps/concentrations. The limitation of claims 7-8: “cyclosporin A" is taught, e.g., in Example 1. The limitation of claim 9: “wherein the cyclosporin component is solubilized in the hydrophobic component present in the composition" is taught in column 3, lines 21-23. The limitations of claim 10: “wherein the hydrophobic component is present in the composition in an amount greater than 0.625% by weight“, of claim 11: "oily material", of claim 12: "vegetable oils" and of claim 13: "castor oil" are taught, e.g., in Examples 1A-D which teach 5.00%, 2.5% and 1.25% of hydrophobic component (castor oil). The limitation of claim 14: “topically administering the composition to the eye" is taught, e.g., in column 5, lines 15-18 and claim 8 of Ding et al. The limitation of claim 15: “wherein the composition comprises an effective amount of an emulsifier

component" is taught in column 3, lines 38-4 and 50-56. The limitations of claim 16-17: "tonicity" and "organic tonicity component" are taught in column 4, lines 12-19. The limitation of claim 18: "polyelectrolyte component in an amount effective in stabilizing the composition" is taught in column 3, lines 64-67 and column 4, lines 1-12. The limitation of claims 19-20 drawn to pH ranges of "of about 7.0 to about 8.0" and "of about 7.2 to about 7.6" are taught, e.g., in Example 1A-1E and in claim 8 of Ding et al. Furthermore, one of ordinary skill in the art would have been motivated to optimize the dosage and specifically the number of times the dosage is provided on a daily basis (e.g., once a day).

Ding et al. do not expressly teach an embodiment comprising both (at the same time) equal to or less than 0.05% of cyclosporin A and less than 0.08 cyclosporin A/castor oil ratio. The closest embodiments are 1D comprising 0.10% of cyclosporin A and 0.08 cyclosporin A/castor oil ratio; **1E comprising equal to 0.05% of cyclosporin A and 0.08 cyclosporin A/castor oil ratio** and 1B comprising 0.20% cyclosporin A and 0.04 cyclosporin A/castor oil ratio. However, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the compositions of Ding et al. (such as 1E) by increasing the amount of castor oil or decreasing the cyclosporin concentration in order to reduce the ratio of the cyclosporin component to hydrophobic component from 0.08 to, e.g., 0.04 as taught by the ranges described in Ding et al. (see, e.g., column 3, lines 18-20) and exemplified in embodiment 1B. Further, it would have been obvious to one skilled in the art to use the beneficial

compositions of Ding et al., which had low irritation level and contained the active agent for corneal allograft rejection prevention as taught by Kaswan and Hunter et al..

With respect to the range of cyclosporin to hydrophobic component, the skilled artisan would have been motivated to do so because such proportions were encompassed by the Ding et al. patent. Please note that compositions with a higher amount of castor oil are encompassed by the Ding et al. claims (e.g., claim 8, embodiment 1B) optimizing the ratio of cyclosporin to hydrophobic components to below 0.08 was taught by Ding et al. in the range 0.02 to 0.12 (e.g., column 3, lines 18-20) and in embodiment 1B (which has 0.04). The adjustment of particular conventional working conditions (e.g., using all the ratios and proportions taught by Ding. et al. and Kaswan) is deemed merely a matter of judicious selection and routine optimization that is well within the purview of the skilled artisan. There is no evidence of criticality of these ranges: “[g]enerally, 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). As such, it would have been obvious to one skilled in the art at the time of invention to determine all optimum and operable conditions [e.g., formulation ranges and proportions such as the proportion of oils], because such conditions are art-recognized result-effective variables that are routinely determined and optimized in the art through routine experimentation. One would have had a reasonable expectation for success because such modifications are routinely determined and optimized in the art through routine

experimentation and because of the guidance provided by Kaswan which spans the instantly claimed range of cyclosporin concentrations (see claims of Kaswan et al.).

From the teaching of the references, 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.

Applicant's arguments

10. The Office rejected claims 1, 4-20, and 37 for nonstatutory obviousness-type double patenting, arguing that the claims are obvious over claims 1-8 of the Ding reference in view of the Kaswan reference. For the reasons the applicants state above, the Kaswan reference gives one of skill in the art no reason to believe that one could use cyclosporin, administered in the doses claimed here, to effectively prevent corneal graft rejection° The applicants respectfully request, therefore, that the Office withdraw the double patenting rejection.

Response to arguments

11. Applicant's arguments have been carefully considered but not deemed persuasive for the reasons of record, for the reasons set forth in paragraph 7.

Specification / Trademarks

12. The use of the trademarks, e.g., Pemulen® (page 20) Purite®, Bio-Cide®, Anthium Dioxide® (page 24) Premulen® (page 26) has been noted in this application.

It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Conclusion

13. No claim is currently allowed.

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

14. THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

15. 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, Cecilia J. Tsang can be reached on (571) 272-0562. 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 1654

MMCG 10/2012

Search Notes	Application/Control No.	Applicant(s)/Patent Under Reexamination
	11897177	ACHEAMPONG ET AL.
	Examiner	Art Unit
	MARCELA M CORDERO GARCIA	1654

SEARCHED

Class	Subclass	Date	Examiner
none	none	12/01/08	MMCG

SEARCH NOTES

Search Notes	Date	Examiner
updated	12/01/08	MMCG
STN searched by STIC (available via SCORE / PAIR)	4/14/08	MMCG
STN searched by STIC (available via SCORE / PAIR)	6/25/09	MMCG
EAST searched (attached)	8/16/09	MMCG
internet search (google.com) terms: restasis, dry eye, vernal conjunctivitis, atopic keratoconjunctivitis, cyclosporin	8/14/09	MMCG
STN searched by STIC (available via SCORE / PAIR)	4/26/10	MMCG
EAST searched (attached)	6/18/10	MMCG
also updated PALM Inventor search	6/18/10	MMCG
internet search (google.com) terms: restasis, corneal or cornea, graft, allograft, transplant, rejection	6/18/10	MMCG
EAST updated (attached)	02/13/2012	MMCG
also updated PALM Inventor search	02/13/2012	MMCG
EAST search (updated)	10/20/2012	MMCG
also ran PALM Inventor search	10/20/2012	MMCG

INTERFERENCE SEARCH

Class	Subclass	Date	Examiner
EAST search			

EAST Search History

EAST Search History (Prior Art)

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	3682	(corneal or cornea) near3 graft near3 rejection	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	ADJ	ON	2012/10/20 19:36
L2	13	(corneal or cornea) near3 graft near3 rejection same (cyclosporin)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	ADJ	ON	2012/10/20 19:36

EAST Search History (Interference)

<This search history is empty>

10/20/2012 7:37:35 PM
C:\Users\mgarcia\Documents\EAST\Workspaces\1166940-b.wsp

PTO/SB/30EFS (07-09)
Approved for use through 07/31/2012. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

REQUEST FOR CONTINUED EXAMINATION(RCE)TRANSMITTAL
(Submitted Only via EFS-Web)

Application Number	11/897,177	Filing Date	2007-08-28	Docket Number (if applicable)	17618CON(AP)	Art Unit	1654
First Named Inventor	Andrew Acheampong			Examiner Name	Marcela M. Cordero Garcia		

This is a Request for Continued Examination (RCE) under 37 CFR 1.114 of the above-identified application.
Request for Continued Examination (RCE) practice under 37 CFR 1.114 does not apply to any utility or plant application filed prior to June 8, 1995, or to any design application. The Instruction Sheet for this form is located at WWW.USPTO.GOV

SUBMISSION REQUIRED UNDER 37 CFR 1.114

Note: If the RCE is proper, any previously filed unentered amendments and amendments enclosed with the RCE will be entered in the order in which they were filed unless applicant instructs otherwise. If applicant does not wish to have any previously filed unentered amendment(s) entered, applicant must request non-entry of such amendment(s).

☐ Previously submitted. If a final Office action is outstanding, any amendments filed after the final Office action may be considered as a submission even if this box is not checked.

- ☐ Consider the arguments in the Appeal Brief or Reply Brief previously filed on _____
- ☐ Other _____

☒ Enclosed

- ☒ Amendment/Reply
- ☐ Information Disclosure Statement (IDS)
- ☐ Affidavit(s)/ Declaration(s)
- ☐ Other _____

MISCELLANEOUS

☐ Suspension of action on the above-identified application is requested under 37 CFR 1.103(c) for a period of months _____
(Period of suspension shall not exceed 3 months; Fee under 37 CFR 1.17(i) required)

☐ Other _____

FEES

☒ **The RCE fee under 37 CFR 1.17(e) is required by 37 CFR 1.114 when the RCE is filed.**
The Director is hereby authorized to charge any underpayment of fees, or credit any overpayments, to Deposit Account No 010885

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT REQUIRED

☒ Patent Practitioner Signature

☐ Applicant Signature

PTO/SB/30EFS (07-09)
Approved for use through 07/31/2012. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Signature of Registered U.S. Patent Practitioner			
Signature	/Laura L. Wine/	Date (YYYY-MM-DD)	2013-04-01
Name	Laura L. Wine	Registration Number	68681

This collection of information is required by 37 CFR 1.114. 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 12 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.

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

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.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Andrew Acheampong, *et al.*	Examiner: Marcela M. Cordero Garcia
Serial No.: 11/897,177	Art Unit: 1654
Filed: August 28, 2007	Confirmation No.: 3860
For: METHODS OF PROVIDING THERAPEUTIC EFFECTS USING CYCLOSPORIN COMPONENTS	Docket No.: 17618CON(AP)

RESPONSE TO FINAL OFFICE ACTION MAILED OCTOBER 30, 2012

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

Dear Sir:

These papers are filed in reply to the Final Office Action mailed October 30, 2012.

The Commissioner is authorized to charge any fee which may be required in connection with this Amendment to deposit account No. 01-0885.

Amendments to the Claims begin at page 2 of this paper.

Remarks begin on page 5 of this paper.

AMENDMENTS TO THE CLAIMS

This list of claims will replace all prior versions of claims presented in this application.

1. (Previously presented) A method of treating or preventing corneal graft rejection, the method comprising administering to an eye of a human or animal, at a frequency of once per day, a composition in the form of an emulsion comprising water, a hydrophobic component, and a cyclosporin component in a therapeutically effective amount equal to or less than 0.05% by weight of the composition, wherein the weight ratio of the cyclosporin component to the hydrophobic component is less than 0.08.

2. – 3. (Canceled)

4. (Previously presented) The method of claim 1 wherein the blood of the human or animal has no detectable concentration of the cyclosporin component.

5. (Previously presented) 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 chromatographylmass spectrometry analytical method.

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

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

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

10. (Original) 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. (Original) The method of claim 1 wherein the hydrophobic component comprises an oily material.

12. (Original) 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. (Original) The method of claim 1 wherein the hydrophobic component comprises castor oil.

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

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

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

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

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

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

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

21. – 36. (Canceled).

37. (Previously presented) The method of claim 1, where the cyclosporin component is in a therapeutically effective amount of less than 0.05% by weight of the composition.

38. (Previously presented) The method of claim 1, wherein the cyclosporin component is in a therapeutically effective amount of 0.05% by weight of the composition.

39. – 41. (Canceled).

