agents and antineoplastic agents
INVENTOR(S): Mittmann, Ulrich; Sachetto, Jean-Pierre
PATENT ASSIGNEE(S): Tillotts Pharma AG, Switz.
SOURCE: PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005123061	A1	20051229	WO 2005-EP6413	20050615

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

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: GB 2004-13730 A 20040618
ED Entered STN: 30 Dec 2005
AB Polyunsatd. fatty acid ("PUFA") or a pharmacol. acceptable salt or derivative thereof (such as EPA and/or DHA) is used in combination with at least one of an immunosuppressive agent or an antineoplastic agent or a pharmacol. acceptable salt or derivative thereof in the treatment of conditions involving acutely or chronically inadequate immune response by topical application of said active agents to at least a portion of the intestinal mucosa. Specific conditions that may be treated include chronic inflammatory disease (e.g. Chrohn's disease and ulcerative colitis) and tumor disease (e.g. bowel cancer and prostate cancer). One advantage of preferred embodiments of the invention is that bioavailability of immunosuppressive or antineoplastic agents is increased. For example, capsules contained fish oil (over 60% of DHA and Incromega 3F60 EPA), Eudragit NE 30D coating, polysorbate 80.
REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L139 ANSWER 60 OF 73 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:1355507 HCAPLUS Full-text
DOCUMENT NUMBER: 144:74884
TITLE: A pharmaceutical compositions containing polyunsaturated fatty acids in combination with immunosuppressive agents and antineoplastic agents
INVENTOR(S): Mittmann, Ulrich; Sachetto, Jean-Pierre
PATENT ASSIGNEE(S): Tillotts Pharma AG, Switz.
SOURCE: PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005123060	A1	20051229	WO 2005-EP6412	20050615

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

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: GB 2004-13729 A 20040618

ED Entered STN: 30 Dec 2005

AB Polyunsatd. fatty acid ("PUFA") or a pharmacol. acceptable salt or derivative thereof (such as EPA and/or DHA) is used in combination with at least one of an immunosuppressive agent or an antineoplastic agent or a pharmacol. acceptable salt or derivative thereof in the treatment of conditions involving acutely or chronically inadequate immune response by topical application of said active agents to at least a portion of the intestinal mucosa. Specific conditions that may be treated include chronic inflammatory disease (e.g. Chrohn's disease and ulcerative colitis) and tumor disease (e.g. bowel cancer and prostate cancer). One advantage of preferred embodiments of the invention is that bioavailability of immunosuppressive or antineoplastic agents is increased. For example, capsules contained fish oil (over 60% of DHA and Incromega 3F60 EPA), Eudragit NE 30D coating, polysorbate 80.

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L139 ANSWER 61 OF 73 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:1223775 HCAPLUS Full-text

DOCUMENT NUMBER: 143:483122

TITLE: Methods and articles for the delivery of drugs to the eye for the treatment of posterior segment diseases

INVENTOR(S): Schultz, Clyde

PATENT ASSIGNEE(S): Directcontact LLC, USA

SOURCE: U.S. Pat. Appl. Publ., 11 pp., Cont.-in-part of U.S. Ser. No. 971,997.
CODEN: USXXCO

DOCUMENT TYPE: **Patent**

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2005255144	A1	20051117	US 2005-102454		20050409
US 2005208102	A1	20050922	US 2004-821718		20040409
US 2005074497	A1	20050407	US 2004-971997		20041022
PRIORITY APPLN. INFO.:			US 2003-461354P	P	20030409
			US 2004-821718	A2	20040409
			US 2004-971997	A2	20041022

ED Entered STN: 18 Nov 2005

AB This invention provides articles and methods for drug delivery including a hydrogel containing one or more drugs for the treatment of a posterior segment disease and/or dry eye conditions. Exemplary drugs are anti-angiogenesis compds. for the treatment of macular degeneration. Allowing passive transference of this drug from a dilute solution into the hydrogel produces the delivery system. The hydrogel, when placed in contact with the eye, delivers the drug. The delivery of the drug is sustained over an extended

period of time, which is of particular utility in the eye, which is periodically flushed with tears. This sustained delivery accelerates the treatment process while avoiding potential damaging effects of localized delivery of high concns. of compds., e.g., from eye drops.

L139 ANSWER 62 OF 73 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:983601 HCAPLUS Full-text
DOCUMENT NUMBER: 143:272523
TITLE: Stable ophthalmic oil-in-water emulsions containing sodium hyaluronate for alleviating dry eye
INVENTOR(S): Yu, Zhi-Jian; Huth, Stanley W.; Crawford, Lauren L.; Cook, James N.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 18 pp., Cont.-in-part of U.S. Ser. No. 802,153.
CODEN: USXXCO
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005196370	A1	20050908	US 2005-98827	20050404
US 2004185068	A1	20040923	US 2003-392375	20030318
US 2004191284	A1	20040930	US 2004-802153	20040317
PRIORITY APPLN. INFO.:			US 2003-392375	A2 20030318
			US 2004-802153	A2 20040317

ED Entered STN: 09 Sep 2005
AB Stable oil-in-water emulsions are described which contain a demulcent for the treatment of dry eye such as sodium hyaluronate. The oil-in-water emulsions are stable and have anti-microbial activity sufficient for use as contact lens disinfecting solns. Thus, an emulsion contained sodium chlorite 65 and WSCP 3 ppm, sodium hyaluronate 0.1, castor oil 1.25, ethoxylated hydrogenated castor oil 1, boric acid 0.6, sodium borate decahydrate 0.035, calcium chloride dihydrate 0.006, MgCl2.6H2O 0.006, KCl 0.14, NaCl 3.5, and water qs to 100%.

L139 ANSWER 63 OF 73 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:902155 HCAPLUS Full-text
DOCUMENT NUMBER: 141:384286
TITLE: Novel encochleation methods, cochleates and methods of use
INVENTOR(S): Mannino, Raphael J.; Gould-Fogerite, Susan; Krause-Elsmore, Sara L.; Delmarre, David; Lu, Ruying
PATENT ASSIGNEE(S): Biodelivery Sciences International, Inc., USA; University of Medicine and Dentistry of New Jersey
SOURCE: PCT Int. Appl., 195 pp.
CODEN: PIXXD2
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004091578	A2	20041028	WO 2004-US11026	20040409
WO 2004091578	C1	20050127		
WO 2004091578	A3	20050331		

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

US 2005013854	A1	20050120	US 2004-822230	20040409
EP 1624858	A2	20060215	EP 2004-759375	20040409

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK

PRIORITY APPLN. INFO.:		
US 2003-461483P	P	20030409
US 2003-463076P	P	20030415
US 2003-499247P	P	20030828
US 2003-502557P	P	20030911
US 2003-532755P	P	20031224
US 2004-537252P	P	20040115
US 2004-556192P	P	20040324
WO 2004-US11026	W	20040409

ED Entered STN: 28 Oct 2004

AB The invention generally relates to cochleate drug delivery vehicles. Disclose are novel methods for making cochleates and cochleate compns. that include introducing a cargo moiety to a liposome in the presence of a solvent. Also disclosed are cochleates and cochleate compns. that include an aggregation inhibitor, and optionally, a cargo moiety. Addnl., anhydrous cochleates that include a protonized cargo moiety, a divalent metal cation and a neg. charge lipid are disclosed. Methods of using the cochleate compns. of the invention, including methods of administration, are also disclosed.

L139 ANSWER 64 OF 73 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:100508 HCAPLUS Full-text
DOCUMENT NUMBER: 140:157440
TITLE: Methods for treating an autoimmune disease using a soluble CTLA4 molecule in combination with a DMARD or NSAID
INVENTOR(S): Cohen, Robert; Carr, Suzette; Hagerty, David; Peach, Robert J.; Becker, Jean-Claude
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 189 pp., Cont.-in-part of U.S. Ser. No. 898,195.
CODEN: USXXCO
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004022787	A1	20040205	US 2003-419008	20030418
US 2003083246	A1	20030501	US 2001-898195	20010702

PRIORITY APPLN. INFO.:		
US 2000-215913P	P	20000703
US 2001-898195	A2	20010702

ED Entered STN: 08 Feb 2004

AB The present invention relates to compns. and methods for treating immune system diseases such as rheumatic disease, by administering to a subject

soluble CTLA4 (cytotoxic T lymphocyte antigen 4) mols. that block endogenous B7 (CD80) mols. from binding their ligands, alone, or in conjunction with other agents including disease modifying anti-rheumatic drugs (DMARDs) or non-steroidal anti-inflammatory drugs (NSAIDs). The soluble CTLA4 mol. comprises the extracellular domain (residues 1-124) of full-length human CTLA4, which may be fused at the N-terminus with the signal peptide of oncostatin M and at the C-terminal end with an Igγ1 constant region. Single-site and double-site CTLA4 mutant sequences are also constructed, including L104E/A29Y-CTLA4/Ig, L104E/A29L-CTLA4/Ig, L104E/A29T-CTLA4/Ig, and L104E/A29W-CTLA4/Ig. CTLA4/Ig administered at 10 mg/kg (plus methotrexate) has superior efficacy in treatment of rheumatoid arthritis compared to placebo (plus methotrexate) based on efficacy parameters of the American Collage of Rheumatol. Core Data Set and Response Definitions (ACR). Binding kinetics to CD86 and CD80, pharmacokinetics, and pharmacodynamics of C-reactive protein, rheumatoid factor, interleukin-2 receptor, interleukin -6, and tumor necrosis factor α are provided.

L139 ANSWER 65 OF 73 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:9767 HCAPLUS Full-text
DOCUMENT NUMBER: 136:74627
TITLE: Drug compositions containing **cyclosporin** and their application as topical systems
INVENTOR(S): Wohlrab, Johannes; Neubert, Reinhard; Jahn, Konstanze
PATENT ASSIGNEE(S): Germany
SOURCE: Ger. Offen., 14 pp.
CODEN: GWXXBX
DOCUMENT TYPE: **Patent**
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 10029404	A1	20020103	DE 2000-10029404	20000615
CA 2470230	AA	20030626	CA 2001-2470230	20011214
WO 2003051385	A1	20030626	WO 2001-EP14749	20011214
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002231703	A1	20030630	AU 2002-231703	20011214
EP 1455810	A1	20040915	EP 2001-991845	20011214
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2001017197	A	20041214	BR 2001-17197	20011214
CN 1582161	A	20050216	CN 2001-823950	20011214
US 2005106189	A1	20050519	US 2003-498656	20011214
JP 2005516931	T2	20050609	JP 2003-552318	20011214
NZ 534061	A	20060127	NZ 2001-534061	20011214
NO 2004003001	A	20040914	NO 2004-3001	20040713
PRIORITY APPLN. INFO.:			DE 2000-10029404 A	20000615
			WO 2001-EP14749 W	20011214

ED Entered STN: 04 Jan 2002

AB The invention concerns emulsions containing **cyclosporin** for the treatment of diseases of the skin and the mucosa of the digestion and urogenital tracts, bronchi, eye: and for the prophylaxis of organ transplant rejection. The compns. can also contain other drugs, e.g. corticosteroids. The emulsions are composed of (weight/weight%): lipophilic phase 1-10; surfactants 1-50; hydrophilic phase 40-80; **cyclosporin** and other drugs 0.1-20. . Thus an emulsion contained (weight/weight%): **cyclosporin A** 2.0; Tagat O2 8.0; Synperonic PE/L101 12.0; isopropylpalmitate 5.0; propylene glycol 48.7; water 24.3.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L139 ANSWER 66 OF 73 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:741944 HCAPLUS Full-text
DOCUMENT NUMBER: 133:301214
TITLE: Eye disorders treatment with **cyclosporin-A** derivatives
INVENTOR(S): Garst, Michael E.
PATENT ASSIGNEE(S): Allergan Sales, Inc., USA
SOURCE: PCT Int. Appl., 32 pp.
CODEN: PIXXD2
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000061168	A1	20001019	WO 2000-US8877	20000404
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6254860	B1	20010703	US 1999-290833	19990413
CA 2369457	AA	20001019	CA 2000-2369457	20000404
EP 1169050	A1	20020109	EP 2000-921645	20000404
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002541207	T2	20021203	JP 2000-610500	20000404
AU 759753	B2	20030501	AU 2000-41935	20000404
NZ 514105	A	20050128	NZ 2000-514105	20000404
US 2001036449	A1	20011101	US 2001-870256	20010530
US 6350442	B2	20020226		

PRIORITY APPLN. INFO.: US 1999-290833 A 19990413
WO 2000-US8877 W 20000404

OTHER SOURCE(S): MARPAT 133:301214
ED Entered STN: 20 Oct 2000
AB A method of treating a disorder in an eye, e.g., an aqueous deficient dry eye state, phacoanaphylactic endophthalmitis, or uveitis, is provided. The method generally includes administering a therapeutically effective amount of a **cyclosporin A** derivative topically to the affected eye. The derivative may be administered as a solution, suspension or ointment in a pharmaceutically acceptable excipient. Sixteen rabbits, 32 eyes are injected intravitreally on day 1 with 500 μg of human serum albumin. Eight rabbits receive no treatment. The other rabbits received 10 μL of 2% ((R)-(Cyclo)alkylthio-Sar)3-(4'-

hydroxy-MeLeu)4-**cyclosporin A** in olive oil applied topically to both eyes 4 times daily beginning 1 h after albumin injection. The degree of intraocular inflammation produced was graded clin. 3 times a week for 3 wk. A marked difference in clin. severity of inflammation between eyes treated with the **cyclosporin A** derivative and control eyes was found.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L139 ANSWER 67 OF 73 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:487224 HCAPLUS Full-text
DOCUMENT NUMBER: 131:125456
TITLE: Method for treating inflammatory diseases using heat shock proteins
INVENTOR(S): Gelfand, Erwin W.; Haczku, Angela Francisca; Lukacs, Katalin Veronika
PATENT ASSIGNEE(S): National Jewish Medical and Research Center, USA
SOURCE: PCT Int. Appl., 69 pp.
CODEN: PIXXD2
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9937319	A1	19990729	WO 1999-US1421	19990122
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
ZA 9900499	A	19990722	ZA 1999-499	19990122
CA 2318263	AA	19990729	CA 1999-2318263	19990122
AU 9923374	A1	19990809	AU 1999-23374	19990122
BR 9907228	A	20001024	BR 1999-7228	19990122
EP 1049483	A1	20001108	EP 1999-903321	19990122
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
TR 200002973	T2	20010221	TR 2000-200002973	19990122
JP 2002509074	T2	20020326	JP 2000-528300	19990122
NO 2000003775	A	20000922	NO 2000-3775	20000721
US 2002006410	A1	20020117	US 2001-932483	20010817
PRIORITY APPLN. INFO.:			US 1998-12330 A	19980123
			WO 1999-US1421 W	19990122

ED Entered STN: 06 Aug 1999
AB A method is provided to protect a mammal from a disease associated with an inflammatory response and in particular from an inflammatory disease characterized by eosinophilia, airway hyperresponsiveness, and/or a Th2-type immune response. The method includes administration of a heat shock protein to a mammal having such a disease. Formulations useful in the present method are also disclosed.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L139 ANSWER 68 OF 73 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1997:278763 HCAPLUS Full-text
DOCUMENT NUMBER: 126:255503

TITLE: Ophthalmic compositions containing hydrocarbonaceous carrier
INVENTOR(S): Kang, Meng-Che
PATENT ASSIGNEE(S): Kang, Meng-Che, Taiwan
SOURCE: Brit. UK Pat. Appl., 12 pp.
CODEN: BAXXDU
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 2302018	A1	19970108	GB 1995-11983	19950613
GB 2302018	B2	19990825		
US 5698533	A	19971216	US 1994-280827	19940726

PRIORITY APPLN. INFO.: US 1994-280827 A 19940726
ED Entered STN: 01 May 1997
AB Compns. contain 0.01-20% drug and 80-99.99% of a hydrocarbonaceous carrier which is a semisolid at room temperature and melts at 30-100°. Typical carriers are petrolatum or lanolin. An emulsifier is optionally present. Suitable drugs for inclusion in the compns. are also listed. Delivery to the eye is particularly in nebulized form. Compns. containing vitamin A and vitamin B12 as active ingredients are exemplified. An ophthalmic composition contained petrolatum 94, camphor 5, menthol 1 g, vitamin A 500,000 IU.

L139 ANSWER 69 OF 73 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1996:359823 HCAPLUS Full-text
DOCUMENT NUMBER: 125:19006
TITLE: Improved topical carriers for mucosal applications
INVENTOR(S): Osborne, David W.
PATENT ASSIGNEE(S): Virotex Corporation, USA
SOURCE: PCT Int. Appl., 11 pp.
CODEN: PIXXD2
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9609829	A1	19960404	WO 1995-US12288	19950926
W: AU, CA, JP, KR				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9537263	A1	19960419	AU 1995-37263	19950926

PRIORITY APPLN. INFO.: US 1994-313418 A 19940927
WO 1995-US12288 W 19950926
ED Entered STN: 21 Jun 1996
AB A topical semisolid composition is claimed for use on mucosal membranes which comprises one or more hydrophilic polymers suspended in a nonaq. matrix. The composition may be combined with a therapeutic agent to assist in healing mucosal lesions. The active agent may be a local anesthetic suitable for treatment of canker sores or Behcet's syndrome, a corticosteroid for treatment of lichen planus, or **cyclosporin A**, or an antimicrobial or antifungal agent. Thus, a formulation can be prepared which contains 4-10% Carbopol, 4-10% Gantrez MS-955, 4-10% cellulose gum, and 70-88% white petrolatum.

L139 ANSWER 70 OF 73 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1996:377098 HCAPLUS Full-text
DOCUMENT NUMBER: 125:26262
TITLE: Eicosapentaenoic acid and/or docosahexaenoic acid for immunosuppressive therapy of autoimmune eye diseases
INVENTOR(S): Yazawa, Kazuyoshi; Oono, Shigeaki; Ishioka, Misaki; Nakamura, Satoshi
PATENT ASSIGNEE(S): Kanagawa Kagaku Kenkyusho Kk, Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 4 pp.
CODEN: JKXXAF
DOCUMENT TYPE: **Patent**
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 08092129	A2	19960409	JP 1993-275999	19931008
PRIORITY APPLN. INFO.:			JP 1993-275999	19931008

ED Entered STN: 29 Jun 1996
AB Eicosapentaenoic acid and/or docosahexaenoic acid are claimed for immunosuppressive therapy of autoimmune eye diseases. Thus, patients with uveitis were treated with the oral immunosuppressant FK 506 or **cyclosporin A** combined with fish oil containing 6% eicosapentaenoic acid and 25% docosahexaenoic acid with satisfactory results.

L139 ANSWER 71 OF 73 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1996:209937 HCAPLUS Full-text
DOCUMENT NUMBER: 124:242363
TITLE: Stable pharmaceutical lipid emulsions containing oils and emulsifiers and lecithins
INVENTOR(S): Suzuki, Hidekazu; Yamazaki, Satoshi; Naito, Yoshikazu; Endo, Kenji; Oguma, Touru; Maeda, Makoto
PATENT ASSIGNEE(S): Wakamoto Pharmaceutical Co., Ltd., Japan
SOURCE: Can. Pat. Appl., 77 pp.
CODEN: CPXXEB
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CA 2153553	AA	19960114	CA 1995-2153553	19950710
US 5693337	A	19971202	US 1995-500087	19950710
EP 700678	A1	19960313	EP 1995-110923	19950712
R: DE, FR, GB, IT				
JP 08081360	A2	19960326	JP 1995-197896	19950712
PRIORITY APPLN. INFO.:			JP 1994-183045 A	19940713

ED Entered STN: 12 Apr 1996
AB A lipid emulsion which comprises (A) an oil component, (B) an emulsifying agent containing yolk lecithin and/or soybean lecithin, and (C) water, wherein the lipid emulsion further comprises citric acid or a pharmaceutically acceptable salt thereof and at least one member selected from the group consisting of methionine, phenylalanine, serine, histidine and pharmaceutically acceptable salts thereof, provided that is does not simultaneously contain methionine and phenylalanine. The emulsion does not change of color and formation of oil drops associated with the conventional natural lecithin-containing lipid emulsions due to the synergistic effect of the foregoing additives. The drug containing lipid emulsion is also excellent

in storage stability and thus the foregoing lipid emulsion can be applied to drugs such as injections, eye drops, nasal drips, lotions or liniments, inhalants and drugs for oral administration or cosmetics such as humectants. A solution of 0.012 g of fluorometholone in 20 mL of ethanol was added to a solution of 20 mL hexane:ethanol (10:1) containing 0.54 g of yolk lecithin and 0.06 g of yolk phosphatidylethanolamine and mixed, followed by evaporation of solvent to obtain a lipid film. To the lipid film was added 5.4 g of soybean oil and 94 mL of 2% glycerin aqueous solution followed by vigorous stirring through shaking to carry out preliminary emulsification. The preliminarily emulsified liquid was passed through microfluidizer 10 times under a pressure of 750 kg/cm2 to emulsify the liquid, the pH value of the emulsified liquid was adjusted to 6.5-7.5 to give a milk white stock lipid emulsion.

L139 ANSWER 72 OF 73 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1996:38846 HCAPLUS Full-text
DOCUMENT NUMBER: 124:66660
TITLE: Lacrimal gland-specific emulsions for topical application to ocular tissue
INVENTOR(S): Ding, Shulin; Tien, Walter L.; Olejnik, Orest
PATENT ASSIGNEE(S): Allergan, Inc., USA
SOURCE: PCT Int. Appl., 27 pp.
CODEN: PIXXD2
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9531211	A1	19951123	WO 1995-US6302	19950517
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US, UZ				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5474979	A	19951212	US 1994-243279	19940517
CA 2190485	AA	19951123	CA 1995-2190485	19950517
CA 2190485	C	20030415		
CA 2309033	AA	19951123	CA 1995-2309033	19950517
CA 2309033	C	20030826		
AU 9526409	A1	19951205	AU 1995-26409	19950517
AU 693213	B2	19980625		
EP 759773	A1	19970305	EP 1995-921294	19950517
EP 759773	B1	20010808		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
CN 1152876	A	19970625	CN 1995-194078	19950517
BR 9507664	A	19971007	BR 1995-7664	19950517
JP 10500414	T2	19980113	JP 1995-529895	19950517
JP 3441462	B2	20030902		
EP 1044678	A1	20001018	EP 2000-202069	19950517
EP 1044678	B1	20030312		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
AT 203911	E	20010815	AT 1995-921294	19950517
ES 2161895	T3	20011216	ES 1995-921294	19950517
PT 759773	T	20020228	PT 1995-921294	19950517
AT 234076	E	20030315	AT 2000-202069	19950517
JP 2003231646	A2	20030819	JP 2003-63234	19950517

PT 1044678	T	20030829	PT 2000-202069		19950517
ES 2194670	T3	20031201	ES 2000-202069		19950517
CN 1288722	A	20010328	CN 2000-120126		20000714
HK 1034190	A1	20051209	HK 2001-104710		20010709
GR 3036945	T3	20020131	GR 2001-401814		20011018
PRIORITY APPLN. INFO.:			US 1994-243279	A	19940517
			CA 1995-2190485	A3	19950517
			EP 1995-921294	A3	19950517
			JP 1995-529895	A3	19950517
			WO 1995-US6302	W	19950517

ED Entered STN: 20 Jan 1996

AB A pharmaceutical composition is disclosed in the form of a nonirritating emulsion which includes at least one **cyclosporin** in admixt. with a higher fatty acid glyceride and polysorbate 80. More particularly, the **cyclosporin** may be **cyclosporine A** and the higher fatty acid glyceride may be castor oil. The composition allows a high comfort level and low irritation potential suitable for delivery of medications to sensitive areas such as ocular tissues with enhanced absorption in the lacrimal gland. In addition, the composition has stability for up to 9 mo without crystallization of **cyclosporin**. For example, an ophthalmic emulsion containing **cyclosporin A** 0.2, castor oil 2.5, Polysorbate-80 1.0, Pemulen 0.05, glycerol 2.2, NaOH q.s., and purified water to 100% was formulated to treat keratoconjunctivitis sicca.

L139 ANSWER 73 OF 73 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1993:140090 HCAPLUS Full-text

DOCUMENT NUMBER: 118:140090

TITLE: Effects of steroids and immunosuppressive drugs on endotoxin-uveitis in rabbits

AUTHOR(S): Ohia, Ekanem O.; Mancino, Michael; Kulkarni, Prasad S.

CORPORATE SOURCE: Sch. Med., Univ. Louisville, Louisville, KY, USA

SOURCE: Journal of Ocular Pharmacology (1992), 8(4), 295-307
CODEN: JOPHER; ISSN: 8756-3320