REMARKS

This Reply responds to the Office Action sent October 30, 2012, in which the Office Action rejected Claims 1, 4-20 and 37-38. The Applicants respectfully submit that the claims are in condition for allowance.

Claim Rejections

35 U.S.C. § 103(a)

Claims 1, 4-20 and 37-38 were rejected under 35 U.S.C. § 103(a) as being obvious over "Ding" (US 5474979) in view of "Kaswan" (US 5411952) and "Hunter" (Clin. Exp. Immunol., 1981).

The Applicants submit that neither Ding nor Kaswan nor Hunter teach or render obvious all elements of Claim 1. Specifically, neither Ding nor Kaswan nor Hunter teach, at least, "A method of treating or preventing corneal graft rejection, the method comprising administering to an eye of a human or animal, at a frequency of **once a day**, a composition in the form of an emulsion comprising (…) **a cyclosporin component** in a therapeutically effective amount **equal to or less than 0.05% by weight** of the composition (…)."

None of the cited references disclose both treating patients with a cyclosporin component in a therapeutically effective amount equal to or less than 0.05% by weight at a frequency of once a day. Instead, for example, Ding discloses compositions with a weight percentage of cyclosporin between 0.05% - 0.40% administered eight times a day for seven days. *See* Ding at col. 4, lines 31-44 and col. 5, lines 14-17.

The October 30, 2012 Office Action at page 8, stated that one or ordinary skill in the art would have been motivated to optimize the dosage and specifically the number of times the dosage (in Ding) is provided on a daily basis. The Supreme Court, quoting *In re Kahn*, 441 F.3d 977, 988, 78 USPQ2d 1329, 1336 (Fed. Cir. 2006), stated that "[R]ejections on obviousness cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness." See MPEP § 2141, subsection III. The Applicant submit that no such articulated reasoning or rational underpinning was stated

with respect to the once a day element of Claim 1. Thus, the Applicants request that the rejection be withdrawn.

Moreover, the Applicants submit that one of skill in the art at the time the invention was made would not have reduced their frequency of administration of the compositions disclosed in Ding from eight times a day down to once a day. There is no teaching or suggestion in the reference that such a modification would have a reasonable expectation of success. Rather, notably, Ding discloses that therapeutic levels of cyclosporine were reached after dosage of the Example compositions 1A-1D, which included between 0.10 – 0.40 wt% cyclosporin (higher than the currently claimed range). *See* Ding at col. 5, lines 15-23. The Applicants submit that one of skill would not be motivated to decrease both the concentration of cyclosporin and the frequency of dosage in Ding, as such a modification may not reach therapeutic levels required for successful treatment with the drug.

Claims 4-20 and 37-38

As described above, amended Claim 1 is patentable over Ding in view of Kaswan and Hunter. Claims 4-20 and 37-38 depend directly or indirectly from Claim 1, and thus include all of the features of Claim 1 and recite combinations of the features not taught or suggested by the cited references. Claims 4-20 and 37-38 are patentable for at least the same reasons as Claim 1 and on their own merit. Thus, the Applicants respectfully request that the Examiner withdraw the rejections of Claims 4-20 and 37-38.

Double Patenting

Pending Claims 1, 4-20, and 37-38 also stand rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-8 of Ding in view of Kaswan and Hunter.

The Applicants submit that the obviousness-type double patenting rejection is improper. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims 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 claims. MPEP § 804. The Applicants submit that the claims of the current

application are patentably distinct from the reference claims of Ding, at least, because the claims of the present application recite additional, non-obvious elements not found in the reference claims of Ding.

For example, independent claim 1 of the present application claim a method of treating or preventing corneal graft rejection, the method including administering a composition to an eye of a human or animal at a frequency of once per day. The cited pending claims of Ding claim a pharmaceutical composition. None of the cited pending claims of Ding claim a method of treating or preventing corneal graft rejection, let alone administration of a cyclosporin-containing composition once a day. Modification of the claims of Ding to include once-daily administration would have also been improper for similar reasons as argued above. The Applicants would also like to note that any reference in the Office Action to the contents of the Ding specification as prior art in the double patenting rejection, outside of the definition of claim terms is improper. See MPEP § 804(II)(B)(1) ("When considering whether the invention defined in a claim of an application would have been an obvious variation of the invention defined in the claim of a patent, the disclosure of the patent may not be used as prior art. *General Foods Corp. v. Studiengesellschaft Kohle mbH*, 972 F.2d 1272, 1279, 23 USPQ2d 1839, 1846 (Fed. Cir. 1992)."

Therefore, at least for the reasons stated above, Claim 1 and those claims dependent thereon (i.e. Claims 4-20 and 37-38) are patentably distinct because they are not anticipated by, nor would they have been obvious in view of pending Claims 1-8 of Ding in view of Kaswan and Hunter.

The Applicants request that the rejections be withdrawn, and the Applicants submit that the claims are in condition for allowance.

Respectfully submitted,

Date: April 1, 2013

/Laura L. Wine/

Laura L. Wine
Registration Number 68,681

ALLERGAN
LEGAL DEPARTMENT
2525 Dupont Drive
Irvine, California 92612-1599 Tel: 714/246-6996 Fax: 714/246-4249

Electronic Patent Application Fee Transmittal

Application Number:	11897177
Filing Date:	28-Aug-2007
Title of Invention:	Methods of providing therapeutic effects using cyclosporin components
First Named Inventor/Applicant Name:	Andrew Acheampong
Filer:	Laura Lee Wine/Bonnie Ferguson
Attorney Docket Number:	17618CON (AP)

Filed as Large Entity

Utility under 35 USC 111(a) Filing Fees

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Basic Filing:				
Pages:				
Claims:				
Miscellaneous-Filing:				
Petition:				
Patent-Appeals-and-Interference:				
Post-Allowance-and-Post-Issuance:				
Extension-of-Time:				
Extension - 2 months with $0 paid	1252	1	600	600

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Miscellaneous:				
Request for Continued Examination	1801	1	1200	1200
		Total in USD ($)		**1800**

Electronic Acknowledgement Receipt

EFS ID:	15402677
Application Number:	11897177
International Application Number:	
Confirmation Number:	3860
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/Bonnie Ferguson
Filer Authorized By:	Laura Lee Wine
Attorney Docket Number:	17618CON (AP)
Receipt Date:	01-APR-2013
Filing Date:	28-AUG-2007
Time Stamp:	16:56:05
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	Deposit Account
Payment was successfully received in RAM	$1800
RAM confirmation Number	3540
Deposit Account	010885
Authorized User	

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)

1	Request for Continued Examination (RCE)	RCE-TRANS-17618CON-Laura.pdf	697965 d91bf576a3948516622df709ffe0d494a3c23dcc	no	3
Warnings:					
Information:					
2	Amendment Submitted/Entered with Filing of CPA/RCE	17618CONResp-toFinalOA-4-1-13.pdf	91853 ead51919371102d49397ad0430be7759968ac18a	no	7
Warnings:					
Information:					
3	Fee Worksheet (SB06)	fee-info.pdf	32031 bb10b39b124fbe9c4ac9de4d29c4c70b04eb8dfa	no	2
Warnings:					
Information:					
		Total Files Size (in bytes):	821849		

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.

<u>New Applications Under 35 U.S.C. 111</u>
If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

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

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

PTO/SB/06 (07-06)
Approved for use through 1/31/2007. OMB 0651-0032
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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	Filing Date	☒ To be Mailed
11/897,177	08/28/2007	

APPLICATION AS FILED – PART I

	(Column 1)	(Column 2)	SMALL ENTITY ☐		OR	OTHER THAN SMALL ENTITY	
FOR	NUMBER FILED	NUMBER EXTRA	RATE ($)	FEE ($)		RATE ($)	FEE ($)
☐ BASIC FEE (37 CFR 1.16(a), (b), or (c))	N/A	N/A	N/A			N/A	
☐ SEARCH FEE (37 CFR 1.16(k), (i), or (m))	N/A	N/A	N/A			N/A	
☐ EXAMINATION FEE (37 CFR 1.16(o), (p), or (q))	N/A	N/A	N/A			N/A	
TOTAL CLAIMS (37 CFR 1.16(i))	minus 20 =	*	X $ =		OR	X $ =	
INDEPENDENT CLAIMS (37 CFR 1.16(h))	minus 3 =	*	X $ =			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 $250 ($125 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			TOTAL	

APPLICATION AS AMENDED – PART II

AMENDMENT	04/01/2013	(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA	SMALL ENTITY RATE ($)	ADDITIONAL FEE ($)	OR	OTHER THAN SMALL ENTITY RATE ($)	ADDITIONAL FEE ($)
	Total (37 CFR 1.16(i))	* 20	Minus	** 37	= 0	X $ =		OR	X $80=	0
	Independent (37 CFR 1.16(h))	* 1	Minus	***3	= 0	X $ =		OR	X $420=	0
	☐ 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	0

AMENDMENT		(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA	RATE ($)	ADDITIONAL FEE ($)	OR	RATE ($)	ADDITIONAL FEE ($)
	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 number found in the appropriate box in column 1.

Legal Instrument Examiner:
/ANGELA JOHNSON/

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
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Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
11/897,177	08/28/2007	Andrew Acheampong	17618CON (AP)	3860

51957 7590 04/08/2013

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
04/08/2013	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

Office Action Summary	Application No. 11/897,177	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 *1 April 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) *1,4-20,37 and 38* 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) *1,4-20,37 and 38* 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.

Interim copies:

a)☐ All b)☐ Some c)☐ None of the: Interim copies of the priority documents have been received.

Attachment(s)

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

2) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.

3) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .

4) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 4/1/2013 has been entered.

Any objection or rejection from the previous office action, which is not restated here, is withdrawn.

Status of the claims

2. Claims 1, 4-20, 37-38 are pending in the application. Appropriate correction is required. Claims 1, 4-20, 37-38 are presented for examination on the merits.

Claim Rejections - 35 USC § 103

3. 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.

4. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any

inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim Rejections - 35 USC § 103

5. 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.

6. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 1, 4-20 and 37-38 are rejected under 35 U.S.C. 103(a) as being obvious over Kawashima et al. (US 6,582,718) in view of Ding et al. (US 5,474,979 cited in the IDS of 11/14/07).

Kawashima et al. discloses that effective topical administration of cyclosporin A to the eye would reduce or eliminate to a large extent the systemic side effects by restricting activity to the locus of the condition being treated and proposals to this effect have been made. Kawashima et al. teach that utility and effectiveness of cyclosporin A in treating diseases and conditions of the eye has been hindered until now by the lack of suitable eye-drops which are acceptable to the eye. Eye-drops are required which do not cause patient discomfort and which permit a convenient administration regimen and do not require unduly frequent administration, while providing adequate drug substance delivery both to the external and, in particular, the internal regions of the eye. A further difficulty is the very poor solubility of cyclosporin A in water. This leads often to precipitation of cyclosporin A from aqueous-based eye-drops causing strong irritation of the eye.

Kawashima et al. teach that the ophthalmic compositions are useful for the same indications as other topical ophthalmic compositions containing cyclosporins, for example diseases affecting the cornea, the aqueous, the lens, the iris, the ciliary, the choroid or the retina. The ophthalmic compositions are useful particularly for the treatment of an autoimmune or inflammatory disease or condition of the eye or of the surrounding or associated organs or tissues, that has undesirably elevated immuno-response or inflammatory reaction or event as

part of its etiology. The ophthalmic compositions are useful preferably for treating the anterior or posterior segment of the eye. For example for the treatment of anterior or posteior uveitis, chronic keratitis, keratoconjunctivitis sicca, vernal keratoconjunctivitis, conjunctivitis, including vernal conjunctivitis, or in keratoplasty. The ophthalmic compositions may also be used in the treatment of immunoreactive graft rejection post corneal transplantation, Behcet disease, and autoimmune corneal diseases such as Mooren's ulcer, ocular pemphigus, and rheumatoid ulcer ([0014]).

Kawashima et al. teach that the utility of the ophthalmic compositions and advantageous therapeutic properties can be observed in standard animal models and in standard clinical tests; for example by administering, a few times a day, 0.05 ml to 0.5 ml, preferably 0.1 ml to 0.2 ml, of an ophthalmic composition containing 0.005% to 1.0%, preferably 0.01% to 0.5%, (by weight) of cyclosporin to the eyes of patients exhibiting diseases or conditions of the eye as set forth above. .

The optimal dosage to be administered to a particular patient will vary from patient to patient and from disease to disease and must be considered carefully by the treating physician. However doses in the range of 0.05 ml to 0.5 ml, preferably 0.1 ml to 0.2 ml, of an ophthalmic composition containing 0.005% to 1.0%, preferably 0.01% to 0.5%, (by weight) of cyclosporin may be used. Satisfactory results are obtained by administering droplets of about 0.05 ml a few times a day; for example 1 to 5 times a day ([0015]).

Kawashima et al. do not expressly teach emulsions wherein the ratio of cyclosporin component to the hydrophobic component is than 0.08.

The Ding patent teaches nonirritating pharmaceutical emulsions of cyclosporin with high comfort level and low irritation potential suitable for delivery to sensitive areas such as ocular tissues comprising cyclosporin in admixture with an emulsifying amount of a higher fatty acid glycerol and polysorbate 80. More particularly, the composition may comprise cyclosporin A and the higher fatty acid glyceride may comprise castor oil (e.g., col. 3) The compositions minimize the problems related to unpleasant sensation and syndrome exacerbation by reducing the oil content and dispersing the oil phase in water into an emulsion (col. 2, lines 55-67). In addition, the composition has stability for up to 9 months without crystallization of cyclosporin (e.g., abstract). The emulsions of Ding utilize higher fatty acid glycerides but in combination with polysorbate 80 which results in an emulsion with a high comfort level and low irritation potential suitable for delivery of medications to sensitive areas such as ocular tissues (col. 3, lines 1-5).

The Ding reference goes on to teach a weight ratio of the cyclosporin component to the hydrophobic component (castor oil) below 0.16. More preferably the weight ratio of cyclosporin component to hydrophobic component is between 0.12 and .02 (e.g., column 3). Additionally, Ding provides Examples 1-4 which further illustrate their invention (columns 4-5). It is clear that such compositions, including Examples 1A thru 1E (having as low as 0.05% of cyclosporin) were all intended as therapeutic compositions. Please note that

Example 1D encompasses 0.10 % of cyclosporin and shows ocular bioavailability at a therapeutic level. (e.g., column 5, lines 15-25).

The Ding patent claims pharmaceutical compositions of cyclosporin. The compositions comprise the range from between about 0.05 to and about 0.40% of cyclosporin and castor oil in an amount between 0.625% to about 5.0%, which encompasses the range 0.01 to 0.64 cyclosporin/castor oil and therefore encompasses the instantly claimed range of equal or less than 0.05 % of cyclosporin and less than 0.08 of cyclosporin component/hydrophobic component (e.g., claim 7 of Ding). The pH is 7.2-7.6 as in claim 8 and are suitable for topical application to ocular tissue (claim 8 of Ding). The Ding reference goes on to teach, preferably, that the weight ratio of the cyclosporin to castor oil is below 0.16. More preferably, the weight ratio of cyclosporin to castor oil is between 0.12 and .02 (e.g., column 3).

It would have been obvious to make compositions of the active agent cyclosporin having less than 0.05 % of cyclosporin which were taught by Kawashima to have activity in treating corneal transplantation using the non-irritating emulsions of 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 that Ding et al. teach highly stable non-irritating emulsions with high comfort level and low irritation potential suitable for delivery to sensitive areas such as ocular tissues having 0.05% cyclosporin and with weight ratios of cyclosporin component to hydrophobic component more preferably between 0.12 and 0.02 (e.g., column 3, lines 15-20). One of ordinary skill in the art at the time the invention was made

would have had a reasonable expectation of success given that cyclosporin A was known to be an active agent with immunosuppressive activity in the treatment of corneal graft rejection as taught by Kawashima et al. The limitation of claim 4: “wherein the blood of the human or animal has substantially no detectable concentration of cyclosporin component” and of claim 5: ”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" and the limitation of claim 6: “0.1 ng/mL or less” necessarily read upon the method of Ding et al. since it teaches overlapping steps/concentrations. Further, “[c]laim 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.” (MPEP 2111.04). In the instant case, it does not appear that the limitations following the wherein clause in claims 4-6 introduce any further manipulative difference with respect to Kawashima et al. in view of Ding et al. The limitation of claims 7-8: “cyclosporin A" is taught,

e.g., in Example 1. The limitation of claim 9: “wherein the cyclosporin component is solubilized in the hydrophobic component present in the composition" is taught in column 3, lines 21-23. The limitations of claim 10: “wherein the hydrophobic component is present in the composition in an amount greater than 0.625% by weight“, of claim 11: "oily material", of claim 12: "vegetable oils" and of claim 13: "castor oil" are taught, e.g., in Examples 1A-D which teach 5.00%, 2.5% and 1.25% of hydrophobic component (castor oil). The limitation of claim 14: “topically administering the composition to the eye" is taught, e.g., in column 5, lines 15-18 and claim 8 of Ding et al. The limitation of claim 15: “wherein the composition comprises an effective amount of an emulsifier component” is taught in column 3, lines 38-4 and 50-56. The limitations of claim 16-17: “tonicity" and "organic tonicity component" are taught in column 4, lines 12-19. The limitation of claim 18: “polyelectrolyte component in an amount effective in stabilizing the composition” is taught in column 3, lines 64-67 and column 4, lines 1-12. The limitation of claims 19-20 drawn to pH ranges of "of about 7.0 to about 8.0" and “of about 7.2 to about 7.6” are taught, e.g., in Example 1A-1E and in claim 8 of Ding et al.

With respect to the claimed ranges, the skilled artisan would have been motivated utilize such proportions because they were encompassed by the Ding et al. patent. Please note that compositions with a higher amount of castor oil are encompassed by the Ding et al. claims (e.g., claim 8, embodiment 1B) optimizing the ratio of cyclosporin to hydrophobic components to below 0.08 was taught by Ding et al. in the range 0.02 to 0.12 (e.g., column 3, lines 18-20) and in

embodiment 1B (which has 0.04). There is no evidence of criticality of these ranges: “[g]enerally, 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). Please note that Kawashima et al. teach that doses in the range of 0.05 ml to 0.5 ml, preferably 0.1 ml to 0.2 ml, of an ophthalmic composition containing 0.005% to 1.0%, preferably 0.01% to 0.5%, (by weight) of cyclosporin may be used. Satisfactory results are obtained by administering droplets of about 0.05 ml a few times a day; for example 1 to 5 times a day ([0015]).

Furthermore, it has been held that under KSR that "obvious to try" may be an appropriate test under 103 The Supreme Court stated in KSR:

> When there is motivation "to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to anticipated success, it is likely the product not of innovation but of ordinary skill and common sense. In that instance the fact that a combination was obvious to try might show that it was obvious under § 103." KSR Int’l Co. v. Teleflex Inc., 127 S. Ct. 1727, ___, 82 USPQ2d 1385, 1397 (2007).

The “problem” facing those in the art was the treatment of corneal graft rejection, and there were a limited number of methodologies available to do so. The skilled artisan would have had reason to try these methodologies with the reasonable expectation that at least one would be successful. In the instant case cyclosporin may be delivered using non-hydrophobic compositions (as taught by Kawashima et al.) and emulsions comprising hydrophobic components (as taught by Ding et al.) Thus, treating corneal graft rejection at concentration ranges

known to be active in treating corneal graft rejection and once a day, as also known in the art, with a cyclosporin emulsion which was known to be non-irritating is a "the product not of innovation but of ordinary skill and common sense," leading to the conclusion that invention is not patentable as it would have been obvious.

In addition, KSR forecloses the argument that a specific teaching, suggestion or motivation is required to support a finding of obviousness. See the recent Board decision Ex parte Smith, --USPQ2d--, slip op. at 20, (Bd. Patt. App. & Interf. June 25, 2007) (citing KSR, 82 USPQ2s at 1396) (available at http://www.uspto.gov/web/offices/dcom/bpai/prec/fd071925.pdf).

Double Patenting

8. 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 obviousness-type double patenting rejection is appropriate where the conflicting claims 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 conflicting 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.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

9. Claims 1, 4-20 and 37-38 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 (cited in the IDS of 11/14/07) in view of Kawashima et al. (US 6,582,718).

The Ding patent is relied upon as above. The Ding patent claims pharmaceutical compositions of cyclosporin. The compositions comprise the range from between about 0.05 to and about 0.40% of cyclosporin and castor oil in an amount between 0.625% to about 5.0%, which encompasses the range 0.01 to 0.64 cyclosporin/castor oil and therefore encompasses the instantly claimed range of equal or less than 0.05 and less than 0.08 (e.g., claim 7 of Ding). The pH is 7.2-7.6 as in claim 8 and are suitable for topical application to ocular tissue (claim 8 of Ding).

The Ding reference goes on to teach, preferably, that the weight ratio of the cyclosporin to castor oil is below 0.16. More preferably, the weight ratio of cyclosporin to castor oil is between 0.12 and .02 (e.g., column 3).

Ding et al. do not expressly teach treating or preventing “corneal graft rejection” with their cyclosporin compositions.

Kawashima et al. disclose that effective topical administration of cyclosporin A to the eye would reduce or eliminate to a large extent the systemic side effects by restricting activity to the locus of the condition being treated and proposals to this effect have been made. Kawashima et al. teach that utility and effectiveness of Cyclosporin A in treating diseases and conditions of the eye has been hindered by the lack of suitable eye-drops which are acceptable to the eye. Eye-drops are required which do not cause patient discomfort and which permit a convenient administration regimen and do not require unduly frequent administration, while providing adequate drug substance delivery both to the external and, in particular, the internal regions of the eye. A further difficulty is the very poor solubility of cyclosporin A in water. This leads often to precipitation of cyclosporin A from aqueous-based eye-drops causing strong irritation of the eye.