DOCUMENT TYPE: Journal

LANGUAGE: English

ED Entered STN: 13 Apr 1993

AB Anti-inflammatory actions of dexamethasone (DEXA), **cyclosporin A** (CSA) and rapamycin (RAPA) were assessed on uveitis induced by intravitreal E. coli endotoxin (100 ng) in rabbits at 24 h. In this model, endotoxin caused a breakdown of the blood-aqueous barrier (BAB) and polymorphonuclear neutrophils (PMN) infiltration into the aqueous humor (AH) and iris-ciliary body (ICB). DEXA given i.m. (2 mg/kg), but not topical DEXA (0.1% 6 + daily), inhibited AH leukocytes and protein level. However, both routes caused an inhibition of AH PGE2 and LTB4. In the ICB, i.m. DEXA inhibited PGE2 synthesis and myeloperoxidase (MPO) activity. Both i.m. CSA (25 mg/kg) and i.m. RAPA (10 mg/kg) inhibited the AH leukocytes and protein content and MPO activity in the ICB. RAPA also inhibited protein and eicosanoid (except AH LTB4) levels in both the AH and ICB. Interestingly, castor oil, a vehicle of CSA, also inhibited AH leukocytes and the release of PGE2 into AH and from ICB. In summary, systemic administration of DEXA and other immunosuppressive drugs (CSA and RAPA) inhibited endotoxin-induced uveitis in rabbits.

```
     FILE 'BIOSIS' ENTERED AT 16:26:29 ON 02 OCT 2006
                ACT GAR857BI1AU/A
                ---------
L1   (         1)SEA ABB=ON  PLU=ON  CYCLOSPORIN A/CN
L2   (        44)SEA ABB=ON  PLU=ON  ACHEAMPONG A?/AU
L3   (       117)SEA ABB=ON  PLU=ON  TANG LIU D?/AU
L4   (      4672)SEA ABB=ON  PLU=ON  CHANG J?/AU
L5   (       446)SEA ABB=ON  PLU=ON  POWER D?/AU
L6   (    213487)SEA ABB=ON  PLU=ON  EYE OR  ASTHENOPIA OR CONJUNCTIVAL
                DISEASES OR CORNEAL DISEASES OR EYELID DISEASES OR LACRIMAL
                APPARATUS DISEASES  OR LENS DISEASES OR OCULAR HYPERTENSION
L7   (      7948)SEA ABB=ON  PLU=ON  OCULAR HYPOTENSION  OR OCULAR MOTILITY
                DISORDERS OR OPTIC NERVE DISEASES OR ORBITAL DISEASES OR PUPIL
                DISORDERS  OR REFRACTIVE ERRORS OR RETINAL DISEASES OR
                SCLERAL DISEASES OR UVEAL DISEASES OR VISION DISORDERS OR
                VITREORETINOPATHY OR VITREOUS DETACHMENT
L8   (    124285)SEA ABB=ON  PLU=ON  OIL
L9   (     23151)SEA ABB=ON  PLU=ON  EMULSI?
L10              SEL PLU=ON  L1 1- CHEM :      38 TERMS
L11  (     46884)SEA ABB=ON  PLU=ON  L10
L12  (         0)SEA ABB=ON  PLU=ON  ((L2 OR L3 OR L4 OR L5)) AND ((L6 OR L7))
                AND L8 AND L9 AND L11
L13  (         9)SEA ABB=ON  PLU=ON  ((L2 OR L3 OR L4 OR L5)) AND ((L6 OR L7))
                AND L11
L14              9 SEA ABB=ON  PLU=ON  L12 OR L13
                 ---------

     FILE 'EMBASE' ENTERED AT 16:26:35 ON 02 OCT 2006
                ACT GAR857EM1AU/A
                ---------
L15  (         1)SEA ABB=ON  PLU=ON  CYCLOSPORIN A/CN
L16  (        21)SEA ABB=ON  PLU=ON  ACHEAMPONG A?/AU
L17  (        63)SEA ABB=ON  PLU=ON  TANG LIU D?/AU
L18  (      3346)SEA ABB=ON  PLU=ON  CHANG J?/AU
L19  (       272)SEA ABB=ON  PLU=ON  POWER D?/AU
L20              SEL PLU=ON  L15 1- CHEM :      38 TERMS
L21  (     74476)SEA ABB=ON  PLU=ON  L20
L22  (    301867)SEA ABB=ON  PLU=ON  EYE DISEASE+NT/CT
L23  (      8415)SEA ABB=ON  PLU=ON  EMULSION+NT/CT
L24  (      5657)SEA ABB=ON  PLU=ON  OIL/CT
L25  (     46238)SEA ABB=ON  PLU=ON  D3.60.650./CT
L26  (         0)SEA ABB=ON  PLU=ON  ((L16 OR L17 OR L18 OR L19)) AND L21 AND
                L22 AND L23 AND ((L24 OR L25))
L27  (         2)SEA ABB=ON  PLU=ON  ((L16 OR L17 OR L18 OR L19)) AND L21 AND
                L22 AND L23
L28  (         5)SEA ABB=ON  PLU=ON  ((L16 OR L17 OR L18 OR L19)) AND L21 AND
                L22
L29  (         0)SEA ABB=ON  PLU=ON  ((L16 OR L17 OR L18 OR L19)) AND L21 AND
                L22 AND ((L24 OR L25))
L30              5 SEA ABB=ON  PLU=ON  L26 OR (L27 OR L28 OR L29)
                 ---------

     FILE 'HCAPLUS' ENTERED AT 16:26:39 ON 02 OCT 2006
                ACT GAR857HC1AU/A
                ---------
L31  (        25)SEA ABB=ON  PLU=ON  ACHEAMPONG A?/AU
L32  (        71)SEA ABB=ON  PLU=ON  TANG LIU D?/AU
```

```
L33 (      7140)SEA ABB=ON  PLU=ON  CHANG J?/AU
L34 (       227)SEA ABB=ON  PLU=ON  POWER D?/AU
L35 (         1)SEA ABB=ON  PLU=ON  CYCLOSPORIN A/CN
L36 (     36733)SEA ABB=ON  PLU=ON  EYE, DISEASE+OLD,NT/CT
L37 (     24550)SEA ABB=ON  PLU=ON  EMULSIFYING AGENTS/CT
L38 (    388102)SEA ABB=ON  PLU=ON  OILS+OLD,NT/CT
L39             SEL PLU=ON  L35 1- CHEM :      38 TERMS
L40 (     23233)SEA ABB=ON  PLU=ON  L39
L41 (         1)SEA ABB=ON  PLU=ON  ((L31 OR L32 OR L33 OR L34)) AND L40 AND
                L36 AND L37 AND L38
L42 (        29)SEA ABB=ON  PLU=ON  ((L31 OR L32 OR L33 OR L34)) AND L40
L43 (         4)SEA ABB=ON  PLU=ON  L42 AND ((L36 OR L37 OR L38))
L44           4 SEA ABB=ON  PLU=ON  L41 OR L43
              ---------

     FILE 'MEDLINE' ENTERED AT 16:26:46 ON 02 OCT 2006
              ACT GAR857MD1AU/A
              ---------
L45 (        24)SEA ABB=ON  PLU=ON  ACHEAMPONG A?/AU
L46 (        63)SEA ABB=ON  PLU=ON  TANG LIU D?/AU
L47 (      3663)SEA ABB=ON  PLU=ON  CHANG J?/AU
L48 (       322)SEA ABB=ON  PLU=ON  POWER D?/AU
L49 (         1)SEA ABB=ON  PLU=ON  CYCLOSPORIN A/CN
L50 (      9221)SEA ABB=ON  PLU=ON  EMULSIONS+NT/CT
L51 (       124)SEA ABB=ON  PLU=ON  EMULSIFYING AGENTS/CT
L52 (     34652)SEA ABB=ON  PLU=ON  OILS+NT/CT
L53 (         0)SEA ABB=ON  PLU=ON  L45 AND L46 AND L47 AND L48
L54             SEL PLU=ON  L49 1- CHEM :      38 TERMS
L55 (     39885)SEA ABB=ON  PLU=ON  L54
L56 (    320609)SEA ABB=ON  PLU=ON  EYE DISEASES+NT/CT
L57 (         0)SEA ABB=ON  PLU=ON  ((L45 OR L46 OR L47 OR L48)) AND L56 AND
                L55 AND ((L50 OR L51)) AND L52
L58 (         2)SEA ABB=ON  PLU=ON  ((L45 OR L46 OR L47 OR L48)) AND L56 AND
                L55 AND ((L50 OR L51))
L59 (         0)SEA ABB=ON  PLU=ON  ((L45 OR L46 OR L47 OR L48)) AND L56 AND
                L55 AND L52
L60 (         5)SEA ABB=ON  PLU=ON  ((L45 OR L46 OR L47 OR L48)) AND L56 AND
                L55
L61 (         5)SEA ABB=ON  PLU=ON  (L57 OR L58 OR L59 OR L60)
L62           5 SEA ABB=ON  PLU=ON  L61 OR L53
              ---------

     FILE 'WPIX' ENTERED AT 16:26:51 ON 02 OCT 2006
              ACT GRA857WX1AU/A
              ---------
L63 (         1)SEA ABB=ON  PLU=ON  CYCLOSPORIN A/CN
L64 (         1)SEA ABB=ON  PLU=ON  ACHEAMPONG A?/AU
L65 (         7)SEA ABB=ON  PLU=ON  TANG LIU D?/AU
L66 (      3666)SEA ABB=ON  PLU=ON  CHANG J?/AU
L67 (        57)SEA ABB=ON  PLU=ON  POWER D?/AU
L68             SEL PLU=ON  L63 1- CHEM :      38 TERMS
L69 (      2231)SEA ABB=ON  PLU=ON  L68
L70 (       959)SEA ABB=ON  PLU=ON  RA0135/DCN OR 90981-1-0-0/DCRE
L71           6 SEA ABB=ON  PLU=ON  ((L64 OR L65 OR L66 OR L67)) AND ((L69 OR
                L70))
              ---------
              D QUE L14

     FILE 'BIOSIS' ENTERED AT 16:29:16 ON 02 OCT 2006
              D QUE L14
```

```
     FILE 'EMBASE' ENTERED AT 16:29:36 ON 02 OCT 2006
                D QUE L30

     FILE 'HCAPLUS' ENTERED AT 16:29:47 ON 02 OCT 2006
                D QUE L44

     FILE 'MEDLINE' ENTERED AT 16:30:01 ON 02 OCT 2006
                D QUE L62

     FILE 'WPIX' ENTERED AT 16:30:10 ON 02 OCT 2006
                D QUE L71

     FILE 'MEDLINE, BIOSIS, EMBASE, WPIX, HCAPLUS' ENTERED AT 16:31:07 ON 02
     OCT 2006
L72           19 DUP REM L62 L14 L30 L71 L44 (10 DUPLICATES REMOVED)
                     ANSWERS '1-5' FROM FILE MEDLINE
                     ANSWERS '6-11' FROM FILE BIOSIS
                     ANSWERS '12-13' FROM FILE EMBASE
                     ANSWERS '14-19' FROM FILE WPIX
                D IALL 1-5
                D IALL 6-11
                D IALL 12-13
                D IALL ABEQ TECH 14-19

     FILE 'BIOSIS' ENTERED AT 16:34:09 ON 02 OCT 2006
                ACT GRA857BI1/A
                ---------
L73 (          1)SEA ABB=ON  PLU=ON  CYCLOSPORIN A/CN
L74 (     213487)SEA ABB=ON  PLU=ON  EYE OR  ASTHENOPIA OR CONJUNCTIVAL
                  DISEASES OR CORNEAL DISEASES OR EYELID DISEASES OR LACRIMAL
                  APPARATUS DISEASES  OR LENS DISEASES OR OCULAR HYPERTENSION
L75 (       7948)SEA ABB=ON  PLU=ON  OCULAR HYPOTENSION  OR OCULAR MOTILITY
                  DISORDERS OR OPTIC NERVE DISEASES OR ORBITAL DISEASES OR PUPIL
                  DISORDERS  OR REFRACTIVE ERRORS OR RETINAL DISEASES OR
                  SCLERAL DISEASES OR UVEAL DISEASES OR VISION DISORDERS OR
                  VITREORETINOPATHY OR VITREOUS DETACHMENT
L76 (     124285)SEA ABB=ON  PLU=ON  OIL
L77 (      23151)SEA ABB=ON  PLU=ON  EMULSI?
L78              SEL PLU=ON  L73 1- CHEM :      38 TERMS
L79 (      46884)SEA ABB=ON  PLU=ON  L78
L80 (          8)SEA ABB=ON  PLU=ON  ((L74 OR L75)) AND L76 AND L77 AND L79
L81            8 SEA ABB=ON  PLU=ON  L80 NOT PY>2004
                ---------

     FILE 'EMBASE' ENTERED AT 16:34:16 ON 02 OCT 2006
                ACT GRA857EM1/A
                ---------
L82 (          1)SEA ABB=ON  PLU=ON  CYCLOSPORIN A/CN
L83              SEL PLU=ON  L82 1- CHEM :      38 TERMS
L84 (      74476)SEA ABB=ON  PLU=ON  L83
L85 (     301867)SEA ABB=ON  PLU=ON  EYE DISEASE+NT/CT
L86 (       5657)SEA ABB=ON  PLU=ON  OIL/CT
L87 (      46238)SEA ABB=ON  PLU=ON  D3.60.650./CT
L88 (     225955)SEA ABB=ON  PLU=ON  L85/MAJ
L89 (         22)SEA ABB=ON  PLU=ON  L88 AND L84 AND ((L86 OR L87))
L90 (         17)SEA ABB=ON  PLU=ON  L89 NOT PY>2004
L91 (        416)SEA ABB=ON  PLU=ON  L84(L)TP/CT
L92 (         12)SEA ABB=ON  PLU=ON  L91 AND L85 AND ((L86 OR L87))
L93 (          9)SEA ABB=ON  PLU=ON  L92 NOT PY>2004
```

```
L94           21 SEA ABB=ON  PLU=ON  L90 OR L93
                 ---------

     FILE 'HCAPLUS' ENTERED AT 16:34:17 ON 02 OCT 2006
                 ACT GAR857HC1/A
                 ---------
L95 (          1)SEA ABB=ON  PLU=ON  CYCLOSPORIN A/CN
L96 (      36733)SEA ABB=ON  PLU=ON  EYE, DISEASE+OLD,NT/CT
L97 (      24550)SEA ABB=ON  PLU=ON  EMULSIFYING AGENTS/CT
L98 (     388102)SEA ABB=ON  PLU=ON  OILS+OLD,NT/CT
L99               SEL PLU=ON  L95 1- CHEM :      38 TERMS
L100(      23233)SEA FILE=HCAPLUS ABB=ON  PLU=ON  L99
L101(          2)SEA FILE=HCAPLUS ABB=ON  PLU=ON  L100 AND L96 AND L97 AND L98
L102(          4)SEA FILE=HCAPLUS ABB=ON  PLU=ON  L96 AND L100 AND L97
L103(         17)SEA FILE=HCAPLUS ABB=ON  PLU=ON  L96 AND L100 AND L98
L104(      28869)SEA FILE=HCAPLUS ABB=ON  PLU=ON  EMULSIONS/CT
L105(          1)SEA FILE=HCAPLUS ABB=ON  PLU=ON  L96 AND L100 AND L104 AND L98
L106(          2)SEA FILE=HCAPLUS ABB=ON  PLU=ON  L96 AND L100 AND L104
L107(         20)SEA FILE=HCAPLUS ABB=ON  PLU=ON  (L101 OR L102 OR L103 OR L105
L108(         19)SEA FILE=HCAPLUS ABB=ON  PLU=ON  L107 AND PATENT/DT
L109(          1)SEA FILE=HCAPLUS ABB=ON  PLU=ON  L107 NOT L108
L110(         19)SEA FILE=HCAPLUS ABB=ON  PLU=ON  ((L108 OR L109)) NOT (PRY>2004
L111          18 SEA ABB=ON  PLU=ON  L110 NOT LIPOSOMAL COCHLEATE/TI
                 ---------

     FILE 'MEDLINE' ENTERED AT 16:34:19 ON 02 OCT 2006
                 ACT GAR857MD1/A
                 ---------
L112(          1)SEA FILE=REGISTRY ABB=ON  PLU=ON  CYCLOSPORIN A/CN
L113(       9221)SEA FILE=MEDLINE ABB=ON  PLU=ON  EMULSIONS+NT/CT
L114(        124)SEA FILE=MEDLINE ABB=ON  PLU=ON  EMULSIFYING AGENTS/CT
L115(      34652)SEA FILE=MEDLINE ABB=ON  PLU=ON  OILS+NT/CT
L116              SEL PLU=ON  L112 1- CHEM :      38 TERMS
L117(      39885)SEA FILE=MEDLINE ABB=ON  PLU=ON  L116
L118(     320609)SEA FILE=MEDLINE ABB=ON  PLU=ON  EYE DISEASES+NT/CT
L119(          1)SEA FILE=MEDLINE ABB=ON  PLU=ON  L118 AND L117 AND ((L113 OR L1
L120(         19)SEA FILE=MEDLINE ABB=ON  PLU=ON  L118 AND L117 AND ((L113 OR L1
L121(          4)SEA FILE=MEDLINE ABB=ON  PLU=ON  L118 AND L117 AND L115
L122          16 SEA ABB=ON  PLU=ON  ((L119 OR L120 OR L121)) NOT PY>2004
                 ---------

     FILE 'WPIX' ENTERED AT 16:34:21 ON 02 OCT 2006
                 ACT GRA857WX1/A
                 ---------
L123(          1)SEA FILE=REGISTRY ABB=ON  PLU=ON  CYCLOSPORIN A/CN
L124(      73228)SEA FILE=WPIX ABB=ON  PLU=ON  EYE/BI,ABEX OR  ASTHENOPIA/BI,ABE
L125(        650)SEA FILE=WPIX ABB=ON  PLU=ON  OCULAR HYPOTENSION/BI,ABEX  OR OC
L126(     444197)SEA FILE=WPIX ABB=ON  PLU=ON  OIL/BI,ABEX
L127(     169370)SEA FILE=WPIX ABB=ON  PLU=ON  EMULSI?/BI,ABEX OR (A10-B03 OR B1
L128(        598)SEA FILE=WPIX ABB=ON  PLU=ON  (K04-E01 OR H06-B09 OR G06-F01B)/
L129              SEL PLU=ON  L123 1- CHEM :      38 TERMS
L130(       2231)SEA FILE=WPIX ABB=ON  PLU=ON  L129
L131(        959)SEA FILE=WPIX ABB=ON  PLU=ON  RA0135/DCN OR 90981-1-0-0/DCRE
L132(         20)SEA FILE=WPIX ABB=ON  PLU=ON  ((L130 OR L131)) AND ((L124 OR L1
L133          17 SEA ABB=ON  PLU=ON  L132 NOT PRY>2004
                 ---------

     FILE 'BIOSIS' ENTERED AT 16:36:17 ON 02 OCT 2006
                 D QUE L81
L134           8 SEA ABB=ON  PLU=ON  L81 NOT L14
```

```
     FILE 'EMBASE' ENTERED AT 16:36:48 ON 02 OCT 2006
                D QUE L94
L135         21 SEA ABB=ON  PLU=ON  L94 NOT L30

     FILE 'HCAPLUS' ENTERED AT 16:37:21 ON 02 OCT 2006
                D QUE L111
L136         17 SEA ABB=ON  PLU=ON  L111 NOT L44

     FILE 'MEDLINE' ENTERED AT 16:37:49 ON 02 OCT 2006
                D QUE L122
L137         14 SEA ABB=ON  PLU=ON  L122 NOT L62

     FILE 'WPIX' ENTERED AT 16:38:39 ON 02 OCT 2006
                D QUE L133
L138         16 SEA ABB=ON  PLU=ON  L133 NOT L71

     FILE 'MEDLINE, BIOSIS, EMBASE, WPIX, HCAPLUS' ENTERED AT 16:39:41 ON 02
     OCT 2006
L139         73 DUP REM L137 L134 L135 L138 L136 (3 DUPLICATES REMOVED)
                     ANSWERS '1-14' FROM FILE MEDLINE
                     ANSWERS '15-21' FROM FILE BIOSIS
                     ANSWERS '22-41' FROM FILE EMBASE
                     ANSWERS '42-57' FROM FILE WPIX
                     ANSWERS '58-73' FROM FILE HCAPLUS
                D IALL 1-14
                D IALL 15-21
                D IALL 22-41
                D IALL ABEQ TECH 42-57
                D IBIB ED ABS 58-73


=>
```

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.
10/927,857	08/27/2004	Andrew Acheampong	D-3111	2409

33197 7590 10/13/2006

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

EXAMINER	
CORDERO GARCIA, MARCELA M	

ART UNIT	PAPER NUMBER
1654	

DATE MAILED: 10/13/2006

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

Office Action Summary	Application No.	Applicant(s)	
	10/927,857	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 an eye of a human or animal, classified, e.g., in class 514, subclass 11.

II. Claims 21-36, drawn to a composition for treating an eye of a human or animal, classified, e.g., in class 530, subclass 317.

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 instantly claimed compositions may also be used, e.g., to treat skin infections.

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.

In addition, this application contains claims directed to the following patentably distinct species: the many and multiple compositions encompassed by the instant claims (e.g. claim 21), the many and multiple diseases to be treated (e.g., claim 2) and methods thereof. The species are independent or distinct because each composition

has a different ratio of components and/or chemically different hydrophobic components.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species [i.e., elect a single composition indicating all its components: the cyclosporin used (e.g., claims 23-24), the % per weight of the cyclosporin component, the hydrophobic component (e.g., claim 28), and the weight ratio of the cyclosporin component to the hydrophobic component. In addition, if Group I is elected, please also elect a single type of condition to be treated (see e.g., claim 2)] 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 and 21 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, Ph.D.
Patent Examiner
Art Unit 1654

MMMCG 09/06

Cecilia J. Tsang
Supervisory Patent Examiner
Technology Center 1600

RECEIVED
CENTRAL FAX CENTER
NOV 10 2006

TRANSMITTAL FORM

(to be used for all correspondence after initial filing)

Application Number	10/927,857
Filing Date	8/27/2004
First Named Inventor	Acheampong
Group Art Unit	1654
Examiner Name	Cordero Garcia, M.M.
Attorney Docket Number	D-3111

Total Number of Pages in This Submission

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)*

Remarks

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

Firm Name	Stout, Uxa, Buyan & Mullins, LLP		
Signature	Frank J. Uxa		
Printed Name	Frank J. Uxa		
Date	11/10/2006	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	Janet McGhee		
Typed or printed name	Janet McGhee	Date	11/10/2006

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Appl. No.	: 10/927,857	Confirmation No. 2409
Applicant	: Acheampong	
Filed	: 08/27/2004	
Title	: METHODS OF PROVIDING THERAPEUTIC EFFECTS USING CYCLOSPORINE COMPONENTS	
TC/A.U.	: 1654	
Examiner	: CORDERO GARCIA, M.M.	
Docket No.	: D-3111	
Customer No.	: 33197	

CERTIFICATE OF FACSIMILE TRANSMISSION

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

November 10, 2006 Janet McGhee

RESPONSE TO RESTRICTION REQUIREMENT AND ELECTION OF SPECIES REQUIREMENT

Commissioner for Patents
Po Box 1450
Alexandria, VA 22313-1450

Sir:

This is in response to the Examiner's communication mailed October 13, 2006, which included a Restriction Requirement and an Election of Species Requirement.

The Examiner has required restriction between the Group I Claims, that is Claims 1-20, drawn to a method of treating an eye of a human or animal, and Group II Claims, that is Claims 21-36, drawn to a composition for treating an eye of a human or animal.

Applicant provisionally elects the Group II claims, that is claims 21-36.

The Examiner has also required election of a single disclosed composition species indicating the cyclosporine, the percent by weight of the cyclosporine component, the hydrophobic component and the weight ratio of the cyclosporine component to the hydrophobic component.

Applicant provisionally elects the species comprising cyclosporin A, a cyclosporine component concentration of less than 0.1% by weight, vegetable oils as the hydrophobic component and a weight ratio of the cyclosporine component to the hydrophobic component of less than 0.08.

The claims which read on this elected species include claims 21-36.

Applicant traverses the restriction requirement and the election of species requirement.

Independent method claim 1 appears to include all the limitations of independent composition claim 21. The present method claims and the present composition claims are thus closely related so that the Patent and Trademark Office is placed under no undue burden in considering and examining all the present claims in the above-identified application.

With regard to the election of species requirement, the definitions of a cyclosporine component and a hydrophobic component are clearly set forth in the present specification. The cyclosporine component concentration and weight ratio of cyclosporine component to hydrophobic component are set forth in the independent claims. The different species identified by the Examiner are closely related and can be considered and examined

together without placing an undue burden on the Patent and Trademark Office.

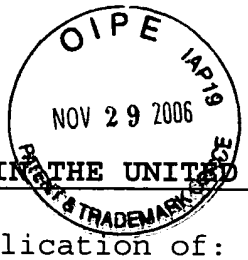
In view of the above, applicant respectfully requests that the restriction requirement and the election of species requirement be withdrawn.

Applicant respectfully requests early and favorable action in the above-identified application.

Respectfully submitted,

Frank J. Uxa
Attorney for Applicant
Reg. No. 25,612
4 Venture, Suite 300
Irvine, CA 92618
(949) 450-1750
Facsimile (494) 450-1764

D-3111



TFW

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

PATENT

In re application of:
Acheampong et al.) Group Art Unit: 1654
)
Serial No. 10/927,857) Examiner: Unknown
)
Filed: August 27, 2004)
)
For: METHODS OF PROVIDING)
THERAPEUTIC EFFECTS USING)
CYCLOSPORIN COMPONENTS)

I hereby certify that this correspondent is being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Commissioner for Patents, PO Box 1450, Alexandria, VA 22313-1450, on or before

November 27, 2006
Date

Alicia Curran

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

SUPPLEMENTAL 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.

Respectfully submitted,

Frank J. Uxa
Attorney for Applicant
Reg. No. 25,612
4 Venture, Suite 300
Irvine, CA 92618
(949) 450-1750
Facsimile (949) 450-1764

FJUxa/ac

U.S. DEPARTMENT OF COMMERCE
PATENT AND TRADEMARK OFFICE
FORM PTO-1449

LIST OF ART CITED BY APPLICANT

ATTY. DOCKET: D-3111	SERIAL NO.: 10/927,857
APPLICANT: Acheampong et al	TITLE: Methods of Providing Therapeutic Effects Using Cyclosporine Components
FILING DATE: August 27, 2004	GROUP: 1654

U.S. PATENT DOCUMENTS

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

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
	CQ	D.E. Lopatin. Chemical compositions and functions of Saliva. 8/24/2001, 31 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.

LIST OF ART CITED BY APPLICANT

ATTY. DOCKET: D-3111	SERIAL NO.: 10/927,857
APPLICANT: Acheampong et al	TITLE: Methods of Providing Therapeutic Effects Using Cyclosporine Components
FILING DATE: August 27, 2004	GROUP: 1654

	CR	Gunduz et al, "Topical Cyclosporin Treatment of Keratoconjunctivitis Sicca in Se condary 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.

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.

EAST Search History

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L2	1919	cyclosporine.clm. or cyclosporin.clm.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2006/12/27 18:27
L3	384	l2 and (hydrophobic.clm. or oil.clm.)	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2006/12/27 18:28
L4	12	l2 and (hydrophobic.clm. or oil.clm.) and allergan	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2006/12/27 18:52

EAST Search History

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L10	47	cyclosporine near3 oil	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2006/12/27 19:28

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.
10/927,857	08/27/2004	Andrew Acheampong	D-3111	2409

33197 7590 01/17/2007

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

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

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/17/2007	PAPER

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

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/927,857	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 *10 November 2006*.

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) *1-20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21-36* 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 *12/04, 3/05, 11/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This Office Action is in response to the reply received on November 10, 2006. Claims 1-36 are pending in the application.

Applicant elected with traverse Group II, claims 21-36, drawn to a composition for treating an eye of a human or animal. In addition, Applicant elected with traverse the species comprising "cyclosporin A, a cyclosporine component concentration of less than 0.1%, vegetable oils as the hydrophobic component, and a weight ratio of the cyclosporine component to the hydrophobic component of less than 0.08".

Applicant argues that the independent method claim 1 appears to include all the limitations of independent composition claim 21 and therefore it would not be undue burden in considering and examining all claims. Applicant also argues that the definitions of the hydrophobic component are clearly set forth in the present specification and that the concentration and weight ratios of the cyclosporine component are set forth in the independent claims. Applicant's arguments have been considered but not deemed persuasive for the reasons of record and because of the following arguments: The instant restriction is between the product (Group II) and a process of using thereof (Group I). 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 claimed cyclosporine compositions may also be used to

study, e.g., the stability of emulsions, emulsion particle size and/or tandem mass spectrometric fragmentation patterns of cyclosporine compounds. 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. Because these inventions are independent or distinct for the reasons given above and there would be a serious burden on the examiner if restriction is not required because the inventions require a different field of search (see MPEP § 808.02), restriction for examination purposes as indicated is proper. Thus, it would be an undue burden to examine all of the above inventions in one application and therefore, the restriction requirement is still deemed proper and is therefore made FINAL.

Please note that, as set forth in the previous Office Action, pursuant to the procedures set forth in MPEP § 821.04(B), the claims directed to the process of making or using an allowable product, and previously withdrawn from consideration as a result of a restriction requirement, would be rejoined and fully examined for patentability under 37 CFR 1.104 after the elected product (as in this instant case) has found to be allowable.

In regards to the species requirement traversal, Applicant's arguments have been carefully considered but not deemed persuasive because as set forth in the previous Office Action, this application contains claims directed to patentably distinct species: the many and multiple compositions encompassed by

the instant claims and methods thereof. The species are independent or distinct because the instant compositions are drawn to a multitude of compositions (and methods thereof) encompassing cyclosporin A and derivatives and functional analogs thereof (or mixtures thereof) in combination with a hydrophobic component encompassing vegetable oils, animal oils, mineral oils, synthetic oils, non-oily hydrophobic components and mixtures thereof combined so that the weight of the cyclosporine component to the weight of the hydrophobic component is less than 0.08. The instant compositions (and methods thereof) are drawn to a large number of combinations, e.g., (cyclosporin A/castor oil) in a ratio of 0.02, (cyclosporine derivative/corn oil) in a ratio of 0.03, (cyclosporin A+cyclosporine derivative/castor oil+mineral oil) in a ratio of 0.007, (cyclosporin Analog/non-oily hydrophobe) in a ratio of 0.001; and so forth. The cyclosporine component encompasses cyclosporine, any derivatives thereof and any functional analogs thereof, which are drawn to a plethora of different chemical formulas. The hydrophobic component encompasses, e.g., vegetable oils, animal oils, mineral oils, synthetic oils and mixtures thereof, non-oily hydrophobic substances and so forth. The combinations of cyclosporine/hydrophobic components and the ratios variations for the combinations above encompass countless different and distinct compositions thereby meeting the species requirement. Therefore, the election requirement is still deemed proper and is therefore made FINAL.

Claims 1-20 are withdrawn as not drawn to the elected invention.

Claims 21-36 are presented for examination on the merits as they read upon the instantly elected species, i.e., "a composition comprising cyclosporin A, a cyclosporine component concentration of less than 0.1%, vegetable oils as the hydrophobic component, and a weight ratio of the cyclosporine component to the hydrophobic component of less than 0.08".

Claim Rejections - 35 USC § 112

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

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

Claims 21-36 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The MPEP states that the purpose of the written description requirement is to ensure that the inventor had possession, as of the filing date of the application, of the specific subject matter later claimed by him. The courts have stated:

> "To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is

> claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966." Regents of the University of California v. Eli Lilly & Co., 43 USPQ2d 1398.

The MPEP lists factors that can be used to determine if sufficient evidence of possession has been furnished in the disclosure of the Application. These include "level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention. Disclosure of any combination of such identifying characteristics that distinguish the claimed invention from other materials and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient." MPEP 2163.

Further, for a broad generic claim, the specification must provide adequate written description to identify the genus of the claim. In Regents of the University of California v. Eli Lilly & Co., the court stated:

> "A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials. Fiers, 984 F.2d at 1171, 25 USPQ2d at 1606; In re Smythe, 480 F.2d 1376, 1383, 178 USPQ 279, 284-85 (CCPA 1973) ("In other cases, particularly but not necessarily, chemical cases, where there is unpredictability in performance of certain species or subcombinations other than those specifically enumerated, one skilled in the art may be found not to have been placed in possession of a genus. . . ."). Regents of the University of California v. Eli Lilly & Co., 43 USPQ2d 1398.

The MPEP further states that if a biomolecule is described only by a functional characteristic, without any disclosed correlation between function and structure of the sequence, it is "not sufficient characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence." MPEP 2163. The MPEP does state that for generic claim the genus can be adequately described if the disclosure presents a sufficient number of representative species that encompass the genus. MPEP 2163. If the genus has a substantial variance, the disclosure must describe a sufficient variety of species to reflect the variation within that genus. See MPEP 2163. Although the MPEP does not define what constitute a sufficient number of representative, the Courts have indicated what do not constitute a representative number species to adequately describe a broad generic. In Gostelli, the Court determined that the disclosure of two chemical compounds within a subgenus did not describe that subgenus. In re Gostelli, 872 F.2d at 1012, 10 USPQ2d at 1618.

In the instant case, the claims are drawn to a composition for treating an eye of a human or an animal, comprising an emulsion comprising water, a hydrophobic component, and a cyclosporine component in a therapeutically effective amount of less than 0.1% by weight, the weight ratio of the cyclosporine component to the hydrophobic component being less than 0.08. The "hydrophobic component" is not limited to any compound with hydrophobicity including any type of oils, fatty acid glycerides and any other hydrophobic-type compounds (e.g., pages 15-16) and the "cyclosporine component" is not limited to cyclosporine but to any cyclosporin A derivatives and mixtures thereof having similar functionality to cyclosporine (e.g., pages 11-12). As stated earlier, the MPEP states that written description for a genus can be achieved by a representative number of species within a

broad generic. It is unquestionable claim 21 is a broad generic with respect all possible compounds encompassed by the claims. The possible structural variations are limitless to any class of polymer with any biomolecule. It must not be forgotten that the MPEP states that if a biomolecule is described only by a functional characteristic (e.g., hydrophobic), without any disclosed correlation between function and structure of the sequence, it is not sufficient characteristic for written description purposes, even when accompanied by a method of obtaining the claimed compound (see MPEP 2163). Here, though the claims may recite some functional characteristics, the claims lack written description because there is no disclosure of a correlation between function and structure of the hydrophobic component beyond compounds disclosed in the examples in the specification (see, e.g., page 26). In addition, one of skill in the art would not know how to find and use all the instantly claimed derivatives of cyclosporine based on the guidance presented, since it basically provides a guidance in terms of functionality, but the functionality is disclosed, i.e., is the functionality of the cyclosporine derivatives that functionality depending on its physical, chemical, bonding, spectrometric, biological, antibiotic or any other properties? The recitation of a few chemical modifications is not sufficient in light of the examples presented (i.e., a single example with cyclosporin A and a comparison formulation). Moreover, the specification lack sufficient variety of species to reflect this variance in the genus since the specification provides examples only one single example of a composition encompassed by the instant claims: with cyclosporin A (as the cyclosporine compound) and castor oil (as the hydrophobic component) and does not encompass any other species from the very broad genus that is claimed in Claim 21. The description requirement of the patent statute requires a description of an invention, not an indication of a result that

one might achieve if one made that invention. See In re Wilder, 736 F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate."). Accordingly, it is deemed that the specification fails to provide adequate written description for the genus of the claims and does not reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the entire scope of the claimed invention.

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 21-36 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.

Claim 21 is rendered vague and indefinite because it is unclear as what kind of derivatives of cyclosporine. The instant disclosure teaches that the term derivatives refers to compounds having structures sufficiently similar to the cyclosporine so as to function in a manner substantially similar to, or substantially identical to cyclosporine. However, the metes and bounds for such derivatives are not clearly delineated since it is unclear what kind of specific functionality one would look at in order to find the instant derivatives of the molecule cyclosporine.

Claim 21 is also rendered vague and indefinite by the recitation of the term "hydrophobic component". The metes and bounds of this component and therefore of the compositions thereof are not well delineated. The instant disclosure teaches that "any suitable hydrophobic component may be employed", however it is not clear what a suitable hydrophobic component is, e.g., does it encompass any and all compounds that are predominantly hydrophobic such as, e.g., fullerenes, hydrophobic cellulose, polyethylene and so forth. In addition, does this term encompass a hydrophilic compound possessing a hydrophobic area? If so, what size of a molecule needs to be hydrophobic in order to make a compound suitably hydrophobic and therefore usable within the instantly claimed compositions.

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 21-36 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 12/27/04).

Ding et al. teach a composition for treating an eye of a human or animal comprising an emulsion comprising water, a hydrophobic component, and cyclosporine component in a therapeutically effective amount of less than 0.1% by weight, the weight ratio of the cyclosporine 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. do not expressly teach the weight ratio of the cyclosporine component to the hydrophobic component being less than 0.08.

Ding et al. teach that the weight ratio of the cyclosporine component to the hydrophobic component may be preferably varied between 0.12 and 0.02 (see, e.g., column 3, lines 19-20).

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. (e.g., Example 1D) by increasing the amount of castor oil in order to reduce the ratio of the cyclosporine component to hydrophobic component from 0.08 to, e.g., 0.02 as taught by Ding et al. (see, e.g., column 3, lines 30-37). The skilled artisan would have been motivated to do so because the compositions encompass castor oil from 0.625% (as in Example 1E) or higher up to 5.0% (see, and Ding et al., claim 8). 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) and because optimizing the ratio of cyclosporine/hydrophobic components to below 0.08 was taught by Ding et al. (e.g., column 3, lines 30-37). Please note that the limitation of claim 22 (wherein the blood of the human has substantially no detectable concentration of the cyclosporine component after application of the composition) would necessarily exist in a composition with the instantly claimed limitations as taught above. The limitation of claim 23 and 24 is taught, e.g., in column 3, lines 30-37; the limitation of claim 25 is taught in column 3, lines 21-27 and 57-67; the limitation of claim 26-27 is taught by Example 1D, the limitation of claims 28-29 is taught in column 3, lines 5-14; the limitation of claim 30 is taught by Ding et al.'s claim 8; the limitation of claim 31 is taught in column 3, line 38-40; the limitations of claim 32-33 is taught in column 4, lines 12-19; the limitation of claim 34 is taught in column 3, lines 64-67 and column 4, lines 1-12; the limitations of claims 35-36 is taught in Example 1D.

Thus the invention as a whole was clearly prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Claims 21-36 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 12/27/04) in view of Ding et al. (Pharm. Res, 1997).

Ding et al. (US 5,474,979) teach a composition for treating an eye of a human or animal comprising an emulsion comprising water, a hydrophobic component, and cyclosporine component in a therapeutically effective amount of

less than 0.1% by weight, the weight ratio of the cyclosporine 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. do not expressly teach the weight ratio of the cyclosporine component to the hydrophobic component being less than 0.08.

Ding et al. (Pharm Res, 1997) teach a composition for treating an eye of a huma comprising an emulsion comprising water, a hydrophobic component, and cyclosporine component the weight ration of the cyclosporine component (cyclosporine) to the hydrophobic component (castor oil, a vegetable oil) is 0.074. The composition is a pH-adjusted, oil-in water emulsion with a polysorbate 80 as primary emulsifier and a polyelectrolyte (such as Pemulen) (see entire abstract, e.g., lines 1-12).

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. in US '979 (e.g., Example 1D) by increasing the amount of castor oil in order to reduce the ratio of the cyclosporine component to hydrophobic component from 0.08 to, e.g., 0.074 as taught by Ding et al. in Pharm. Res. (see, e.g., column 3, lines 30-37). The skilled artisan would have been motivated to do so because Ding et al. (Pharm. Res.) teaches that the compositions with 0.074 cyclosporin/castor oil are stable at room temperature for at least 18 months. 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) and because optimizing the ratio of cyclosporine/hydrophobic components to below

0.08 was taught by Ding et al. US '979 (e.g., column 3, lines 30-37) and Pharm. Res. (abstract, line 12). Thus the invention as a whole was clearly prima facie obvious to one of ordinary skill in the art at the time the invention was made. Please note that the limitation of claim 22 (wherein the blood of the human has substantially no detectable concentration of the cyclosporine component after application of the composition) would necessarily exist in a composition with the instantly claimed limitations as taught above. The limitation of claim 23 and 24 is taught, e.g., in column 3, lines 30-37; the limitation of claim 25 is taught, e.g., in column 3, lines 21-27 and 57-67; the limitation of claim 26-27 is taught by Example 1D, the limitation of claims 28-29 is taught in column 3, lines 5-14; the limitation of claim 30 is taught by Ding et al.'s claim 8; the limitation of claim 31 is taught in column 3, line 38-40; the limitations of claim 32-33 is taught in column 4, lines 12-19; the limitation of claim 34 is taught in column 3, lines 64-67 and column 4, lines 1-12; the limitations of claims 35-36 is taught in Example 1D.

Double Patenting

Claims 21-36 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-8 of U.S. Patent No. 5,474,979. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instantly claimed invention and the invention claimed in US '979 are both drawn to a composition for treating an eye of a human or animal comprising an emulsion comprising water, a hydrophobic component, and cyclosporine component in a therapeutically

effective amount of less than 0.1% by weight, the weight ratio of the cyclosporine component to the hydrophobic component being less than 0.08. (See, e.g., Example 1D and column 3, lines 19-20 teaching that the weight ratio of cyclosporin A to castor oil is preferably between 0.12 and 0.02. In addition, see claim 8, encompassing species within the instantly claimed compositions).

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-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, PhD
Patent Examiner
Art Unit 1654

MMCG 12/06

1/8/07
ANISH GUPTA
PRIMARY EXAMINER

Form PTO-1449

DEC 27 2004

U.S. PATENT & TRADEMARK OFFICE

INFORMATION DISCLOSURE CITATION IN AN APPLICATION

(Use several sheets if necessary)

Docket No.: D-3111	Application No.: 10/927,857
Applicant: Acheampong et al.	
Filing Date: August 27, 2004	Group Art Unit: 1636

U. S. PATENT DOCUMENTS

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

MMCG	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.*
MMCG	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
/Marcela M Cordero Garcia/	12/26/2006

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 the applicant.

Form PTO-1449

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

Docket No.: D-3111	Application No.: 10/927,857
Applicant: Acheampong et al.	
Filing Date: August 27, 2004	Group Art Unit: 1636

U. S. PATENT DOCUMENTS

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

MMCG	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.*
MMCG	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
/Marcela M Cordero Garcia/	12/26/2006

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 the applicant.