Kawashima et al. teach that their ophthalmic compositions are useful for the same indications as other topical ophthalmic compositions containing cyclosporins, for example diseases affecting the cornea, the aqueous, the lens, the iris, the ciliary, the choroid or the retina. The ophthalmic compositions are useful particularly for the treatment of an autoimmune or inflammatory disease or

condition of the eye or of the surrounding or associated organs or tissues, that has undesirably elevated immuno-response or inflammatory reaction or event as part of its etiology. The ophthalmic compositions are useful preferably for treating the anterior or posterior segment of the eye. For example for the treatment of anterior or posteior uveitis, chronic keratititis, keratoconjunctivitis sicca, vernal keratoconjunctivitis, conjunctivitis, including vernal conjunctivitis, or in keratoplasty. The ophthalmic compositions may also be used in the treatment of immunoreactive graft rejection post corneal transplantation, Behcet disease, and autoimmune corneal diseases such as Mooren's ulcer, ocular pemphigus, and rheumatoid ulcer ([0014]).

Kawashima et al. teach that the utility of the ophthalmic compositions and advantageous therapeutic properties can be observed in standard animal models and in standard clinical tests; for example by administering, a few times a day, 0.05 ml to 0.5 ml, preferably 0.1 ml to 0.2 ml, of an ophthalmic composition containing 0.005% to 1.0%, preferably 0.01% to 0.5%, (by weight) of cyclosporin to the eyes of patients exhibiting diseases or conditions of the eye as set forth above. .

The optimal dosage to be administered to a particular patient will vary from patient to patient and from disease to disease and must be considered carefully by the treating physician. However doses in the range of 0.05 ml to 0.5 ml, preferably 0.1 ml to 0.2 ml, of an ophthalmic composition containing 0.005% to 1.0%, preferably 0.01% to 0.5%, (by weight) of cyclosporin may be used.

Satisfactory results are obtained by administering droplets of about 0.05 ml a few times a day; for example 1 to 5 times a day ([0015]).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to utilize, e.g., the pharmaceutical compositions of Ding et al. to treat or prevent corneal transplantation rejection using cyclosporin as the active agent. One of ordinary skill in the art at the time the invention was made would have been motivated to do so produce other methods of treating corneal transplantation rejection with decreased irritation in the eyes and decreased systemic side effects and also to produce therapeutic methods of highly stable compositions. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success since cyclosporin A was known to be an active agent in the treatment of corneal graft rejection as taught by Kawashima et al. and included doses in the range of 0.05 ml to 0.5 ml, preferably 0.1 ml to 0.2 ml, of an ophthalmic composition containing 0.005% to 1.0%, preferably 0.01% to 0.5%, (by weight) of cyclosporin and satisfactory results in treatments were obtained by administering droplets of about 0.05 ml a few times a day; for example 1 to 5 times a day ([0015]) of Kawashima.

With respect to the range of cyclosporin to hydrophobic component, the skilled artisan would have been motivated to do so because such proportions were encompassed by the Ding et al. patent. Please note that compositions with a higher amount of castor oil are encompassed by the Ding et al. claims (e.g., claim 8, embodiment 1B) optimizing the ratio of cyclosporin to hydrophobic components to below 0.08 was taught by Ding et al. in the range 0.02 to 0.12

(e.g., column 3, lines 18-20) and in embodiment 1B (which has 0.04). The adjustment of particular conventional working conditions (e.g., using all the ratios and proportions taught by Ding. et al.) with amounts of active agent for treating corneal graft disease is deemed merely a matter of judicious selection and routine optimization that is well within the purview of the skilled artisan. There is no evidence of criticality of these ranges: “[g]enerally, 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)

Furthermore, it has been held that under KSR that "obvious to try" may be an appropriate test under 103 The Supreme Court stated in KSR:

> When there is motivation "to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to anticipated success, it is likely the product not of innovation but of ordinary skill and common sense. In that instance the fact that a combination was obvious to try might show that it was obvious under § 103." KSR Int’l Co. v. Teleflex Inc., 127 S. Ct. 1727, ___, 82 USPQ2d 1385, 1397 (2007).

The “problem” facing those in the art was the treatment of corneal graft rejection, and there were a limited number of methodologies available to do so. The skilled artisan would have had reason to try these methodologies with the reasonable expectation that at least one would be successful. In the instant case cyclosporin may be delivered using non-hydrophobic compositions (as taught by Kawashima et al.) and emulsions comprising hydrophobic components (as taught by Ding et al.) Thus, treating corneal graft rejection at concentration ranges

known to be active in treating corneal graft rejection and once a day, as also known in the art, with a cyclosporin emulsion which was known to be non-irritating is a "the product not of innovation but of ordinary skill and common sense," leading to the conclusion that invention is not patentable as it would have been obvious.

In addition, KSR forecloses the argument that a specific teaching, suggestion or motivation is required to support a finding of obviousness. See the recent Board decision Ex parte Smith, --USPQ2d--, slip op. at 20, (Bd. Patt. App. & Interf. June 25, 2007) (citing KSR, 82 USPQ2s at 1396) (available at http://www.uspto.gov/web/offices/dcom/bpai/prec/fd071925.pdf).

Conclusion

10. No claim is currently allowed.

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

11. 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 04/2013

Notice of References Cited	Application/Control No. 11/897,177	Applicant(s)/Patent Under Reexamination ACHEAMPONG ET AL.	
	Examiner MARCELA M. CORDERO	Art Unit 1658	Page 1 of 1

U.S. PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Name	Classification
*	A	US-6,582,718	06-2003	Kawashima et al.	424/427
	B	US-			
	C	US-			
	D	US-			
	E	US-			
	F	US-			
	G	US-			
	H	US-			
	I	US-			
	J	US-			
	K	US-			
	L	US-			
	M	US-			

FOREIGN PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Country	Name	Classification
	N					
	O					
	P					
	Q					
	R					
	S					
	T					

NON-PATENT DOCUMENTS

*		Include as applicable: Author, Title Date, Publisher, Edition or Volume, Pertinent Pages)
	U	
	V	
	W	
	X	

*A copy of this reference is not being furnished with this Office action. (See MPEP § 707.05(a).)
Dates in MM-YYYY format are publication dates. Classifications may be US or foreign.

EAST Search History

EAST Search History (Prior Art)

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	13	corneal near3 graft near3 rejection same cyclosporin	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	ADJ	ON	2013/04/02 20:24
L2	0	cornea near3 graft near3 (rejection or transplantation) same cyclosporin	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	ADJ	ON	2013/04/02 21:19
L3	13	corneal near3 graft near3 (rejection or transplantation) same cyclosporin	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	ADJ	ON	2013/04/02 21:19
L4	17	corneal near3 graft near3 (rejection or transplantation or transplant) same cyclosporin	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	ADJ	ON	2013/04/02 21:19

EAST Search History (Interference)

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4/2/2013 9:21:48 PM
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Search Notes	Application/Control No.	Applicant(s)/Patent Under Reexamination
	11897177	ACHEAMPONG ET AL.
	Examiner	Art Unit
	MARCELA M CORDERO GARCIA	1654

CPC- SEARCHED		
Symbol	Date	Examiner

CPC COMBINATION SETS - SEARCHED		
Symbol	Date	Examiner

US CLASSIFICATION SEARCHED			
Class	Subclass	Date	Examiner
none	none	12/01/08	MMCG

SEARCH NOTES		
Search Notes	Date	Examiner
updated	12/01/08	MMCG
STN searched by STIC (available via SCORE / PAIR)	4/14/08	MMCG
STN searched by STIC (available via SCORE / PAIR)	6/25/09	MMCG
EAST searched (attached)	8/16/09	MMCG
internet search (google.com) terms: restasis, dry eye, vernal conjunctivitis, atopic keratoconjunctivitis, cyclosporin	8/14/09	MMCG
STN searched by STIC (available via SCORE / PAIR)	4/26/10	MMCG
EAST searched (attached)	6/18/10	MMCG
also updated PALM Inventor search	6/18/10	MMCG
internet search (google.com) terms: restasis, corneal or cornea, graft, allograft, transplant, rejection	6/18/10	MMCG
EAST updated (attached)	02/13/2012	MMCG
also updated PALM Inventor search	02/13/2012	MMCG
EAST search (updated)	10/20/2012	MMCG
also ran PALM Inventor search	10/20/2012	MMCG
EAST search (attached)	4/2/2013	MMCG
also updated PALM Inventor search	4/2/2013	MMCG

INTERFERENCE SEARCH			
US Class/ CPC Symbol	**US Subclass / CPC Group**	**Date**	**Examiner**
EAST search			

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:

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City		State		Zip	
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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	July 2, 2013
Name	Debra D. Condino, Reg. No. 31,007	Telephone	714-246-2368
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.**

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

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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.
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PTO/SB/96 (01-08)
Approved for use through 07/31/2008. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

STATEMENT UNDER 37 CFR 3.73(b)

Applicant/Patent Owner: Acheampong et al

Application No./Patent No.: 10/927,857 Filed/Issue Date: 08/27/2004

Entitled: METHODS OF PROVIDING THERAPEUTIC EFFECTS USING CYCLOSPORIN COMPONENTS

ALLERGAN, INC., a Corporation
(Name of Assignee) (Type of Assignee, e.g., corporation, partnership, university, government agency, etc.)

states that it is:

1. [X] the assignee of the entire right, title, and interest; or

2. [ ] an assignee of less than the entire right, title and interest
(The extent (by percentage) of its ownership interest is_____ %)

in the patent application/patent identified above by virtue of either:

A. [X] An assignment from the inventor(s) of the patent application/patent identified above. The assignment was recorded in the United States Patent and Trademark Office at Reel 015749, Frame 0698, or for which a copy thereof is attached.

OR

B. [ ] A chain of title from the inventor(s), of the patent application/patent identified above, to the current assignee as follows:

1. From: _____ To: _____
The document was recorded in the United States Patent and Trademark Office at
Reel _____, Frame _____, or for which a copy thereof is attached.

2. From: _____ To: _____
The document was recorded in the United States Patent and Trademark Office at
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[ ] Additional documents in the chain of title are listed on a supplemental sheet.

[ ] As required by 37 CFR 3.73(b)(1)(i), the documentary evidence of the chain of title from the original owner to the assignee was, or concurrently is being, submitted for recordation pursuant to 37 CFR 3.11.

[NOTE: A separate copy (*i.e.*, a true copy of the original assignment document(s)) must be submitted to Assignment Division in accordance with 37 CFR Part 3, to record the assignment in the records of the USPTO. See MPEP 302.08]

The undersigned (whose title is supplied below) is authorized to act on behalf of the assignee.

Debra D. Condino — July 2, 2013
Signature — Date

Debra D. Condino — 714.246.2388
Printed or Typed Name — Telephone Number

Assistant Secretary
Title

UNITED STATES PATENT AND TRADEMARK OFFICE

UNDER SECRETARY OF COMMERCE FOR INTELLECTUAL PROPERTY AND
DIRECTOR OF THE UNITED STATES PATENT AND TRADEMARK OFFICE

MARCH 09, 2005

PTAS

102830605A

ALLERGAN, INC.
FRANK J. UXA
PO BOX 19534
2525 DUPONT DR.
IRVINE, CA 92612

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ASSIGNOR:
ACHEAMPONG, ANDREW DOC DATE: 08/12/2004

ASSIGNOR:
TANG-LIU, DIANE DOC DATE: 08/12/2004

ASSIGNOR:
CHANG, JAMES N. DOC DATE: 08/12/2004

ASSIGNOR:
POWER, DAVID F. DOC DATE: 08/12/2004

ASSIGNEE:
ALLERGAN, INC.
2525 DUPONT DRIVE
IRVINE, CALIFORNIA 92612

OPT

SERIAL NUMBER: 10927857 FILING DATE: 08/27/2004
PATENT NUMBER: ISSUE DATE:
TITLE: METHODS OF PROVIDING THERAPEUTIC EFFECTS USING CYCLOSPORIN COMPONENTS

JEEVON JONES, EXAMINER
ASSIGNMENT DIVISION
OFFICE OF PUBLIC RECORDS

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(Rev. 6-93)
OMB No. 0651-0011 (exp. 4/94)

RECORDATION FORM COVER SHEET
09-07-2004

U.S. DEPARTMENT OF COMMERCE
Patent and Trademark Office
0-3119

102830605

To the Honorable Commissioner of Patents and Trademarks: Please record the attached original documents or copy thereof.

1. Name of conveying party(ies): 8-27-04
ANDREW ACHEAMPONG
DIANE TANG-LIU
JAMES N. CHANG
DAVID F. POWER

Additional name(s) of conveying party(ies) attached? ☐ Yes ☒ No

2. Name and address of receiving party(ies)
Name: ALLERGAN, INC.
Internal Address:

Received
MAR 16 2005
LEGAL/PATENTS

Street Address: 2525 DUPONT DRIVE
IRVINE, CA 92612

Additional name(s) & address(es) attached? ☐ Yes ☒ No

10587 U.S. PTO
10/927857
082704

3. Nature of conveyance:
☒ Assignment ☐ Merger
☐ Security Agreement ☐ Change of Name
☐ Other: _____
Execution Date: August 12, 2004

4. Application number(s) or patent number(s):
If this document is being filed together with a new application, the execution date of the application is: August 12, 2004
A. Patent Application No.(s) B. Patent No. (s)
Additional numbers attached? ☐ Yes ☒ No

5. Name and address of party to whom correspondence concerning document should be mailed:
Name: ALLERGAN, INC.
Internal Address: PO BOX 19534
Street Address: 2525 DUPONT DRIVE
IRVINE, CA 92612

6. Total number of applications and patents involved: 1

7. Total fee (37 CFR 3.41).....$ 40
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9. Statement and signature.
To the best of my knowledge and belief, the foregoing information is true and correct and any attached copy is a true copy of the original document.

FRANK J. UXA
Name of Person Signing

Signature

8/27/04
Date

09/03/2004 RBETHUNE 00000002 01 0885 10927857
01 FC:8021 40.00 DP

Total number of pages including cover sheet, attachments and document: 4

Mail documents to be recorded with required cover sheet information to:
Commissioner of Patents & Trademarks,
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D-3111

ASSIGNMENT

WHEREAS, we, **ANDREW ACHEAMPONG**, of the County of Orange, State of California, **DIANE TANG-LIU**, of the County of Orange, State of California, **JAMES N. CHANG**, of the County of Orange, State of California and **DAVID F. POWER**, of the County of Orange, State of California, have invented certain new and useful improvements in **METHODS OF PROVIDING THERAPEUTIC EFFECTS USING CYCLOSPORIN COMPONENTS**, which said **ANDREW ACHEAMPONG**, has this 12 day of AUGUST, 2004, which said **DIANE TANG-LIU**, has this 12 day of AUGUST, 2004, which said **JAMES N. CHANG**, has this 12 day of AUGUST, 2004, and which said **DAVID F. POWER** has this 12 day of AUGUST, 2004, executed application papers for United States Letters Patent thereon; and

NOW, THEREFORE, in consideration of ONE DOLLAR ($1.00) and other valuable consideration paid to us by Allergan, Inc., having its principal place of business at 2525 Dupont Drive, Irvine, CA 92612, receipt of which is hereby acknowledged, and intending to be legally bound, we do hereby assign unto said Allergan, Inc., its successors, and assigns, the entire right, title and interest in and to the said invention, said executed application, any divisional, continuation and continuation-in-part of said application, and all Letters Patent of the United States and all foreign countries to be obtained therefore;

We further assign to said Allergan, Inc. the right, optionally in its own name or in the names of its related companies, to apply for, obtain and maintain in all countries foreign to the United States, patent and/or Utility Model applications for said invention, including the full right to claim for any such application the benefits of any priority rights based on said executed United States application;

And we agree to execute further instruments (including divisional, continuation, continuation-in-part or reissue applications or other instruments) proper to effectuate the premises, this agreement to be binding upon my heirs, executors, and administrators;

And we request the Commissioner of Patents and Trademarks of the United States, and any official of any country or countries foreign to the United States whose duty it is to issue patents on applications as aforesaid, to issue Letters Patent in accordance herewith.

Executed this 12 day of August, 2004.

A Acheampong
ANDREW ACHEAMPONG

State of California)
) ss
County of Orange)

On this 12th day of AUGUST, 2004, before me, MARY Lou MCNAUL, personally appeared **ANDREW ACHEAMPONG** ~~personally known to me or~~ proved to me on the basis of satisfactory evidence to be the person(s) whose name(s) is/~~are~~ subscribed to the within instrument and ~~acknowledged~~ to me that ~~he/she/they~~ executed the ~~same~~ in ~~his/her/their~~ authorized capacity(~~ies~~), and that by ~~his/her/their~~ signature(~~s~~) on the instrument the person(~~s~~) or the entity upon behalf of which the person(~~s~~) acted, executed the instrument.

WITNESS my hand and official seal.

Mary Lou McNaul
Notary Public

SEAL

MARY LOU MC NAUL
Commission # 1401794
Notary Public - California
Orange County
My Comm. Expires Aug 14, 2007

Executed this 12th day of August, 2004.

DIANE TANG-LIU

State of California)
) ss
County of Orange)

On this 12th day of AUGUST, 2004, before me, MARY LOU MCNOWN, personally appeared **DIANE TANG-LIU** ~~personally known to me or~~ proved to me on the basis of satisfactory evidence to be the person(s) whose name(s) ~~is/are~~ subscribed to the within instrument and acknowledged to me that ~~he/she/they~~ executed the same in ~~his/her/their~~ authorized capacity(~~ies~~), and that by ~~his/her/their~~ signature(s) on the instrument the person(s) or the entity upon behalf of which the person(s) acted, executed the instrument.

WITNESS my hand and official seal.

Mary Lou McNown
Notary Public

MARY LOU MC NOWN
Commission # 1431736
Notary Public - California
Orange County
My Comm. Expires Aug 16, 2007

SEAL

Executed this 12 day of August, 2004.

JAMES N. CHANG

State of California)
) ss
County of Orange)

On this 12th day of AUGUST, 2004, before me, MARY LOU MC NOWN, personally appeared **JAMES N. CHANG** ~~personally known to me or~~ proved to me on the basis of satisfactory evidence to be the person(s) whose name(s) ~~is/are~~ subscribed to the within instrument and acknowledged to me that ~~he/she/they~~ executed the same in ~~his/her/their~~ authorized capacity(~~ies~~), and that by ~~his/her/their~~ signature(s) on the instrument the person(s) or the entity upon behalf of which the person(s) acted, executed the instrument.

WITNESS my hand and official seal.

Mary Lou McNown
Notary Public

SEAL

MARY LOU MC NOWN
Commission # 1431736
Notary Public - California
Orange County
My Comm. Expires Aug 16, 2007

Executed this 12 day of August, 2004.

DAVID F. POWER

State of California)
) ss
County of Orange)

On this 12th day of AUGUST, 2004, before me, MARY LOU McNOUN, personally appeared **DAVID F. POWER** ~~personally known to me or~~ proved to me on the basis of satisfactory evidence to be the person(s) whose name(s) is/are subscribed to the within inst ument and acknowledged to me that he/she/they executed the same in his/her/their aut orized capacity(ies), and that by his/her/their signature(s) on the instrument the person(s) or the entity upon behalf of which the person(s) acted, executed the instrument.

WITNESS my hand and official seal.

Mary Lou McNoun
Notary Public

SEAL

MARY LOU MC NOUN
Commission # 1401734
Notary Public - California
Orange County
My Comm. Expires Aug 14, 2007

Electronic Acknowledgement Receipt

EFS ID:	16214544
Application Number:	11897177
International Application Number:	
Confirmation Number:	3860
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/Bonnie Ferguson
Filer Authorized By:	Laura Lee Wine
Attorney Docket Number:	17618CON (AP)
Receipt Date:	02-JUL-2013
Filing Date:	28-AUG-2007
Time Stamp:	11:45:38
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	Power of Attorney	17618CON-POA-373-7-1-13-C.pdf	613142 474517f9fb07cd38de7ed1cb6372959186c3c251	no	9

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

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

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

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Andrew Acheampong, et al.	Examiner: Cordero Garcia, Marcela M.
Serial No.: 11/897,177	Art Unit: 1658
Filed: August 28, 2007	Confirmation No.: 3860
For: METHODS OF PROVIDING THERAPEUTIC EFFECTS USING CYCLOSPORIN COMPONENTS	Docket No.: 17618CON(AP)

RESPONSE TO NON-FINAL OFFICE ACTION MAILED APRIL 8, 2013

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

Dear Sir:

These papers are filed in reply to the Non-Final Office Action mailed April 8, 2013.

The Commissioner is authorized to charge any fee which may be required in connection with this Amendment to deposit account No. 01-0885.

Amendments to the Claims begin at page 2 of this paper.

Remarks begin on page 5 of this paper.

AMENDMENTS TO THE CLAIMS

The following claims replace all claims previously 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. (**Currently Amended**) A method of treating or preventing corneal graft rejection, the method comprising administering to an eye of a human or animal, at a frequency of once per day, a composition in the form of an emulsion comprising water, polysorbate 80, a hydrophobic component, and a cyclosporin component in a therapeutically effective amount equal to or less than 0.05% by weight of the composition, wherein the weight ratio of the cyclosporin component to the hydrophobic component is less than 0.08.

2. – 3. (Canceled)

4. (Previously Presented) The method of claim 1 wherein the blood of the human or animal has no detectable concentration of the cyclosporin component.

5. (Previously Presented) 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 chromatographylmass spectrometry analytical method.

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

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

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

10. (Original) 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. (Original) The method of claim 1 wherein the hydrophobic component comprises an oily material.

12. (Original) 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. (Original) The method of claim 1 wherein the hydrophobic component comprises castor oil.

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

15. (Canceled)

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

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

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

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

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

21. – 36. (Canceled).

37. (Previously Presented) The method of claim 1, where the cyclosporin component is in a therapeutically effective amount of less than 0.05% by weight of the composition.

38. (Previously Presented) The method of claim 1, wherein the cyclosporin component is in a therapeutically effective amount of 0.05% by weight of the composition.

39. – 41. (Canceled).

REMARKS

This Reply responds to the Non-Final Office Action sent April 8, 2013, in which the Office Action rejected Claims 1, 4-20 and 37-38. Claim 1 has been amended. Claim 15 has been canceled. Thus, Claims 1, 4-14, 16-20, and 37-38 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 specification and claims. The Applicants respectfully submits that the claims are in condition for allowance.