Form PTO-1449	Docket No.: D-3111	Application No.: 10/927,857
INFORMATION DISCLOSURE CITATION IN AN APPLICATION (Use several sheets if necessary)	Applicant: Acheampong et al.	
	Filing Date: August 27, 2004	Group Art Unit: 1636

U. S. PATENT DOCUMENTS

EXAMINER INITIAL	DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE
MMCG	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			
MMCG	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	
	AB	
	AC	
	AD	
	AE	
	AF	
	AG	
	AH	

EXAMINER	DATE CONSIDERED
/Marcela M Cordero Garcia/	12/26/2006

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 the applicant.

Form PTO-1449	Docket No.: D-3111	Application No.: 10/927,857
INFORMATION DISCLOSURE CITATION IN AN APPLICATION (Use several sheets if necessary)	Applicant: Acheampong et al.	
	Filing Date: August 27, 2004	Group Art Unit: 1636

U. S. PATENT DOCUMENTS

EXAMINER INITIAL	DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE
MMCG	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.			
MMCG	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	
	AB	
	AC	
	AD	
	AE	
	AF	
	AG	

EXAMINER	DATE CONSIDERED
/Marcela M Cordero Garcia/	12/26/2006

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 the applicant.

Form PTO-1449

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

Docket No.: D-3111	Application No.: 10/927,857
Applicant: Acheampong et al.	
Filing Date: August 27, 2004	Group Art Unit: 1636

U. S. PATENT DOCUMENTS

EXAMINER INITIAL	DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE
MMCG	2001/0036449 A1	11/2001	Garst			

FOREIGN PATENT DOCUMENTS

	DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION YES	TRANSLATION NO

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

	AA	
	AB	
	AC	
	AD	
	AE	
	AF	
	AG	
	AH	

EXAMINER	DATE CONSIDERED
/Marcela M Cordero Garcia/	12/26/2006

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 the applicant.

U.S. DEPARTMENT OF COMMERCE
PATENT AND TRADEMARK OFFICE
FORM PTO-1449

LIST OF ART CITED BY APPLICANT

ATTY. DOCKET: D-3111	SERIAL NO.: 10/927,857
APPLICANT: Acheampong et al	TITLE: Methods of Providing Therapeutic Effects Using Cyclosporine Components
FILING DATE: August 27, 2004	GROUP: 1654

U.S. PATENT DOCUMENTS

*EXAMINER INITIAL		DOCUMENT NO.	DATE	NAME	CLASS	SUB-CLASS	FILING DATE (if applicable)
MMCG	AA	2003/0055028 A1	03/2003	Stergiopoulos et al.			
	AB	5,368,854	11/1994	Rennick			
	AC	4,614,736	09/1986	Delevallee et al.			
MMCG	AD						

FOREIGN PATENT DOCUMENTS

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

OTHER ART

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

MMCG	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
MMCG	CQ	D.E. Lopatin. Chemical compositions and functions of Saliva. 8/24/2001, 31 pages

EXAMINER /Marcela M Cordero Garcia/ DATE CONSIDERED 12/26/2006

*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.

U.S. DEPARTMENT OF COMMERCE
PATENT AND TRADEMARK OFFICE
FORM PTO-1449

LIST OF ART CITED BY APPLICANT

ATTY. DOCKET: D-3111	SERIAL NO.: 10/927,857
APPLICANT: Acheampong et al	TITLE: Methods of Providing Therapeutic Effects Using Cyclosporine Components
FILING DATE: August 27, 2004	GROUP: 1654

MMCG	CR	Gunduz et al, "Topical Cyclosporin Treatment of Keratoconjunctivitis Sicca in Se condary 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
MMCG	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.

EXAMINER /Marcela M Cordero Garcia/ DATE CONSIDERED 12/26/2006

*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.

Notice of References Cited	Application/Control No. 10/927,857	Applicant(s)/Patent Under Reexamination ACHEAMPONG ET AL.	
	Examiner Marcela M. Cordero Garcia	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-6,872,705	03-2005	Lyons, Robert T.	514/13
	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	Kuwano et al. Cyclosporine A Formulation Affects Its Ocular Distribution in Rabbits. Pharm Res January 2002. Vol. 19 No. 1, pages 108-111
	V	Ding et al. Cyclosporine Ophthalmic o/w Emulsion: Formulation and Emulsion Characterization. Pharmaceutical Resaerch 1997. 14(11, suppl):S41 (2 pages).
	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.

UNITED STATES PATENT AND TRADEMARK OFFICE

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

Bib Data Sheet

CONFIRMATION NO. 2409

SERIAL NUMBER	FILING OR 371(c) DATE	CLASS	GROUP ART UNIT	ATTORNEY DOCKET NO.
10/927,857	08/27/2004 RULE	514	1654	D-3111

APPLICANTS

Andrew Acheampong, Irvine, CA; MMC6
Diane Tang-Liu, Newport Beach, CA; MMC6
James N. Chang, Newport Beach, CA; MMC6
David F. Power, Trabuco Canyon, CA; MMC6

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

This appln claims benefit of 60/503,137 09/15/2003 MMC6

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

-NONE-

IF REQUIRED, FOREIGN FILING LICENSE GRANTED
** 10/21/2004

Foreign Priority claimed	STATE OR COUNTRY	SHEETS DRAWING	TOTAL CLAIMS	INDEPENDENT CLAIMS
☐ yes ☑ no	CA	0	36	2

35 USC 119 (a-d) conditions met: ☐ yes ☑ no ☐ Met after Allowance

Verified and Acknowledged: Examiner's Signature MMC6 Initials

ADDRESS
33197

TITLE

Methods of providing therapeutic effects using cyclosporin components

FILING FEE RECEIVED		
1058	FEES: Authority has been given in Paper No. _____ to charge/credit DEPOSIT ACCOUNT No. _____ for following:	☐ All Fees ☐ 1.16 Fees (Filing) ☐ 1.17 Fees (Processing Ext. of time) ☐ 1.18 Fees (Issue) ☐ Other _____ ☐ Credit

Search Notes	Application/Control No.	Applicant(s)/Patent under Reexamination	
	10/927,857	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 (attached)	10/2/2006	MMCG
EAST searched (attached)	12/27/2006	MMCG
also ran PALM inventor search	12/27/2006	MMCG

RECEIVED
CENTRAL FAX CENTER
MAR 27 2007

TRANSMITTAL FORM

(to be used for all correspondence after initial filing)

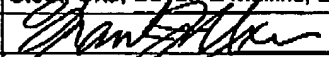
Application Number	11/927,857
Filing Date	8/27/2004
First Named Inventor	Acheampong
Group Art Unit	1654
Examiner Name	Cordero Garcia, M.M.
Total Number of Pages in This Submission	20
Attorney Docket Number	D-3111

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)*

Remarks

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

Firm Name	Stout, Uxa, Buyan & Mullins, LLP		
Signature			
Printed Name	Frank J. Uxa		
Date	3/23/07	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	Alicia Curran		
Typed or printed name	Alicia Curran	Date	3/27/07

RECEIVED
CENTRAL FAX CENTER
MAR 27 2007

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 ($)

Complete if Known	
Application Number	11/927,857
Filing Date	8/27/2004
First Named Inventor	Acheampong
Examiner Name	Cordero Garcia, M.M.
Art Unit	1654
Attorney Docket No.	D-3111

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 Frank J. Uxa

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

☒ Charge any additional fee(s) associated with this communication ☒ Credit any overpayments

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.

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	
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) 0

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 ____ -20 or HP = ____ x Fee ($) ____ Fee Paid ($) ____

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

Indep. Claims ____ -3 or HP = ____ x Fee ($) ____ Fee Paid ($) ____

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

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

Subtotal (2) 0

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).

Total Sheets ____ -100 = ____ Extra Sheets ____ /50= ____ Number of each additional 50 or fraction thereof (round up to a whole number) x Fee ($) ____ = Fee Paid ($) ____

Subtotal (3) 0

4. OTHER FEE(S) Fee Paid ($)

- ☐ Surcharge - Late filing fee or oath/declaration: $130 fee ($65 small entity discount)
- ☐ Non-English Specification: $130 fee (no small entity discount)
- ☐ 1-month extension of time: $120 fee ($60 small entity discount)
- ☐ 2-month extension of time: $450 fee ($225 small entity discount)
- ☐ 3-month extension of time: $1020 fee ($510 small entity discount)
- ☐ 4-month extension of time: $1590 fee ($795 small entity discount)
- ☐ 5-month extension of time: $2160 fee ($1080 small entity discount)
- ☐ Information Disclosure Statement Fee: $180 fee (no small entity discount)
- ☐ Notice of Appeal: $500 fee ($250 small entity discount)
- ☐ Filing a Brief in Support of Appeal: $500 fee ($250 small entity discount)
- ☐ Request for Oral Hearing: $1000 fee ($500 small entity discount)
- ☐ Utility Issue Fee: $1400 fee ($700 small entity discount)
- ☐ Recording each patent assignment per property (times number of properties): $40 fee (no small entity fee discount)
- ☐ Request for Continued Examination: $790 fee ($395 small entity discount)
- ☐ Other: ____

Subtotal (4) 0

SUBMITTED BY

Name (Print/Type)	Frank J. Uxa	Registration No. (Attorney/Agent)	25,612	Telephone	949-450-1750
Signature				Date	3/23/07

RECEIVED
CENTRAL FAX CENTER
MAR 27 2007

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Appl. No. : 10/927,857 Confirmation No. 2409
Applicant : ACHEAMPONG ET AL.
Filed : August 27, 2004
Title : METHODS OF PROVIDING THERAPEUTIC EFFECTS USING CYCLOSPORIN COMPONENTS

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

Docket No. : D-3111
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: March 27, 2007
Name: Alicia Curran

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

AMENDMENT A

Sir:

In response to the Office Action mailed January 17, 2007, please amend the above-identified application as follows:

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

Remarks/Arguments begin on page 7 of this paper.

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

Listing of Claims

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

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

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

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

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

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

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

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

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

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

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

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

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

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

21. (Currently Amended) A composition for treating an eye of a human or animal comprising an emulsion comprising water,

~~a hydrophobic component~~ castor oil, and ~~a cyclosporin component~~ cyclosporin A in a therapeutically effective amount of less than 0.1% by weight, the weight ratio of the ~~cyclosporin component~~ cyclosporin A to the ~~hydrophobic component~~ castor oil being less than 0.08.

22. (Currently Amended) 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~~ cyclosporin A.

23. (Canceled)

24. (Canceled)

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

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

27. (Canceled)

28. (Canceled)

29. (Canceled)

30. (Currently Amended) The composition of claim 21 ~~wherein the administering step comprises topically administering~~

~~the composition to the eye of the human~~ having a make-up so that when the composition is topically 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 A.

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

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

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

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

35. (Original) 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. (Original) 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 composition of claim 21 which includes 1.25% by weight of castor oil.

38. (New) The composition of claim 21 which includes 0.05% by weight of cyclosporin A.

39. (New) The composition of claim 38 which includes 1.25% by weight of castor oil.

40. (New) A composition for treating an eye of a human or animal comprising an emulsion comprising water, 1.25% by weight of castor oil and 0.05% by weight of cyclosporin A, the weight ratio of the cyclosporin A to the castor oil being 0.04.

Remarks

The above-identified application has been carefully reviewed in light of the Office Action mailed January 17, 2007.

Without conceding the correctness of any of the Examiner's rejections, applicant has amended certain of the present claims to facilitate prosecution of the above-identified application to an early allowance. Applicant expressly reserves the right to seek patent protection for the original claims and for any other claims supported by the above-identified application in one or more related applications.

Specifically, claim 21 has been amended to refer to castor oil rather than a hydrophobic component; and to cyclosporin A instead of a cyclosporin component. Claims 22 and 26 have been amended to be consistent with the amendments to claim 21. Claim 30 has been amended to read more clearly. Claims 23, 24 and 27-29 have been canceled in view of the amendments to claim 21. New claims 37-40 have been added and are directed to embodiments for which patent protection is sought.

Each of the amendments and the new claims is fully supported by the present specification and the claims as originally filed.

Claims 1-20 have been withdrawn as being directed to a non-elected invention. Applicant hereby requests rejoinder of these method of use claims when the composition claims are found to be allowable.

Claims 21-36 have been rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. Claims 21-36 have been rejected under 35 U.S.C. 112, second paragraph.

In view of the above-noted amendments, applicant submits that the present claims 21, 22, 25, 26 and 30-40 satisfy the

requirements of 35 U.S.C. 112, first and second paragraphs. Therefore, applicant respectfully requests that both these rejections under 35 U.S.C. 112 be withdrawn.

Claims 21-36 have been rejected under 35 U.S.C. 103(a) as being obvious over Ding et al U.S. Patent No. 5,474,979 (hereinafter Ding et al Patent). Claims 21-36 have been rejected under 35 U.S.C. 103(a) as being obvious over Ding et al Patent in view of Ding et al (Pharm. Res., 1997) (hereinafter Ding et al Publication). Applicant traverses each of these rejections as it pertains to the present claims 21, 22, 25, 26 and 30-40.

Independent claim 21 is directed to a composition for treating an eye of a human or animal. The composition comprises an emulsion comprising castor oil and cyclosporin A in a therapeutically effective amount of less than 0.1% by weight. In addition, as recited in claim 21, the weight ratio of the cyclosporin A to the castor oil is less than 0.08.

New independent claim 40 is directed to a composition for treating an eye of a human or animal comprising an emulsion comprising water, 1.25% by weight of castor oil and 0.05% by weight of cyclosporin A, and the weight ratio of the cyclosporin to the castor oil is 0.04.

The present compositions provide substantial advantages. For example, as illustrated in Example 1 of the present specification, Composition II, a composition in accordance with the present invention, and Composition I, a composition having a higher concentration of cyclosporin A, are tested in use for the

treatment of dry eye disease. In relevant part, the make-ups of these two compositions are as follows[1]:

	Composition I wt%	Composition II wt%
Cyclosporin A	0.1	0.05
Castor Oil	1.25	1.25
Weight Ratio of Cyclosporin A to Castor Oil	0.08	0.04

[1]Each composition includes the same weight percent of Polysorbate 80, Premulen®, and Glycerin; and includes sodium hydroxide and water, and has a pH of 7.2-7.6.

Each of 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.

Using relatively large 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 slit-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 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 Composition I.

Ding et al Patent discloses a composition comprising cyclosporin A in admixture with an emulsifying amount of castor oil and polysorbate 80. Ding et al Patent discloses that preferably the composition has a weight ratio of castor oil to polysorbate 80 between about 0.3 and about 30 and a weight ratio of cyclosporin A to castor oil of below 0.16. Ding et al Patent discloses that 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 0.02. See Ding et al Patent, column 3, lines 15-20. In Example 1, Ding et al

Patent discloses a series of five (5) cyclosporin A-containing emulsions. In relevant part, the make-ups of these five (5) emulsions are as follows[(2)]:

	Composition, wt%				
	A	B	C	D	E
Cyclosporin A	0.40%	0.20%	0.20%	0.10%	0.05%
Castor Oil	5.00%	5.00%	2.50%	1.25%	0.625%
Weight Ratio of Cyclosporin A to Castor Oil	0.08	0.04	0.08	0.08	0.08

[(2)]Each composition includes the same weight percent of Polysorbate 80, Premulen®, and Glycerin; and includes sodium hydroxide and water, and has a pH of 7.2-7.6.

Each of the above-noted emulsions of Ding et al Patent has a weight ratio of cyclosporin A to castor oil of 0.08, except for Composition B, which includes a relatively large amount of cyclosporin A (0.2%) outside the range of cyclosporin A concentrations recited in the present claims, and has a cyclosporin A to castor oil weight ratio of 0.04. Ding et al Patent placed no significance on Composition B relative to Compositions A, C and D of Example 1. Moreover, Composition D, specifically cited by the Examiner, includes more cyclosporin A than in the presently claimed compositions, as well as having a weight ratio of cyclosporin A to castor oil outside the range recited in the present claims.

Claim 8 of Ding et al Patent discloses compositions having make ups similar to those of Example 1 of Ding et al Patent.

The Examiner's citation of Ding et al Patent column 3, lines 30-37 is not understood.

Ding et al Patent does not specifically disclose, teach or suggest the present invention. For example, Ding et al Patent does not specifically disclose, teach or even suggest a composition comprising an emulsion comprising water, castor oil and cyclosporin A in an amount of less than 0.1% by weight, for example, 0.05% by weight, with the weight ratio of cyclosporin A to castor oil being less than 0.08 and/or the castor oil being 1.25% by weight of the composition, as recited in the present claims. Moreover, Ding et al Patent does not specifically disclose, teach or even suggest the substantial, even surprising advantages of the present compositions, for example, in terms of efficacy in treating dry eye disease, more rapid breaking down or resolving the emulsion in the eye and mitigation against undesirable side effects and potential drug interactions, obtained in accordance with the present invention.