Claim Rejections

35 U.S.C. § 103

Claims 1, 4-20 and 37-38 are rejected under 35 U.S.C. 103(a) as being obvious over Kawashima et al. (US 6,582,718) in view of Ding et al. (US 5,474,979 cited in the IDS of 11/14/07).

Claim 1

While the Applicants do not acquiesce to the rejection, in order to expedite prosecution, Claim 1 has been amended to recite:

> A method of treating or preventing corneal graft rejection, the method comprising administering to an eye of a human or animal, at a frequency of once per day, a composition in the form of an emulsion comprising water, **polysorbate 80**, a hydrophobic component, and a cyclosporin component in a therapeutically effective amount equal to or less than 0.05% by weight of the composition, wherein the weight ratio of the cyclosporin component to the hydrophobic component is less than 0.08.

Claim 1 (emphasis added).

The Applicants submit that amended Claim 1 is patentable over Kawashima in view of Ding because one of skill would not have combined the teachings of Kawashima with Ding, at least, because Kawashima teaches away from their combination. It is improper to combine references where the references teach away from their combination. See MPEP § 2145(X)(D)(2).

Kawashima discloses that polysorbate 80 has not been used successfully for formulating medical substances with low solubility in water (such as cyclosporin):

> In an attempt to solve these problems, studies have been conducted with various surfactants which are currently used for formulating medical substances with low

> solubility in water, especially the most commonly used surfactants polysorbate 80 and polyoxyethylene hydrogenated castor oil. **However, polysorbate 80 was found to have a poor solubilizing effect, when used for the preparation of eye-drops, and the dissolution of cyclosporin was not sufficient.**

Kawashima at col. 2, lines 22-29 (emphasis added).

Thus, the Applicants submit that one of skill looking at the Kawashima reference as a whole would have not reasonably expected success in combining teachings from Kawashima with Ding to form the composition currently claimed in amended Claim 1, which includes **polysorbate 80,** because Kawashima explicitly teaches away from ophthalmic formulations including polysorbate 80.

Thus, at least for the reasons recited above, the cited references taken alone or in combination with another reference would not anticipate amended Claim 1 nor render it obvious. The Applicants respectfully request that the rejection be withdrawn.

Claims 4-20 and 37-38

As described above, amended Claim 1 is patentable over Kawashima in view of Ding. Claims 4-20 and 37-38 depend directly or indirectly from Claim 1, and thus include all of the features of Claim 1 and recite combinations of the features not taught or suggested by the cited references. Claims 4-20 and 37-38 are patentable for at least the same reasons as Claim 1 and on their own merit.

Specifically, the Applicants would also like to submit that Claims 11-13 are patentable over Kawashima in view of Ding because one of skill would not have combined the teachings of Kawshima with Ding, at least, because Kawashima teaches away from their combination.

Kawashima discloses that oils have posed problems in formulating cyclosporin-based compositions:

> Efforts have been made to overcome these difficulties by dissolving cyclosporin A in vegetable oils (Ophthalmology, 96, 1144-1150 (1989)) and by clatherating cyclosporin A with cyclodextrin (Japanese unexamined Patent Publication SHO-64-85921/1989).
>
> **In oily solution, however, cyclosporin A is poorly distributed in the eyes** (Folia Ophthalmologica Japonica, 40, (5), 902-908 (1989)), and a high concentration (2%) of cyclosporin A is needed for clinical treatment (Ophthalmology, 96, 1144-1150 (1989)). **Further, these oily eye drops tend to cause a disagreeable feeling to the eyes.**

Kawashima, col. 1, line 65 – col. 2, line 8 (emphasis added).

> In an attempt to solve these problems, studies have been conducted with various surfactants which are currently used for formulating medical substances with low solubility in water, especially the most commonly used surfactants polysorbate 80 and **polyoxyethylene hydrogenated castor oil**. (…) **Polyoxyethylene hydrogenated castor oil was found to strongly irritate the eyes when used in eye-drops**.

Kawashima at col. 2, lines 22-31 (emphasis added).

Thus, the Applicants submit that one of skill looking at the Kawashima reference as a whole would have not reasonably expected success in combining teachings from Kawashima with Ding to form the composition currently claimed in Claims 11-13, which include **oily materials; vegetable oils, animal oils, mineral oils, synthetic oils and mixtures thereof; and castor oil**, respectively, because Kawashima explicitly teaches away from ophthalmic formulations including oils. This is further evidenced by the fact that Kawashima specifically claims an oil-free composition as their formulation. *See* Kawashima, claim 1.

Thus, the Applicants respectfully request that the Examiner withdraw the rejections of Claims 4-20 and 37-38.

Thus the Applicants respectfully request that the claim rejections under 35 U.S.C. § 103(a) be withdrawn.

Double Patenting

Claims 1, 4-20 and 37-38 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-8 of Ding (U.S. Patent No. 5,474,979) in view of Kawashima et al. (US 6,582,718).

The Applicants submit that the obviousness-type double patenting rejection is improper. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims 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 claims. MPEP § 804. The Applicants submit that the claims of the current application are patentably distinct from the reference claims of Ding, at least, because the claims of the present application recite additional, non-obvious elements not found in the reference claims of Ding.

For example, independent claim 1 of the present application claims a method of treating or preventing corneal graft rejection. The cited claims of Ding claim a pharmaceutical composition. None of the cited pending claims of Ding claim a method of treating or preventing corneal graft rejection. Modification of the claims of Ding to include a method of treatment of corneal graft rejection or any other limitation disclosed in Kawashima would have also been improper for similar reasons as argued above. The Applicants would also like to note that any reference in the Office Action to the contents of the Ding specification as prior art in the double patenting rejection, outside of the definition of claim terms is improper. See MPEP § 804(II)(B)(1) ("When considering whether the invention defined in a claim of an application would have been an obvious variation of the invention defined in the claim of a patent, the disclosure of the patent may not be used as prior art." *General Foods Corp. v. Studiengesellschaft Kohle mbH*, 972 F.2d 1272, 1279, 23 USPQ2d 1839, 1846 (Fed. Cir. 1992)).

Therefore, at least for the reasons stated above, Claim 1 and those claims dependent thereon (i.e. Claims 4-20 and 37-38) are patentably distinct because they are not anticipated by, nor would they have been obvious in view of pending Claims 1-8 of Ding in view of Kawashima.

The Applicants request that the rejections be withdrawn, and the Applicants submit that the claims are in condition for allowance.

Respectfully submitted,

Date: July 8, 2013

/Laura L. Wine/

Laura L. Wine
Registration Number 68,681

ALLERGAN
LEGAL DEPARTMENT
2525 Dupont Drive
Irvine, California 92612-1599 Tel: 714/246-6996 Fax: 714/246-4249

Electronic Acknowledgement Receipt

EFS ID:	16256654
Application Number:	11897177
International Application Number:	
Confirmation Number:	3860
Title of Invention:	Methods of providing therapeutic effects using cyclosporin components
First Named Inventor/Applicant Name:	Andrew Acheampong
Customer Number:	51957
Filer:	Laura Lee Wine
Filer Authorized By:	
Attorney Docket Number:	17618CON (AP)
Receipt Date:	08-JUL-2013
Filing Date:	28-AUG-2007
Time Stamp:	18:45:15
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	Amendment/Req. Reconsideration-After Non-Final Reject	17618CON_Response_to_NonFinalOA3.pdf	158483 5967cdcc5caac43135e1c68944bcd98ee8cb5e98	no	8

Warnings:	
Information:	

Total Files Size (in bytes):	158483

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.

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

PATENT APPLICATION FEE DETERMINATION RECORD Substitute for Form PTO-875	Application or Docket Number 11/897,177	Filing Date 08/28/2007	☐ To be Mailed

ENTITY: ☒ LARGE ☐ SMALL ☐ MICRO

APPLICATION AS FILED – PART I

	(Column 1)	(Column 2)		
FOR	NUMBER FILED	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	07/08/2013	(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))	* 19	Minus	** 37	= 0	X $80 =	0
	Independent (37 CFR 1.16(h))	* 1	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
/PAMELA YOUNG/

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
11/897,177	08/28/2007	Andrew Acheampong	17618CON (AP)

CONFIRMATION NO. 3860

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

POA ACCEPTANCE LETTER

OC000000062462743

Date Mailed: 07/12/2013

NOTICE OF ACCEPTANCE OF POWER OF ATTORNEY

This is in response to the Power of Attorney filed 07/02/2013.

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.

/tpetros/

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

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

NOTICE OF ALLOWANCE AND FEE(S) DUE

51957 7590 08/26/2013

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

EXAMINER
CORDERO GARCIA, MARCELA M

ART UNIT	PAPER NUMBER
1658	

DATE MAILED: 08/26/2013

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
11/897,177	08/28/2007	Andrew Acheampong	17618CON (AP)	3860

TITLE OF INVENTION: METHODS OF PROVIDING THERAPEUTIC EFFECTS USING CYCLOSPORIN COMPONENTS

APPLN. TYPE	ENTITY STATUS	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	UNDISCOUNTED	$1780	$300	$0	$2080	11/26/2013

THE APPLICATION IDENTIFIED ABOVE HAS BEEN EXAMINED AND IS ALLOWED FOR ISSUANCE AS A PATENT. PROSECUTION ON THE MERITS IS CLOSED. THIS NOTICE OF ALLOWANCE IS NOT A GRANT OF PATENT RIGHTS. THIS APPLICATION IS SUBJECT TO WITHDRAWAL FROM ISSUE AT THE INITIATIVE OF THE OFFICE OR UPON PETITION BY THE APPLICANT. SEE 37 CFR 1.313 AND MPEP 1308.

THE ISSUE FEE AND PUBLICATION FEE (IF REQUIRED) MUST BE PAID WITHIN THREE MONTHS FROM THE MAILING DATE OF THIS NOTICE OR THIS APPLICATION SHALL BE REGARDED AS ABANDONED. THIS STATUTORY PERIOD CANNOT BE EXTENDED. SEE 35 U.S.C. 151. THE ISSUE FEE DUE INDICATED ABOVE DOES NOT REFLECT A CREDIT FOR ANY PREVIOUSLY PAID ISSUE FEE IN THIS APPLICATION. IF AN ISSUE FEE HAS PREVIOUSLY BEEN PAID IN THIS APPLICATION (AS SHOWN ABOVE), THE RETURN OF PART B OF THIS FORM WILL BE CONSIDERED A REQUEST TO REAPPLY THE PREVIOUSLY PAID ISSUE FEE TOWARD THE ISSUE FEE NOW DUE.

HOW TO REPLY TO THIS NOTICE:

I. Review the ENTITY STATUS shown above. If the ENTITY STATUS is shown as SMALL or MICRO, verify whether entitlement to that entity status still applies.

If the ENTITY STATUS is the same as shown above, pay the TOTAL FEE(S) DUE shown above.

If the ENTITY STATUS is changed from that shown above, on PART B - FEE(S) TRANSMITTAL, complete section number 5 titled "Change in Entity Status (from status indicated above)".

For purposes of this notice, small entity fees are 1/2 the amount of undiscounted fees, and micro entity fees are 1/2 the amount of small entity fees.