Contrary to the Examiner's contention, Ding et al Patent does not teach or even suggest optimizing the weight ratio of cyclosporin A/castor oil to below 0.08. In fact, since four of the five compositions tested in Example 1 of Ding et al Patent have such a weight ratio of 0.08, Ding et al Patent appears to consider 0.08 the optimum weight ratio of cyclosporin A to castor oil. As noted above, Ding et al Patent does not specifically distinguish between compositions having relatively wide variations in cyclosporin A concentrations and castor oil concentrations, such as Compositions A, B, C and D of Example 1 of this reference. Thus, applicant submits that Ding et al Patent actually teaches away from the presently claimed compositions and the substantial, surprising advantages of such compositions obtained by applicant.

Simply put, Ding et al Patent provides no motivation nor any other proper basis to one of ordinary skill in the art to extend the teachings of Ding et al Patent to make obvious the present compositions having the compositional parameters recited in the present claims, let alone obtaining the substantial, surprising advantages of the present compositions obtained by applicant.

Therefore, applicant submits that claims 21, 22, 25, 26 and 30-40 are unobvious from and patentable over Ding et al Patent under 35 U.S.C. 103(b).

The Examiner relies on Ding et al Publication to supplement the teachings of Ding et al Patent.

The disclosure and deficiencies of Ding et al Patent are discussed above and are resubmitted here.

Ding et al Publication discloses a stable, pH-adjusted, oil-in-water emulsion using castor oil as the internal phase to solubilize cyclosporine, polysorbate 80 as the primary emulsifier and a polyelectrolyte as a stabilizer. Ding et al Publication discloses that the concentration of cyclosporin in the oil globule is formulated at a level of 7.4% w/w, meaning that the weight ratio of the cyclosporine to castor oil is 0.074/0.926 or 0.08.

Ding et al Publication does not disclose, teach or suggest the present invention. For example, Ding et al Publication does not disclose a composition with any specific cyclosporin A concentration, let alone a composition having a cyclosporin A concentration of less than 0.1% by weight, for example, 0.05% by weight, as recited in the present claims. In addition, Ding et al Publication does not disclose, teach or even suggest a composition in which the weight ratio of cyclosporin A to castor oil is less than 0.08 and/or the castor oil is 1.25% by weight

of the composition, as recited in the present claims. By disclosing only a composition having a weight ratio of cyclosporin to castor oil of 0.08, Ding et al Publication reinforces the apparent teaching of Ding et al Patent that the optimum weight ratio of cyclosporin A to castor oil is 0.08. To a large extent, Ding et al Publication actually teaches away from the present claims.

The combination of Ding et al Patent and Ding et al Publication does not disclose, teach or suggest the present invention. For example, this combination of references does not disclose, teach or suggest compositions comprising less than 0.1% by weight, for example 0.05% by weight, of cyclosporin A and castor oil in which the weight ratio of cyclosporin A to castor oil is less than 0.08 and/or the castor oil is 1.25% by weight of the composition, let alone the substantial and even surprising advantages of such compositions obtained by applicant.

As noted above, both Ding et al Patent and Ding et al Publication actually teach away from the present invention. These references provide no motivation nor any other proper basis to one of ordinary skill in the art to make obvious the compositions recited in the present invention, let alone obtain the substantial surprising advantages of the present compositions obtained by applicant. Simply put, Ding et al Publication does not supply the deficiencies apparent in the teachings of Ding et al Publication with respect to the present claims.

In view of the above, applicant submits that claims 21, 22, 25, 26 and 30-40 are unobvious from and patentable over Ding et al Patent in view of Ding et al Publication under 35 U.S.C. 103(a).

Claims 21-36 have been rejected on the ground of non-statutory obviousness-type double patenting as being unpatentable over claims 1-8 of Ding et al Patent. Applicant traverses these rejections as it pertains to claims 21, 22, 25, 26 and 30-40.

For substantially the same reasons, as stated above, that the present claims are patentable over Ding et al Patent, so too are the present claims patentable over claims 1-8 of Ding et al Patent.

For example, none of claims 1-8 of Ding et al Patent specifically disclose, teach or suggest the present invention. To illustrate, none of claims 1-8 of Ding et al Patent specifically disclose, teach or even suggest a composition comprising less than 0.1% by weight, for example, 0.05% by weight, of cyclosporin A, and castor oil in which the weight ratio of cyclosporin A to castor oil is less than 0.08 and/or the castor oil is 1.25% by weight of the composition, as recited in the present claims, let alone the substantial, surprising advantages of such compositions, discussed above, obtained by applicant.

The Examiner states that claim 8 of Ding et al Patent encompasses species within the instantly claimed compositions. Applicant disagrees.

Claim 8 does not specifically disclose compositions including less than 0.1% by weight of cyclosporin A in which the weight ratio of cyclosporin A to castor oil is less than 0.08, as in the presently claimed compositions. Moreover, the relatively wide ranges of cyclosporin A and castor oil concentrations recited in claim 8 of Ding et al Patent actually lead away from the present claims, and the substantial and

surprising advantages of the presently claimed compositions obtained by applicant.

To a large extent, the disclosure of claim 8 of Ding et al Patent is similar to that of Example 1 of Ding et al Patent, which has been discussed previously. Claim 8, like Example 1, of Ding et al Patent does not distinguish one composition from the other compositions. Neither does column 3, lines 19-20 of Ding et al Patent, cited by the Examiner. As noted previously, Ding et al Patent does not teach optimizing the weight ratio of cyclosporin A to castor oil to below 0.08. Rather, since four of the five compositions tested in Example 1 of Ding et al Patent have such a weight ratio of 0.08, Ding et al Patent appears to consider 0.08 the optimum weight ratio of cyclosporin A to castor oil.

None of the Compositions A, B, C, D and E of Ding et al Patent specifically disclose, teach or suggest the presently claimed compositions. As noted previously, Ding et al Patent does not distinguish the Compositions of Example 1, one from the other. In effect, the claims, including claim 8, of Ding et al Patent discloses that compositions with relatively wide ranges of concentrations of cyclosporin A and castor oil have similar properties. Such teaching actually leads away from the presently claimed compositions and the substantial, surprising advantages, discussed previously, obtained by applicant relative to compositions encompassed by the claims of Ding et al Patent.

In view of the above, applicant submits that claims 21, 22, 25, 26 and 30-40 are patentable over the claims of Ding et al Patent, and respectfully requests that the obviousness-type double patenting rejection based on claims 1-8 of Ding et al Patent be withdrawn.

Each of the present dependent claims is separately patentable over the prior art. For example, none of the prior art, taken single or in any combination, disclose, teach or even suggest the present compositions including the additional feature or features recited in any of the present dependent claims. Therefore, applicant submits that all of the present claims are separately patentable over the prior art.

In conclusion, applicant has shown that the present claims satisfy the requirements of 35 U.S.C. 112, first and second paragraphs; are unobvious from and patentable over the prior art; and are not subject to obviousness type double patenting based on claims 1-8 of Ding et al Patent. Therefore, applicant submits that the present claims, that is claims 21, 22, 25, 26 and 30-40, are allowable and respectfully requests the Examiner to pass the above-identified application to issuance at an early date. Should any matters remain unresolved, applicant requests the Examiner to telephone applicant's attorney at the telephone number given below.

Respectfully submitted,

Date: 3/23/07

Frank J Uxa
Attorney for Applicant
Registration No. 25,612
4 Venture, Suite 300
Irvine, California 92618
(949) 450-1750
(949) 450-1764 Facsimile

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

PATENT APPLICATION FEE DETERMINATION RECORD

Substitute for Form PTO-875

Application or Docket Number	Filing Date	☐ To be Mailed
10/927,857	08/27/2004	

APPLICATION AS FILED – PART I

FOR	(Column 1) NUMBER FILED	(Column 2) NUMBER EXTRA	SMALL ENTITY RATE ($)	SMALL ENTITY FEE ($)	OR	OTHER THAN SMALL ENTITY RATE ($)	OTHER THAN SMALL ENTITY FEE ($)
☐ BASIC FEE (37 CFR 1.16(a), (b), or (c))	N/A	N/A	N/A			N/A	
☐ 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	03/27/2007	(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))	* 35	Minus	** 36	= 0	X $ =		OR	X $50=	0
	Independent (37 CFR 1.16(h))	* 3	Minus	***3	= 0	X $ =		OR	X $200=	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:
Rozenia Harmon

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.
10/927,857	08/27/2004	Andrew Acheampong	D-3111	2409

33197 7590 07/02/2007

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
07/02/2007	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)	
	10/927,857	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 *27 March 2007*.

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) *1-22,25-26, 30-40* 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) *1-22,25,26 and 30-40* 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: _____.

DETAILED ACTION

This Office Action is in response to the reply received on March 27, 2007.

Claims 1-22, 25-26, 30-40 are pending in the application. New claims 37-40 have been added. Any rejection from the previous office action, which is not restated here, is withdrawn.

Claims 1-20 are withdrawn as not drawn to the elected invention. Claims 21-22, 25-26 and 30-36 were originally examined as they read upon the instantly elected species, i.e., "a composition comprising cyclosporin A, a cyclosporine component concentration of less than 0.1%, vegetable oils as the hydrophobic component, and a weight ratio of the cyclosporine component to the hydrophobic component of less than 0.08".

Applicant has now amended claims 21-22, 25-26 substituting the term "cyclosporine component" for "cyclosporin A" and the term "hydrophobic component" for "castor oil". Applicant has also amended claim 30 to include the limitation "having a make-up so that when the composition is topically 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 A."

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 1-22, 25-26, 30-40 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 12/27/04).

Ding et al. teach a composition for treating an eye of a human or animal comprising an emulsion comprising water, a hydrophobic component, and cyclosporine component in a therapeutically effective amount of less than 0.1% by weight, the weight ratio of the cyclosporine 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. do not expressly teach the weight ratio of the cyclosporine component to the hydrophobic component being less than 0.08.

Ding et al. teach that the weight ratio of the cyclosporine component to the hydrophobic component may be preferably varied between 0.12 and 0.02 (see, e.g., column 3, lines 19-20). 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 21) 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 21 "the weight ratio of he cyclosporin A to the castor oil being less than 0.08".

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. (e.g., Example 1D) by increasing the amount of castor oil or decreasing the cyclosporine concentration in order to reduce the ratio of the cyclosporine component to hydrophobic component from 0.08 to, e.g., 0.02 as taught by Ding et al. (see, e.g., column 3, lines 18-20). Following the ranges taught by claim 8 of Ding et al. as above one skilled in the art would readily envisage the claimed composition. The skilled artisan would have been motivated to do so because the compositions taught by Ding et al. teach (see 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 21) 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 21 "the weight ratio of he cyclosporin A to the castor oil being less than 0.08" and therefore one skilled in the art would have readily envisaged compositions reading upon the limitations of the instantly claimed compositions. 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) and because optimizing the ratio of cyclosporine/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). Please note that the limitation of claim 22 (wherein the blood of the human has substantially no detectable concentration of the cyclosporine component after application of the composition) would necessarily read upon a composition with the instantly claimed limitations as taught above. The limitation of claim 25 is taught in column 3, lines 21-27 and 57-67; the limitation of claim 26 is taught, e.g., in Example 1D, the limitation of claim 30 is taught by Ding et al.'s claim 8; the limitation of claim 31 is taught in column 3, lines 38-40; the limitations of claim 32-33 is taught in column 4, lines 12-19; the limitation of claim 34 is taught in column 3, lines 64-67 and column 4, lines 1-12; the limitations of claims 35-36 are taught, e.g., in Example 1D, column 4, line 43. The limitations of claims 37-40 are not expressly taught, but the claimed species reads upon the instant range as taught with sufficient specificity by the motivation set forth above (0.05% by weight of cyclosporin A, which is the lower limit of the range as claimed in claim 8, 1.25% of castor oil, which is within the range taught by Ding et al. of 0.625% to 5.0% for castor oil, and 0.04 is encompassed by the range of ratios taught at column 3, lines 18-20, 0.02-0.12). The adjustment of particular conventional working conditions (e.g., determining appropriate concentrations and ratios within such compositions) is deemed merely a matter of judicious selection and routine optimization that is well within the purview of the skilled artisan.

Thus the invention as a whole was clearly prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Applicant's arguments

Applicant argues that Ding et al. Patent discloses a composition comprising cyclosporin A in admixture with an emulsifying amount of castor oil and polysorbate 80. Ding et al. Patent discloses that preferably the composition has a weight ratio of castor oil to polysorbate 80 between about 0.3 and about 30 and a weight ratio of cyclosporin A to castor oil below 0.16. Ding et al. Patent discloses that more preferably the weight ratio of castor oil to polysorbate 80 is between 0.5 and 12.5 and the weight of cyclosporine to castor oil between 0.12 and 0.02. (e.g., column 3, lines 15-20). In example 1, Ding et al. Patent discloses a series of five (5) cyclosporin A-containing emulsions. In relevant part, the make-ups of these five emulsions are as follows, with each composition including the same weight percent of polysorbate 80, Permulen ®, and Glycerin; and includes sodium hydroxide and water, and has a pH of 7.2-7.6::

	A	B	C	D	E
Cyclosporin A	0.40%	0.2%	0.2	0.10%	0.05%
Castor Oil	5.00%	5.00%	2.5%	1.25%	.625%
Weight ratio Cyclosporin A/Castor Oil	0.08	0.04	0.08	0.08	0.08

Each of the above-noted emulsions of Ding et al. Patent has a weight ratio of cyclosporin A to castor oil of 0.08, except for Composition B, which includes a relatively large amount of cyclosporin A (0.2%) outside the range of cyclosporine concentrations recited in the present claims (upper limit 0.1%), and has a cyclosporin A to castor oil

weight ratio of 0.04. Ding et al placed no significance on Composition B relative to Compositions A, C or D of Example 1. Moreover, Composition D, specifically cited by the Examiner, includes more cyclosporin A than in the presently claimed inventions, as well as having a weight ratio of cyclosporin A to castor oil outside the range recited in the present claims.

Claim 8 of Ding et al. Patent discloses compositions having make ups similar to those of Example 1 of Ding et al. Patent. The Examiner's citation of Ding et al. Patent of column 3, lines 30-37 is not understood.

Ding et al. Patent does not specifically disclose, teach or suggest the present invention. For example, Ding et al. Patent does not specifically disclose, teach or even suggest a composition comprising an emulsion comprising water, castor oil and cyclosporin A in an amount of less than 0.1 % by weight, for example, 0.05% by weight, with the weight ratio of cyclosporin A to castor oil being less than 0.08 and/or the castor oil being 1.25 % by weight of the composition, as recited in the present claims. Moreover, Ding et al. Patent does not specifically disclose, teach or even suggest the substantial, even surprising efficacy in treating dry eye disease, more rapid breaking down or resolving the emulsion in the eye and mitigation against undesirable side effects and potential drug interactions, obtained in accordance with the present invention.

Contrary to the Examiner's contention, Ding et al. Patent does not teach or even suggest optimizing the weight ratio of cyclosporin A/castor oil to below 0.08. In fact, since four of the five compositions tested in Example 1 of Ding et al Patent have such a

weight ratio of 0.08, Ding et al Patent appears to consider 0.08 the optimum weight ratio of cyclosporin A to castor oil. As noted above, Ding et al. Patent does not specifically distinguish between compositions having relatively wide variations in cyclosporin A concentrations and castor oil concentrations. Thus, Applicant submits that Ding et al. Patent actually teaches away from the presently claimed compositions and the substantial, surprising advantages of such compositions obtained by Applicant.

Simply put, Ding et al. Patent provides no motivation nor any other proper basis to one of ordinary skill in the art to extend the teachings of Ding et al Patent to make obvious the present compositions having the compositional parameters recited in the present claims, let alone obtaining the substantial, surprising advantages of the present composition.

The Examiner relies on Ding et al. Publication to supplement the teachings of Ding et al. Patent. The disclosure and deficiencies of Ding et al. Patent are discussed above and are resubmitted here.

Ding et al. Publication discloses a stable, pH-adjusted, oil-in-water emulsion using castor oil as the internal phase to solubilize cyclosporine, polysorbate 80 as the primary emulsifier and a polyelectrolyte as a stabilizer. Ding et al. publication discloses that the concentration of cyclosporin in the oil globule is formulated at a level of 7.4% w/w/, meaning that the weight ratio of the cyclosporine to castor oil is 0.074/0.926 or 0.08.

Ding et al. Publication does not disclose, teach or suggest the present invention. For example, Ding et al. Publication does not disclose a composition with any specific

cyclosporin A concentration, let alone a composition having a cyclosporin concentration of less than 0.1% by weight., for example, 0.05% by weight, as recited in the present claims. In addition, Ding et al. Publication does not disclose, teach or even suggest a composition in which the weight ratio of cyclosporin A to castor oil is less than 0.08 and/or the castor oil is 1.25% by weight of the composition, as recited in the present claims. By disclosing only a composition having a weight ratio of cyclosporin to castor oil of 0.08, Ding et al. Publication reinforces the apparent teaching of Ding et al. Patent that the optimum weight ratio of cyclosporin A to castor oil is 0.08. To a large extent, Ding et al. Publication actually teaches away from the present claims.