II. PART B - FEE(S) TRANSMITTAL, or its equivalent, must be completed and returned to the United States Patent and Trademark Office (USPTO) with your ISSUE FEE and PUBLICATION FEE (if required). If you are charging the fee(s) to your deposit account, section "4b" of Part B - Fee(s) Transmittal should be completed and an extra copy of the form should be submitted. If an equivalent of Part B is filed, a request to reapply a previously paid issue fee must be clearly made, and delays in processing may occur due to the difficulty in recognizing the paper as an equivalent of Part B.

III. All communications regarding this application must give the application number. Please direct all communications prior to issuance to Mail Stop ISSUE FEE unless advised to the contrary.

IMPORTANT REMINDER: Utility patents issuing on applications filed on or after Dec. 12, 1980 may require payment of maintenance fees. It is patentee's responsibility to ensure timely payment of maintenance fees when due.

PART B - FEE(S) TRANSMITTAL

Complete and send this form, together with applicable fee(s), to: Mail **Mail Stop ISSUE FEE**
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450
or Fax (571)-273-2885

INSTRUCTIONS: This form should be used for transmitting the ISSUE FEE and PUBLICATION FEE (if required). Blocks 1 through 5 should be completed where appropriate. All further correspondence including the Patent, advance orders and notification of maintenance fees will be mailed to the current correspondence address as indicated unless corrected below or directed otherwise in Block 1, by (a) specifying a new correspondence address; and/or (b) indicating a separate "FEE ADDRESS" for maintenance fee notifications.

CURRENT CORRESPONDENCE ADDRESS (Note: Use Block 1 for any change of address)

51957 7590 08/26/2013
ALLERGAN, INC.
2525 DUPONT DRIVE, T2-7H
IRVINE, CA 92612-1599

Note: A certificate of mailing can only be used for domestic mailings of the Fee(s) Transmittal. This certificate cannot be used for any other accompanying papers. Each additional paper, such as an assignment or formal drawing, must have its own certificate of mailing or transmission.

Certificate of Mailing or Transmission

I hereby certify that this Fee(s) Transmittal is being deposited with the United States Postal Service with sufficient postage for first class mail in an envelope addressed to the Mail Stop ISSUE FEE address above, or being facsimile transmitted to the USPTO (571) 273-2885, on the date indicated below.

(Depositor's name)
(Signature)
(Date)

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
11/897,177	08/28/2007	Andrew Acheampong	17618CON (AP)	3860

TITLE OF INVENTION: METHODS OF PROVIDING THERAPEUTIC EFFECTS USING CYCLOSPORIN COMPONENTS

APPLN. TYPE	ENTITY STATUS	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	UNDISCOUNTED	$1780	$300	$0	$2080	11/26/2013

EXAMINER	ART UNIT	CLASS-SUBCLASS
CORDERO GARCIA, MARCELA M	1658	514-020500

1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.363).

❑ Change of correspondence address (or Change of Correspondence Address form PTO/SB/122) attached.

❑ "Fee Address" indication (or "Fee Address" Indication form PTO/SB/47; Rev 03-02 or more recent) attached. **Use of a Customer Number is required.**

2. For printing on the patent front page, list

(1) the names of up to 3 registered patent attorneys or agents OR, alternatively,

(2) the name of a single firm (having as a member a registered attorney or agent) and the names of up to 2 registered patent attorneys or agents. If no name is listed, no name will be printed.

1 _____
2 _____
3 _____

3. ASSIGNEE NAME AND RESIDENCE DATA TO BE PRINTED ON THE PATENT (print or type)

PLEASE NOTE: Unless an assignee is identified below, no assignee data will appear on the patent. If an assignee is identified below, the document has been filed for recordation as set forth in 37 CFR 3.11. Completion of this form is NOT a substitute for filing an assignment.

(A) NAME OF ASSIGNEE (B) RESIDENCE: (CITY and STATE OR COUNTRY)

Please check the appropriate assignee category or categories (will not be printed on the patent) : ❑ Individual ❑ Corporation or other private group entity ❑ Government

4a. The following fee(s) are submitted:

❑ Issue Fee

❑ Publication Fee (No small entity discount permitted)

❑ Advance Order - # of Copies _____

4b. Payment of Fee(s): **(Please first reapply any previously paid issue fee shown above)**

❑ A check is enclosed.

❑ Payment by credit card. Form PTO-2038 is attached.

❑ The Director is hereby authorized to charge the required fee(s), any deficiency, or credit any overpayment, to Deposit Account Number _____ (enclose an extra copy of this form).

5. **Change in Entity Status** (from status indicated above)

❑ Applicant certifying micro entity status. See 37 CFR 1.29

NOTE: Absent a valid certification of Micro Entity Status (see form PTO/SB/15A and 15B), issue fee payment in the micro entity amount will not be accepted at the risk of application abandonment.

❑ Applicant asserting small entity status. See 37 CFR 1.27

NOTE: If the application was previously under micro entity status, checking this box will be taken to be a notification of loss of entitlement to micro entity status.

❑ Applicant changing to regular undiscounted fee status.

NOTE: Checking this box will be taken to be a notification of loss of entitlement to small or micro entity status, as applicable.

NOTE: The Issue Fee and Publication Fee (if required) will not be accepted from anyone other than the applicant; a registered attorney or agent; or the assignee or other party in interest as shown by the records of the United States Patent and Trademark Office.

Authorized Signature _____ Date _____

Typed or printed name _____ Registration No. _____

This collection of information is required by 37 CFR 1.311. 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 12 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, Virginia 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

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.

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.
11/897,177	08/28/2007	Andrew Acheampong	17618CON (AP)	3860

51957 7590 08/26/2013

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

EXAMINER	
CORDERO GARCIA, MARCELA M	
ART UNIT	PAPER NUMBER
1658	

DATE MAILED: 08/26/2013

Determination of Patent Term Adjustment under 35 U.S.C. 154 (b)
(application filed on or after May 29, 2000)

The Patent Term Adjustment to date is 0 day(s). If the issue fee is paid on the date that is three months after the mailing date of this notice and the patent issues on the Tuesday before the date that is 28 weeks (six and a half months) after the mailing date of this notice, the Patent Term Adjustment will be 0 day(s).

If a Continued Prosecution Application (CPA) was filed in the above-identified application, the filing date that determines Patent Term Adjustment is the filing date of the most recent CPA.

Applicant will be able to obtain more detailed information by accessing the Patent Application Information Retrieval (PAIR) WEB site (http://pair.uspto.gov).

Any questions regarding the Patent Term Extension or Adjustment determination should be directed to the Office of Patent Legal Administration at (571)-272-7702. Questions relating to issue and publication fee payments should be directed to the Customer Service Center of the Office of Patent Publication at 1-(888)-786-0101 or (571)-272-4200.

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.

Examiner-Initiated Interview Summary	**Application No.** 11/897,177	**Applicant(s)** ACHEAMPONG ET AL.	
	Examiner MARCELA M. CORDERO GARCIA	**Art Unit** 1658	

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

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

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

Date of Interview: *8/19/2013*.

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: *1*.

Identification of prior art discussed: *N/A*.

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...)

Examiner contacted Applicant's representative to discuss potential amendments that would place the application in condition for allowance. Such amendments were approved by Applicant's representative (see attached Examiner's amendment).

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	

Notice of Allowability	Application No. 11/897,177	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--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to *7/8/2013*.
   ☐ A declaration(s)/affidavit(s) under **37 CFR 1.130(b)** was/were filed on_____.
2. ☐ 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.
3. ☒ The allowed claim(s) is/are *1,4-14,16-20,37 and 38*. As a result of the allowed claim(s), 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 .
4. ☐ 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)).

   * Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

   Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).
6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☐ Notice of References Cited (PTO-892)
2. ☐ Information Disclosure Statements (PTO/SB/08), Paper No./Mail Date _____
3. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
4. ☒ Interview Summary (PTO-413), Paper No./Mail Date *20130819* .
5. ☒ Examiner's Amendment/Comment
6. ☐ Examiner's Statement of Reasons for Allowance
7. ☐ Other _____.

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

EXAMINER'S AMENDMENT

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Laura L. Wine on 8/19/2013.

The application has been amended as follows:

IN THE CLAIMS:

Claim 1 (Currently amended) A method of treating or preventing corneal graft rejection, the method comprising administering to an eye of a human or animal in need thereof, at a frequency of once per day, a composition in the form of an emulsion comprising water, polysorbate 80, a hydrophobic component, and a cyclosporin component in a therapeutically effective amount equal to or less than 0.05% by weight of the composition, wherein the weight ratio of the cyclosporin component to the hydrophobic component is less than 0.08.

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 08/2013

Examiner-Initiated Interview Summary	**Application No.** 11/897,177	**Applicant(s)** ACHEAMPONG ET AL.	
	Examiner MARCELA M. CORDERO GARCIA	**Art Unit** 1658	

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

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

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

Date of Interview: *8/19/2013*.

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: *1*.

Identification of prior art discussed: *N/A*.

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...)

Examiner contacted Applicant's representative to discuss potential amendments that would place the application in condition for allowance. Such amendments were approved by Applicant's representative (see attached Examiner's amendment).

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	

EAST Search History

EAST Search History (Prior Art)

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L6	28	cyclosporin same (corneal or cornea) same (transplant or rejection) and polysorbate	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	ADJ	ON	2013/08/19 18:17
L9	25	cyclosporin same (corneal or cornea) same (transplant or rejection) and polysorbate and (hydrophobic or oil)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	ADJ	ON	2013/08/19 18:57

EAST Search History (Interference)

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L7	10	cyclosporin same (corneal or cornea) same (transplant or rejection) and polysorbate	USPAT; UPAD	ADJ	ON	2013/08/19 18:55
L8	10	cyclosporin same (corneal or cornea) same (transplant or rejection) and polysorbate and (hydrophobic or oil)	USPAT; UPAD	ADJ	ON	2013/08/19 18:57

8/19/2013 6:58:08 PM
C:\Users\mgarcia\Documents\EAST\Workspaces\1166940-b.wsp

Search Notes	Application/Control No.	Applicant(s)/Patent Under Reexamination
	11897177	ACHEAMPONG ET AL.
	Examiner	Art Unit
	MARCELA M CORDERO GARCIA	1654

CPC- SEARCHED		
Symbol	Date	Examiner

CPC COMBINATION SETS - SEARCHED		
Symbol	Date	Examiner

US CLASSIFICATION SEARCHED			
Class	Subclass	Date	Examiner
none	none	12/01/08	MMCG

SEARCH NOTES		
Search Notes	Date	Examiner
updated	12/01/08	MMCG
STN searched by STIC (available via SCORE / PAIR)	4/14/08	MMCG
STN searched by STIC (available via SCORE / PAIR)	6/25/09	MMCG
EAST searched (attached)	8/16/09	MMCG
internet search (google.com) terms: restasis, dry eye, vernal conjunctivitis, atopic keratoconjunctivitis, cyclosporin	8/14/09	MMCG
STN searched by STIC (available via SCORE / PAIR)	4/26/10	MMCG
EAST searched (attached)	6/18/10	MMCG
also updated PALM Inventor search	6/18/10	MMCG
internet search (google.com) terms: restasis, corneal or cornea, graft, allograft, transplant, rejection	6/18/10	MMCG
EAST updated (attached)	02/13/2012	MMCG
also updated PALM Inventor search	02/13/2012	MMCG
EAST search (updated)	10/20/2012	MMCG
also ran PALM Inventor search	10/20/2012	MMCG
EAST search (attached)	4/2/2013	MMCG
also updated PALM Inventor search	4/2/2013	MMCG
EAST updated (attached)	8/19/2013	MMCG
also updated PALM Inventor search	8/19/2013	MMCG