The combination of Ding et al. Patent and Ding et al. Publication does not disclose, teach or suggest the present invention. For example, this combination of references does not disclose, teach or suggest compositions comprising less than 0.1% by weight, for example 0,05% by weight, of cyclosporin A and castor oil in which the weight ratio of cyclosporin A to castor oil is less than 0.08 and/or the castor oil is 1.25% by weight of the composition, let alone the substantial and even surprising advantages of such compositions obtained by applicant.

Applicant also argues (pages 10 and 11) that the present compositions provide substantial advantages. For example, as illustrated in Example 1 of the present specification, Composition II, a composition in accordance with the present invention, and Composition I, a composition having a higher concentration of cyclosporin A, are

tested in use for the treatment of dry eye disease. In relevant part, the make-ups of these two compositions are as follows:.

	Composition I, wt%	Composition II, wt%
Cyclosporin A	0.1	0.05
Castor Oil	1.25	1.25
Weight Ratio of Cyclosporin A To Castor Oil	0.08	0.04

Note: each composition includes the same weight percent of polysorbate 80, premulen, glycerin and includes sodium hydroxide and water, and has a pH of 7.2 to 7.6

Each of 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 efficacy in treating dry eye disease.

Using relatively large amounts of castor oil, with reduced amounts of cyclosporine 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 cyclosporine 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 measure by slit-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 aide effects and potential drug interactions. Prescribing physicians can prescribe Composition II to more patients and/or with fewer restrictions and/or with reduced risk of the occurrence of adverse effects, drug interactions and the like, relative to Composition I.

Response to Arguments

Applicant's arguments above have been fully considered but they are not persuasive.

According to MPEP 2144.05:

> "In the case where the claimed ranges "overlap or lie inside ranges disclosed by the prior art" a prima facie case of obviousness exists. In re Wertheim, 541 F.2d 257, 191 USPQ 90 (CCPA 1976); In re Woodruff, 919 F.2d 1575, 16 USPQ2d 1934 (Fed.Cir. 1990) (The prior art taught carbon monoxide concentrations of "about 1-5%" while the

claim was limited to "more than 5%." The court held that "about 1-5%" allowed for concentrations slightly above 5% thus the ranges overlapped.); In re Geisler, 116 F.3d 1465, 1469-71, 43 USPQ2d 1362, 1365-66 (Fed. Cir. 1997) (Claim reciting thickness of a protective layer as falling within a range of "50 to 100 Angstroms" considered prima facie obvious in view of prior art reference teaching that "for suitable protection, the thickness of the protective layer should be not less than about 10 nm [i.e., 100 Angstroms]." The court stated that "by stating that suitable protection' is provided if the protective layer is about' 100 Angstroms thick, [the prior art reference] directly teaches the use of a thickness within [applicant's] claimed range."). Similarly, a prima facie case of obviousness exists where the claimed ranges and prior art ranges do not overlap but are close enough that one skilled in the art would have expected them to have the same properties. Titanium Metals Corp. of America v. Banner, 778 F.2d 775, 227 USPQ 773 (Fed. Cir. 1985) (Court held as proper a rejection of a claim directed to an alloy of "having 0.8% nickel, 0.3% molybdenum, up to 0.1% iron, balance titanium" as obvious over a reference disclosing alloys of 0.75% nickel, 0.25% molybdenum, balance titanium and 0.94% nickel, 0.31% molybdenum, balance titanium.). "[A] prior art reference that discloses a range encompassing a somewhat narrower claimed range is sufficient to establish a prima facie case of obviousness." In re Peterson, 315 F .3d 1325, 1330, 65 USPQ2d 1379, 1382-83 (Fed. Cir. 2003). >See also In re Harris, 409 F.3d 1339, 74 USPQ2d 1951 (Fed. Cir. 2005) (claimed alloy held obvious over prior art alloy that taught ranges of weight percentages overlapping, and in most instances completely encompassing, claimed ranges; furthermore, narrower ranges taught by reference overlapped all but one range in claimed invention."

The Ding et al. Patent does indeed disclose, teaches and suggest the present invention, and it is not deemed to teach away from the present invention (MPEP 2145) because: The skilled artisan would have been motivated to do so because the compositions taught by Ding et al. teach (see 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 21) and between 0.625 and about 5.0 % castor oil. The corresponding lower ratio to the

lower range limit of 0.05%/5.0% = 0.01 weight ratio of cyclosporin A/castor oil, which reads upon the limitation in claim 21 "the weight ratio of the cyclosporin A to the castor oil being less than 0.08" and therefore one skilled in the art would have readily envisaged the instant compositions. 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) and because optimizing the ratio of cyclosporine/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). In addition, Applicant's arguments with respect to the Examples provided by the disclosure of Ding et al. Patent claiming that such examples teach away from the invention have been carefully considered by Examiner but not deemed persuasive because Ding et al. Patent teaches at column 5, lines 36-43 and column 6, line 1, that:

> "Although there has been hereinabove described a particular pharmaceutical composition in the form of a nonirritating emulsion for the purpose of illustrating the manner in which the invention may be used to advantage, it should be appreciated that the invention is not limited thereto. Accordingly, any and all modifications, variations, or equivalent arrangements, which may occur to those skilled in the art, should be considered to be within the scope of the present invention as defined in the appended claims."

MPEP 2144.05, with regards to Optimization Within Prior Art Conditions or Through Routine Experimentation, states:

> "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. "[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) (Claimed process which was performed at a temperature between 40°C and 80°C and an acid concentration between 25% and 70%

> was held to be prima facie obvious over a reference process which differed from the claims only in that the reference process was performed at a temperature of 100°C and an acid concentration of 10%.); see also Peterson, 315 F.3d at 1330, 65 USPQ2d at 1382 ("The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages."); In re Hoeschele, 406 F.2d 1403, 160 USPQ 809 (CCPA 1969) (Claimed elastomeric polyurethanes which fell within the broad scope of the references were held to be unpatentable thereover because, among other reasons, there was no evidence of the criticality of the claimed ranges of molecular weight or molar proportions.). For more recent cases applying this principle, see Merck & Co. Inc. v. Biocraft Laboratories Inc., 874 F.2d 804, 10 USPQ2d 1843 (Fed. Cir.), cert. denied, 493 U.S. 975 (1989); In re Kulling, 897 F.2d 1147, 14 USPQ2 1056 (Fed.Cir. 1990); and In re Geisler, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997).

Thus, the adjustment of particular conventional working conditions (e.g., determining appropriate concentrations and ratios within such compositions) is deemed merely a matter of judicious selection and routine optimization that is well within the purview of the skilled artisan, based on the teaching set forth in claim 8 and column 3, lines 18-20 as described above.

> .See also MPEP 2145: "Furthermore, "the prior art's mere disclosure of more than one alternative does not constitute a teaching away from any of these alternatives because such disclosure does not criticize, discredit, or otherwise discourage the solution claimed...." In re Fulton, 391 F.3d 1195, 1201, 73 USPQ2d 1141, 1146 (Fed. Cir. 2004)."

With respect to the unexpected results arguments set in Applicant's response, Examiner notes that the arguments provided for only 2 compositions (Composition I and II), and that they found that both compositions provide substantially equal overall efficacy in treating dry eye disease. The results presented do not actually compare

between the instant invention and the closest prior art as set forth above, including the complete range claimed by Ding et al. In other words, Ding et al. encompasses both Compositions I and II, within its scope. In addition, the arguments and evidence presented are not commensurate in scope with the instant invention, since they are limited to a single point within the concentrations and ranges disclosed.

> According to MPEP 2144.05: Applicants can rebut a prima facie case of obviousness based on overlapping ranges by showing the criticality of the claimed range. "The law is replete with cases in which the difference between the claimed invention and the prior art is some range or other variable within the claims. . . . In such a situation, the applicant must show that the particular range is critical, generally by showing that the claimed range achieves unexpected results relative to the prior art range." In re Woodruff, 919 F.2d 1575, 16 USPQ2d 1934 (Fed. Cir. 1990).

> MPEP 716.02(d) [R-2] states:

> "Whether the unexpected results are the result of unexpectedly improved results or a property not taught by the prior art, the "objective evidence of nonobviousness must be commensurate in scope with the claims which the evidence is offered to support." In other words, the showing of unexpected results must be reviewed to see if the results occur over the entire claimed range. In re Clemens, 622 F.2d 1029, 1036, 206 USPQ 289, 296 (CCPA 1980) (Claims were directed to a process for removing corrosion at "elevated temperatures" using a certain ion exchange resin (with the exception of claim 8 which recited a temperature in excess of 100C). Appellant demonstrated unexpected results via comparative tests with the prior art ion exchange resin at 110C and 130C. The court affirmed the rejection of claims 1-7 and 9-10 because the term "elevated temperatures" encompassed temperatures as low as 60C where the prior art ion exchange resin was known to perform well. The rejection of claim 8, directed to a temperature in excess of 100C, was reversed.). See also In re Peterson, 315 F.3d 1325, 1329-31, 65 USPQ2d 1379, 1382-85 (Fed. Cir. 2003) (data showing improved alloy strength with the addition of 2% rhenium did not evidence unexpected results for the entire claimed range of about 1-3% rhenium); In re Grasselli, 713 F.2d 731, 741, 218 USPQ 769, 777 (Fed. Cir. 1983) (Claims were directed to certain catalysts containing an alkali metal. Evidence presented to rebut an obviousness rejection compared catalysts

containing sodium with the prior art. The court held this evidence insufficient to rebut the prima facie case because experiments limited to sodium were not commensurate in scope with the claims.)."

Thus the invention as a whole was clearly prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Double Patenting

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).

Claims 21-22, 25-26 and 30-6 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-8 of U.S. Patent No. 5,474,979. Although the conflicting claims are not identical, they are not patentably

distinct from each other because the skilled artisan would have been motivated to do so because the compositions taught by Ding et al. teach (see 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 21) 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 21 "the weight ratio of he cyclosporin A to the castor oil being less than 0.08" and therefore one skilled in the art would have readily envisaged compositions reading upon the limitations of the instantly claimed. Further, the instantly claimed composition encompasses and/or is encompassed by the claimed composition in US '979.

Applicant's arguments

For substantially the same reasons, as stated above, that the present claims are patentable over Ding et al. Patent, so too are the present claims patentable over claims 1-8 of Ding et al Patent.

For example, none of claims 1-8 of Ding et al. Patent specifically disclose, teach or suggest the present invention. To illustrate, none of the claims 1-8 of Ding et al. Patent specifically disclose, teach or even suggest a composition comprising less than 0.1 % by weight, for example, 0.05% by weight, of cyclosporin A, and castor oil in which the weight ratio of cyclosporin A to castor oil is less than 0.08 and/or the castor oil is 1.25% by weight of the composition, as recited in the present claims, let alone the substantial, surprising advantages of such compositions, discussed above, obtained by applicant.

The Examiner states that claim 8 of Ding et al. Patent encompasses species within the instantly claimed compositions. Applicant disagrees.

Claim 8 does not specifically disclose compositions including less than 0.1% by weight of cyclosporin A in which the weight ratio of cyclosporin A to castor oil is less than 0.08, as in the presently claimed compositions. Moreover, the relatively wide ranges of cyclosporin A and castor oil concentrations recited in claim 8 of Ding et al. actually lead away from the present claims, and the substantial and surprising advantages of the presently claimed compositions obtained by applicant.

To a large extent, the disclosure of claim 8 of Ding et al. Patent is similar to that of Example 1 of Ding et al. Patent, which has been discussed previously. Claim 8, like Example 1, of Ding et al. Patent, does not distinguish one composition from the other compositions. Neither does column 3, lines 19-20 of the Ding et al. Patent, cited by the Examiner. As noted previously, Ding et al. Patent does not teach optimizing the weight ratio of cyclosporin A to castor oil to below 0.08. Rather, since four of the five compositions tested in Example 1 of Ding et al. Patent have such a weight ratio of 0.08, Ding et al. Patent appears to consider 0.08 the optimum weight ratio of cyclosporin A to castor oil.

Response to Arguments

Applicant's arguments have been carefully considered but not deemed persuasive because of the reasons set forth above.

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 García 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 García
Patent Examiner
Art Unit 1654

MMCG 06/07

6/25/07
ANISH GUPTA
PRIMARY EXAMINER

Search Notes

Application/Control No.	Applicant(s)/Patent under Reexamination
10/927,857	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
updated	6/20/2007	MMCG

TRANSMITTAL FORM

(to be used for all correspondence after initial filing)

Application Number	10/927,857
Filing Date	August 27, 2004
First Named Inventor	Acheampong et al.
Group Art Unit	1654
Examiner Name	cordero Garcia, Marcela M.
Total Number of Pages In This Submission: 19	Attorney Docket Number: D-3111

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)*

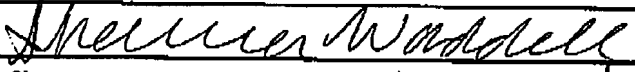
Remarks

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

Firm Name	Stout, Uxa, Buyan & Mullins, LLP		
Signature			
Printed Name	Carlos A. Fisher		
Date	August 27th 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	Shaunna Waddell	Date	Aug. 27 2007

RECEIVED
CENTRAL FAX CENTER

AUG 2 7 2007

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Appl. No.	: 10/927,857	Confirmation No. 2409
Applicant	: ACHEAMPONG ET AL.	
Filed	: August 27, 2004	
Title	: METHODS OF PROVIDING THERAPEUTIC EFFECTS USING CYCLOSPORIN COMPONENTS	
TC/A.U.	: 1654	
Examiner	: Cordero Garcia, Marcela M.	
Docket No.	: D-3111	
Customer No.	: 33197	

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

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: August 27, 2007

Name: Shawanna Waddell

AMENDMENT B

Sir:

In response to the Office Action mailed July 2, 2007, please amend the above-identified application as follows:

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

Remarks/Arguments begin on page 7 of this paper.

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

Listing of Claims

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

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

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

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

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

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

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

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

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

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

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

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

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

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

21. (Currently Amended) A <u>therapeutically effective</u> composition for treating an eye of a human or animal comprising

an emulsion comprising water, castor oil, and cyclosporin A in a therapeutically effective amount of less than 0.1% by weight, the weight ratio of the cyclosporin A to the castor oil being less than 0.08.

22. (Previously presented) 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 A.

23. (Canceled)

24. (Canceled)

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

26. (Currently Amended) The composition of claim 21 wherein the castor oil is present in an amount greater than 0.625% by weight of the composition.

27. (Canceled)

28. (Canceled)

29. (Canceled)

30. (Previously presented) The composition of claim 21 having a make-up so that when the composition is topically 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 A.

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

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

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

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

35. (Original) 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. (Original) 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. (Previously presented) The composition of claim 21 which includes 1.25% by weight of castor oil.

38. (Previously presented) The composition of claim 21 which includes 0.05% by weight of cyclosporin A.

39. (Previously presented) The composition of claim 38 which includes 1.25% by weight of castor oil.

40. (Previously presented) A composition for treating an eye of a human or animal comprising an emulsion comprising water, 1.25% by weight of castor oil and 0.05% by weight of cyclosporin A, the weight ratio of the cyclosporin A to the castor oil being 0.04.

Remarks

Applicants have the following comments in reply to the Office Action mailed July 2, 2007 (the "Office Action"). The above-identified application has been carefully reviewed in light of the Office Action mailed January 17, 2007.

Rejections Pursuant to 35 USC 103(a)

Claims 1-22, 25-26 and 30-40 have been finally rejected as allegedly obvious over Ding et al., (US Patent Serial No. 5474979). Applicants believe that the Examiner may have intended to specify claims 21-22 (rather than 1-22), 25-26 and 30-40, since claims 1-20 have been withdrawn and are no longer being prosecuted. If Applicants are in error in the regard they ask that the Examiner so indicate in the next communication to Applicants.

Upon a review of the Examiner's comments, Applicants hereby traverse this rejection for the following reasons.

Obviousness is a mixed question of law and fact. The United States Supreme Court's decision in *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 nonobviousness of the subject matter is determined." 383 U.S. at 17, 148 U.S.P.Q. at 467.

In applying this test in the case before it, the *Graham* Court found that the differences between the prior art and Graham's invention rendered the invention obvious because "a person having ordinary skill in the prior art . . . would immediately see that the thing to do was what Graham did. . . ." 383 U.S. at 24, 148 U.S.P.Q. at 469 (emphasis added). In other words, when the invention is predictable in light of the prior art in such a way as would permit the person of ordinary skill in the art to "immediately see" the claimed invention, the invention is obvious.

The Supreme Court's recent decision in *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. ___, __ U.S.P.Q.2d___ (2007) affirms in every regard the standards set forth in Graham. Moreover, the *KSR* court indicated that in a proper rejection on obviousness grounds the Examiner must articulate reasoning with some rational underpinning to support the legal conclusion of obviousness, *id.*, slip op. at 14, such as "a reason that would have prompted a person of ordinary skill in the relevant field to combine the [known] elements in the way the claimed new invention does." *Id.*, slip op. at 15.

The presently claimed invention is drawn in claim 21 to a composition for treating an eye of a human or animal comprising an emulsion comprising water, castor oil, and cyclosporin A in a therapeutically effective amount of less than 0.1% by weight, the weight ratio of the cyclosporin A to the castor oil being less than 0.08.