INTERFERENCE SEARCH			
US Class/ CPC Symbol	**US Subclass / CPC Group**	**Date**	**Examiner**
EAST searched	attached	8/19/2013	MMCG

Issue Classification	Application/Control No.	Applicant(s)/Patent Under Reexamination
	11897177	ACHEAMPONG ET AL.
	Examiner	**Art Unit**
	MARCELA M CORDERO GARCIA	1658

CPC		
Symbol	**Type**	**Version**

CPC Combination Sets				
Symbol	**Type**	**Set**	**Ranking**	**Version**

NONE (Assistant Examiner) (Date)		**Total Claims Allowed:** 19	
/MARCELA M CORDERO GARCIA/ Primary Examiner.Art Unit 1658 (Primary Examiner)	08/19/2013 (Date)	O.G. Print Claim(s) 1	O.G. Print Figure none

Issue Classification	Application/Control No.	Applicant(s)/Patent Under Reexamination
	11897177	ACHEAMPONG ET AL.
	Examiner	**Art Unit**
	MARCELA M CORDERO GARCIA	1658

US ORIGINAL CLASSIFICATION		INTERNATIONAL CLASSIFICATION										
CLASS	SUBCLASS	CLAIMED					NON-CLAIMED					
514	20.5	A	6	1	K	38 / 13 (2006.01.01)						
CROSS REFERENCE(S)		A	6	1	K	38 / 00 (2006.01.01)						
		A	6	1	P	9 / 10 (2006.01.01)						
CLASS	SUBCLASS (ONE SUBCLASS PER BLOCK)	A	6	1	P	27 / 02 (2006.01.01)						
514	20.8											

NONE (Assistant Examiner)	(Date)	**Total Claims Allowed:** 19	
/MARCELA M CORDERO GARCIA/ Primary Examiner.Art Unit 1658 (Primary Examiner)	08/19/2013 (Date)	O.G. Print Claim(s) 1	O.G. Print Figure none

Issue Classification	Application/Control No.	Applicant(s)/Patent Under Reexamination
	11897177	ACHEAMPONG ET AL.
	Examiner	**Art Unit**
	MARCELA M CORDERO GARCIA	1658

☒ Claims renumbered in the same order as presented by applicant ☐ CPA ☐ T.D. ☐ R.1.47

Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original

NONE (Assistant Examiner)	(Date)	**Total Claims Allowed:** 19	
/MARCELA M CORDERO GARCIA/ Primary Examiner.Art Unit 1658 (Primary Examiner)	08/19/2013 (Date)	O.G. Print Claim(s) 1	O.G. Print Figure none

PART B - FEE(S) TRANSMITTAL

Complete and send this form, together with applicable fee(s), to: Mail **Mail Stop ISSUE FEE**
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450
or Fax (571)-273-2885

INSTRUCTIONS: This form should be used for transmitting the ISSUE FEE and PUBLICATION FEE (if required). Blocks 1 through 5 should be completed where appropriate. All further correspondence including the Patent, advance orders and notification of maintenance fees will be mailed to the current correspondence address as indicated unless corrected below or directed otherwise in Block 1, by (a) specifying a new correspondence address; and/or (b) indicating a separate "FEE ADDRESS" for maintenance fee notifications.

CURRENT CORRESPONDENCE ADDRESS (Note: Use Block 1 for any change of address)

51957 7590 08/26/2013
ALLERGAN, INC.
2525 DUPONT DRIVE, T2-7H
IRVINE, CA 92612-1599

Note: A certificate of mailing can only be used for domestic mailings of the Fee(s) Transmittal. This certificate cannot be used for any other accompanying papers. Each additional paper, such as an assignment or formal drawing, must have its own certificate of mailing or transmission.

Certificate of Mailing or Transmission
I hereby certify that this Fee(s) Transmittal is being deposited with the United States Postal Service with sufficient postage for first class mail in an envelope addressed to the Mail Stop ISSUE FEE address above, or being facsimile transmitted to the USPTO (571) 273-2885, on the date indicated below.

Alexis Swan	(Depositor's name)
/Alexis Swan/	(Signature)
November 25, 2013	(Date)

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
11/897,177	08/28/2007	Andrew Acheampong	17618CON (AP)	3860

TITLE OF INVENTION: METHODS OF PROVIDING THERAPEUTIC EFFECTS USING CYCLOSPORIN COMPONENTS

APPLN. TYPE	ENTITY STATUS	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	UNDISCOUNTED	$1780	$300	$0	$2080	11/26/2013

EXAMINER	ART UNIT	CLASS-SUBCLASS
CORDERO GARCIA, MARCELA M	1658	514-020500

1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.363).
☐ Change of correspondence address (or Change of Correspondence Address form PTO/SB/122) attached.
☐ "Fee Address" indication (or "Fee Address" Indication form PTO/SB/47; Rev 03-02 or more recent) attached. **Use of a Customer Number is required.**

2. For printing on the patent front page, list
(1) the names of up to 3 registered patent attorneys or agents OR, alternatively,
(2) the name of a single firm (having as a member a registered attorney or agent) and the names of up to 2 registered patent attorneys or agents. If no name is listed, no name will be printed.

1 Laura L. Wine
2 Joel B. German
3

3. ASSIGNEE NAME AND RESIDENCE DATA TO BE PRINTED ON THE PATENT (print or type)

PLEASE NOTE: Unless an assignee is identified below, no assignee data will appear on the patent. If an assignee is identified below, the document has been filed for recordation as set forth in 37 CFR 3.11. Completion of this form is NOT a substitute for filing an assignment.

(A) NAME OF ASSIGNEE: Allergan, Inc.
(B) RESIDENCE: (CITY and STATE OR COUNTRY): Irvine, CA

Please check the appropriate assignee category or categories (will not be printed on the patent) : ☐ Individual ☒ Corporation or other private group entity ☐ Government

4a. The following fee(s) are submitted:
☒ Issue Fee
☒ Publication Fee (No small entity discount permitted)
☐ Advance Order - # of Copies _____

4b. Payment of Fee(s): **(Please first reapply any previously paid issue fee shown above)**
☐ A check is enclosed.
☐ Payment by credit card. Form PTO-2038 is attached.
☒ The Director is hereby authorized to charge the required fee(s), any deficiency, or credit any overpayment, to Deposit Account Number 010885 (enclose an extra copy of this form).

5. **Change in Entity Status** (from status indicated above)

❑ Applicant certifying micro entity status. See 37 CFR 1.29	NOTE: Absent a valid certification of Micro Entity Status (see form PTO/SB/15A and 15B), issue fee payment in the micro entity amount will not be accepted at the risk of application abandonment.
❑ Applicant asserting small entity status. See 37 CFR 1.27	NOTE: If the application was previously under micro entity status, checking this box will be taken to be a notification of loss of entitlement to micro entity status.
❑ Applicant changing to regular undiscounted fee status.	NOTE: Checking this box will be taken to be a notification of loss of entitlement to small or micro entity status, as applicable.

NOTE: The Issue Fee and Publication Fee (if required) will not be accepted from anyone other than the applicant; a registered attorney or agent; or the assignee or other party in interest as shown by the records of the United States Patent and Trademark Office.

Authorized Signature /Laura L. Wine/ Date November 25, 2013

Typed or printed name Laura L. Wine Registration No. 68,681

This collection of information is required by 37 CFR 1.311. 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 12 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, Virginia 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

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.

Electronic Patent Application Fee Transmittal

Application Number:	11897177
Filing Date:	28-Aug-2007
Title of Invention:	METHODS OF PROVIDING THERAPEUTIC EFFECTS USING CYCLOSPORIN COMPONENTS
First Named Inventor/Applicant Name:	Andrew Acheampong
Filer:	Laura Lee Wine/Alexis Swan
Attorney Docket Number:	17618CON (AP)

Filed as Large Entity

Utility under 35 USC 111(a) Filing Fees

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Basic Filing:				
Pages:				
Claims:				
Miscellaneous-Filing:				
Petition:				
Patent-Appeals-and-Interference:				
Post-Allowance-and-Post-Issuance:				
Utility Appl Issue Fee	1501	1	1780	1780
Publ. Fee- Early, Voluntary, or Normal	1504	1	300	300

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Extension-of-Time:				
Miscellaneous:				
			Total in USD ($)	**2080**

Electronic Acknowledgement Receipt

EFS ID:	17492135
Application Number:	11897177
International Application Number:	
Confirmation Number:	3860
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:	17618CON (AP)
Receipt Date:	25-NOV-2013
Filing Date:	28-AUG-2007
Time Stamp:	14:23:58
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	Deposit Account
Payment was successfully received in RAM	$2080
RAM confirmation Number	779
Deposit Account	010885
Authorized User	

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

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

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

Charge any Additional Fees required under 37 C.F.R. Section 1.19 (Document supply fees)	
Charge any Additional Fees required under 37 C.F.R. Section 1.20 (Post Issuance fees)	
Charge any Additional Fees required under 37 C.F.R. Section 1.21 (Miscellaneous fees and charges)	

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Issue Fee Payment (PTO-85B)	17618CON-Issue-Fee.pdf	2021602 8a48fc611c1db4c233a1ec3bfe922e2bb8157a10	no	2
Warnings:					
Information:					
2	Fee Worksheet (SB06)	fee-info.pdf	32411 ce7b3be71646ad4f2c6ff9591e68b4a0faca5548	no	2
Warnings:					
Information:					
		Total Files Size (in bytes):	2054013		

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.

<u>New Applications Under 35 U.S.C. 111</u>
If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

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

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

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.	ISSUE DATE	PATENT NO.	ATTORNEY DOCKET NO.	CONFIRMATION NO.
11/897,177	12/31/2013	8618064	17618CON (AP)	3860

51957 7590 12/11/2013

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

ISSUE NOTIFICATION

The projected patent number and issue date are specified above.

Determination of Patent Term Adjustment under 35 U.S.C. 154 (b)
(application filed on or after May 29, 2000)

The Patent Term Adjustment is 0 day(s). Any patent to issue from the above-identified application will include an indication of the adjustment on the front page.

If a Continued Prosecution Application (CPA) was filed in the above-identified application, the filing date that determines Patent Term Adjustment is the filing date of the most recent CPA.

Applicant will be able to obtain more detailed information by accessing the Patent Application Information Retrieval (PAIR) WEB site (http://pair.uspto.gov).

Any questions regarding the Patent Term Extension or Adjustment determination should be directed to the Office of Patent Legal Administration at (571)-272-7702. Questions relating to issue and publication fee payments should be directed to the Application Assistance Unit (AAU) of the Office of Data Management (ODM) at (571)-272-4200.

APPLICANT(s) (Please see PAIR WEB site http://pair.uspto.gov for additional applicants):

Andrew Acheampong, Irvine, CA;
Diane Tang-Liu, Newport Beach, CA;
James N. Chang, Newport Beach, CA;
David F. Power, Trabuco Canyon, CA;