Ding, the reference being applied against the pending claims, is characterized by the Office Action as teaching a composition comprising water, a hydrophobic component and a cyclosporin component in a therapeutically effective amount of less that 0.1% by weight.

Ding et al. disclose that the solubility of cyclosporins (including cyclosporine A) is extremely low have made it practically impossible to prepare a pharmaceutical composition containing cyclosporin in an aqueous medium. Moreover, oil based cyclosporin compositions have generally been limited to oral preparations because of the separation of cyclosporin as a solid immediately after it comes into contact with water, such as in the mouth or eye of a patient.

Ding states that "although it is well known that cycclosporin may be used in combination with castor oil, this combination is irritating to sensitive tissues such as the eye." Ding, column 3, lines 43-45.

The Office Action on pages 3 and 4 argues that the presently claimed invention is obvious because Ding discloses weight ratios of cyclosporin to castor oil of from about 0.12 to about 0.02. The Office Action also points to claim 8 of Ding, which claims from about 0.05% to about 0.4% cyclosporin A and from about 0.625% to about 5.0% castor oil.

However, as acknowledged on page 3 of the Office Action, Ding discloses 5 different cyclosporin-containing compositions in Example 1; none of these compositions has a weight ratio of cyclosporin to castor oil of less than 0.8. Thus, while Ding et

al. disclose amounts of each ingredient that are encompassed by the ranges of ingredients given in Ding et al., in practice Ding et al. teaches away from the present composition having less than 0.1% cyclosporin A and a weight ratio of cyclosporin to castor oil of less than 0.08%.

Furthermore, the present specification provides comparative evidence of surprising results in the use of the claimed compositions. Example 1 of the present specification is drawn to a comparison of two different compositions in which percentages are presented by weight; Composition I, which fall outside the scope of the present claims, contains 0.1% cyclosporin A and 1.25% castor oil. This composition therefore has a weight ratio of cyclosporin to castor oil of 0.08. Composition II contains 0.05% cyclosporin and 1.25% castor oil, and thus has a weight ratio of cyclosporin to castor oil of 0.04%.

It was utterly unpredictable, with reference to Ding, that Composition II, containing half the amount of cyclosporin A as Composition I, would provide substantially equivalent overall efficacy against dry eye diseases such as keratoconjunctivitis sicca when applied topically to the eye. See SPECIFICATION at page 26, lines 8 and 9.

It is therefore completely surprising that an equivalently therapeutically effective composition containing a reduced amount of cyclosporin A (below 0.1%) relative to Composition I (and thus a reduced potential for adverse side effects and drug interactions than Composition I) could be made. Using the currently claimed compositions, prescribing physicians can

prescribe e.g., 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 Composition I.

Moreover, it was utterly unpredictable that the concentration of castor oil (1.25%) present in both Composition I and Composition II of the present specification would be substantially non-irritating in human eyes (and therefore useful as required by 35 USC §101) upon use. See SPECIFICATION at page 26, lines 16 and 17. Although the antibiotic effects of the main component of castor oil, ricinoleic acid, are known, oily ocular topical cyclosporin compositions can lead to irritation or a clouding of visual field. Ding, column 2, lines 6 and 7. Indeed, Ding indicates that in rabbit eyes some discomfort and hyperaemia results from topical application of Compositions A-E disclosed therein.

It is therefore clear in the light of the unpredictability of the present invention that a person of ordinary skill in the art would not only not be able to "immediately see" in light of Ding "that the thing to do was what the Applicants did", Graham, 383 U.S. at 24, 148 U.S.P.Q. at 469, but that such a person would have no basis for even attempting to make the claimed compositions.

Furthermore, since the Office Action admits that Ding et al. does not disclose compositions containing less than 0.1% cyclosporin A and weight ratios of cyclosporin to castor oil of of below 0.08%, the statements that "the limitations" of claims

21, 22, 25 26, and 30-40 are taught in various places in Ding is respectfully submitted to be erroneous.

The Examiner relies on Ding et al Publication PHARM. RES. 1997:14:S41 to supplement the teachings of Ding et al Patent. Thus publication consists of an abstract.

Ding et al Publication discloses a stable, pH-adjusted, oil-in-water emulsion using castor oil as the internal phase to solubilize cyclosporine, polysorbate 80 as the primary emulsifier and a polyelectrolyte as a stabilizer. Ding et al Publication discloses that the concentration of cyclosporin in the oil globule is formulated at a level of 7.4% w/w, meaning that the weight ratio of the cyclosporine to castor oil in the oil globule is 0.074/0.926 or 0.08. Ding et al. Publication does not disclose the concentration of cyclosporin or the amount of castor oil.

Thus, Ding et al. Publication adds nothing to e.g., Example 1 of Ding et al. patent. The Office Action appears to concede that the significance of Ding et al. Publication is that it reinforces that teachis of Ding et al. patent that the op[timal weight ratio of cyclosporin to castor oil is 0.8%.

The Office Action cites the Manual of Patent Examining Procedure (MPEP) §2144.05, which states that if a prima facie case of obviousness exists, such a case is rebutted if, as here, the prior art teaches away from the claimed invention.

Ding et al. patent discloses exemplary compositions, all but one having weight ratios the cyclosporine to castor oil of

0.08%, and all but one having cyclosporin concentrations of 0.1% or above. The clear teaching is that an optimal weight ratio is 0.8%. Thus, Ding et al. teaches away from the present invention. Applicants note that the present claim limitations do not use the term "about" with respect to these limitations, and therefore there is no overlap with the exemplary compositions of Example 1.

The Office Action also appears to hold Applicants to a much higher standard than is permissible regarding the evidence of Example 1 of the present specification demonstrating surprising results. The Office Action seems to indicate that the Applicants must provide such evidence over "the complete range claimed by Ding et al.", and that an experiment using a single composition, such as Composition II, cannot prove such results since it is limited to a single point within the concentrations and ranges claimed. Applicants respectfully disagree with this conclusion.

It is clearly evident to the person of ordinary skill in the art that lower concentrations of cyclosporin than 0.1% would result in a reduced potential for adverse side effects and drug interactions than a composition containing higher concentrations of cyclosporin A. Moreover, regarding therapeutic effectiveness, it is not required that a patent application provide evidence that all embodiments of an invention are operative; the Court of Appeals for the Federal Circuit has ruled that even if some of the claimed combinations were inoperative, the claims are not necessarily invalid." *Atlas Powder Co. v. E.I. DuPont de Nemours & Co.*, 750 F2d. 1569, 204 USPQ 409 (Fed. Cir. 1984). In the present case, the utility of the invention depends upon its

therapeutic effectiveness, and the fact that there is some concentration of cyclosporin at which the claimed composition may not be therapeutically effective does not make these claims obvious.

Furthermore, Applicants point out that the Office Action's reasoning regarding surprising results can in no event pertain to claims 37-40, which are drawn to preferred specific embodiments comprising a single concentration of cyclosporin (0.05%) and/or castor oil (1.25%). Any such conclusion can only be improperly reached from a prior knowledge of and a hindsight analysis of the claims in light of the Applicants' own specification.

In view of the above, Applicants submit that claims 21, 22, 25, 26 and 30-40 are unobvious from and patentable over Ding et al Patent in view of Ding et al Publication under 35 U.S.C. 103(a).

Double Patenting

Claims 21-36 have been rejected on the ground of non-statutory obviousness-type double patenting as being unpatentable over claims 1-8 of Ding et al Patent. Applicant traverses these rejections as it pertains to claims 21, 22, 25, 26 and 30-40.

For substantially the same reasons as stated above showing that the present claims are patentable over Ding et al Patent, so too are the present claims patentable over claims 1-8 of Ding et al Patent.

For example, none of claims 1-8 of Ding et al Patent specifically disclose, teach or suggest the present invention. To illustrate, none of claims 1-8 of Ding et al Patent specifically disclose, teach or even suggest a composition comprising less than 0.1% by weight, for example, 0.05% by weight, of cyclosporin A, and castor oil in which the weight ratio of cyclosporin A to castor oil is less than 0.08 and/or the castor oil is 1.25% by weight of the composition, as recited in the present claims, let alone the substantial, surprising advantages of such compositions, discussed above, obtained by Applicants.

The Examiner states that claim 8 of Ding et al Patent encompasses species within the instantly claimed compositions. Applicant disagrees.

Claim 8 does not specifically disclose compositions including less than 0.1% by weight of cyclosporin A in which the weight ratio of cyclosporin A to castor oil is less than 0.08, as in the presently claimed compositions. Moreover, the wide ranges of cyclosporin A and castor oil concentrations recited in claim 8 of Ding et al Patent actually lead away from the present claims, and the substantial and surprising advantages of the presently claimed compositions obtained by Applicants.

To a large extent, the disclosure of claim 8 of Ding et al Publication is similar to that of Example 1 of Ding et al Patent, which has been discussed previously. Claim 8, like Example 1, of Ding et al Patent does not distinguish one composition from the other compositions. Neither does column 3, lines 19-20 of Ding et al Patent, cited by the Examiner. As

noted previously, Ding et al Patent does not teach optimizing the weight ratio of cyclosporin A to castor oil to below 0.08. Rather, since four of the five compositions tested in Example 1 of Ding et al Patent have such a weight ratio of 0.08, Ding et al Patent appears to consider 0.08 the optimum weight ratio of cyclosporin A to castor oil.

None of the Compositions A, B, C, D and E of Ding et al Patent specifically disclose, teach or suggest the presently claimed compositions. As noted previously, Ding et al Patent does not distinguish the Compositions of Example 1, one from the other. In effect, the claims, including claim 8, of Ding et al Patent discloses that compositions with relatively wide ranges of concentrations of cyclosporin A and castor oil have similar properties. Such teaching actually leads away from the presently claimed compositions and the substantial, surprising advantages, discussed previously, obtained by Applicants relative to compositions encompassed by the claims of Ding et al Patent.

Further, nothing in the claims of Ding suggest the specific concentrations and ratios recited in claims 37-40 of the present application.

In view of the above, Applicants submits that claims 21, 22, 25, 26 and 30-40 are patentable over the claims of Ding et al Patent, and respectfully requests that the obviousness-type double patenting rejection based on claims 1-8 of Ding et al Patent be withdrawn.

Each of the present dependent claims is separately patentable over the prior art. For example, none of the prior art, taken single or in any combination, disclose, teach or even suggest the present compositions including the additional feature or features recited in any of the present dependent claims. Therefore, Applicants submits that all of the present claims are separately patentable over the prior art.

In conclusion, Applicants have shown that the present claims satisfy the requirements of 35 U.S.C. 112, first and second paragraphs; are unobvious from and patentable over the prior art; and are not subject to obviousness type double patenting based on claims 1-8 of Ding et al Patent. Therefore, Applicants submits that the present claims, that is claims 21, 22, 25, 26 and 30-40, are allowable and respectfully requests the Examiner to pass the above-identified application to issuance at an early date. Should any matters remain unresolved, Applicants requests the Examiner to telephone Applicants's attorney at the telephone number given below.

Respectfully submitted,

Date: August 27th, 2007

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

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
10/927,857	08/27/2004	

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), (l), 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 03/27/2007	(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))	* 35	Minus	** 36	= 0	X $ =		OR	X $50=	0
Independent (37 CFR 1.16(h))	* 3	Minus	*** 3	= 0	X $ =		OR	X $200=	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

8/27/07

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))	* 35	Minus	** 36	=	X $ =		OR	X $ =	
Independent (37 CFR 1.16(h))	* 3	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	

* 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:
Rozenia Harmon

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.
10/927,857	08/27/2004	Andrew Acheampong	D-3111	2409

33197 7590 09/27/2007

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**
09/27/2007	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.

Advisory Action Before the Filing of an Appeal Brief	**Application No.** 10/927,857	**Applicant(s)** ACHEAMPONG ET AL.
	Examiner Marcela M. Cordero Garcia	**Art Unit** 1654

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

THE REPLY FILED 27 August 2007 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☐ The period for reply expires _____ months from the mailing date of the final rejection.
   b) ☒ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☒ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☒ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: *See Continuation Sheet*. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☒ will not be entered, or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: _____.
   Claim(s) objected to: _____.
   Claim(s) rejected: *21,22,25,26 and 30-40*.
   Claim(s) withdrawn from consideration: *1-20*.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☐ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: _____.
12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08) Paper No(s). _____
13. ☐ Other: _____.

Cecilia J. Tsang
Supervisory Patent Examiner
Technology Center 1600

Marcela M Cordero Garcia
Patent Examiner
Art Unit 1654

Continuation of 3. NOTE: As noted by Applicant, there was a typo in the final rejection and claim 1 should read as claim 21. Claims 1-20 were withdrawn by restriction since they are drawn to a method of using rather than a product. Therefore, the 103 rejection over Ding is over claims 21-22, 25-26 and 30-40 (see the ODP rejection which encompasses the correct claims). Examiner thanks Applicants for clarifying this point. With respect to applicants arguments: 1) Ding et al. discloses that the solubility of cyclosporins is extremely low and that oil based cyclosporin compositions have generally been limited to oral preparations because of the separation of cyclosporin as a solid when it comes into contact with water. Response to 1): Ding et al. teach operative conditions for the eye emulsions which encompass the instant ranges. Moreover, Ding et al. teaches that the compositions are found to be physically stable upon long term storage and that the drug had reasonably high thermodynamic activity yet without crystallization problems (e.g. column 3, lines 20-28). Moreover, Ding et al. teach that the "present invention achieves a stable solution state of cyclosporin. This stable solution state is another important performance characteristic differentiating the present invention from the conventional oil systems. cyclosporin is notorious for its tendency to precipitate out in conventional oil systems in which it is fully dissolved initially." (column 3, lines 57-63). 2) Ding states that "although it is well known that cyclosporin may be used in combination with castor oil, this combination is irritating to sensitive tissues such as the eye." (Ding column 3, lines 43-45). Response to 2) Ding et al. teach in abstract that the compositions have high comfort level and low irritation potential suitable for delivery of medications to sensitive areas such as ocular tissues. In addition, the compositions of Examples 1-4, encompassing up to 5% castor oil (much larger than the instant Composition II of disclosure which has 1.25% of castor oil) were found to cause only slight to mild discomfort and slight hyperemia (e.g., column 5, lines 15-20). The compositions encompassed by the teachings of the Ding et al. patent are non-irritant as taught by the title of the patent "Nonirritating emulsions for sensitive tissue". 3) According to Apliccants, none of the compositions in Example 1 has a weight ration of cyclosporin to castor oil of less than 0.8, therefore Ding et al. teach away for the present composition. Answer to 3). Example 1A is 0.4% cyclosporin / 5.00 % castor oil, which has a ratio of 0.08; Example 1D is 0.1 % cyclosporin and 1.25% castor oil, which also has a ratio of 0.08. In addition the ratios 0.02 to 0.12 are "more preferred" ratios of cyclosporin to castor oil (column 3, lines 17-20), therefore it does not teach away but instead provides ample motivation to make the instantly claimed compositions. 4) Applicants argue unexpected results because when comparing composition 1D of Ding et al. (named composition I in the instant application, comprising 0.1 % cyclosporin and 1.25% castor oil) and composition II which has 0.05% cyclosporin (half as much as composition I) and 1.25% castor oil, composition II provides substantially equivalent overall efficacy against dry eye diseases such as keratoconjunctivitis sicca when applied topically to the eye. Response to 4) The statement that both compositions provide "substantially equivalent overall efficacy" is not unexpected since both compositions are encompassed by the invention of Ding et al. and all the embodiments described therein are considered operative. Moreover, no data is presented to substantiate the arguments besides the statement that the composition II and composition I have substantially overall efficacy. 5) Applicants allege unexpected result encompassing less adverse effects due to the use of a lower amount of cyclosporin. Response to 5) a lower amount of cyclosporin is taught, e.g., at claim 8, which teaches cyclosporin A at 0.05% and therefore the result is not unexpected. Additionally, the less adverse results would be dependent on the lower concentration and are not unexpected and encompassed by the invention of Ding et al. 6) Applicants allege that "it was utterly unpredictable that the concnetration of castor oil (1.25%) present in both composition I and composition II of the present specification would be substantially non-irritating in human eyes upon use. Although the antibiotic effects of the main component of castor oil, ricinoleic acid, are known, oily ocular topical cyclosporin compositions can lead to irritation or a colduing of visual field. Ding , column 2, lines 6 and 7. Indeed Ding indicates that in rabbit eyes some discomfort and hyperaemia results from topical application of compositions A-E disclosed therein. Response to 6) Ding et al. teach in abstract that the compositions have high comfort level and low irritation potential suitable for delivery of medications to sensitive areas such as ocular tissues. In addition, the compositions of Examples 1-4, encompassing up to 5% castor oil (much larger than the instant Composition II of disclosure which has 1.25% of castor oil) were found to cause only slight to mild discomfort and slight hyperemia (e.g., column 5, lines 15-20). The compositions encompassed by the teachings of the Ding et al. patent are non-irritant as taught by the title of the patent "Nonirritating emulsions for sensitive tissue". 7) Applicants allege that the limitations as pointed out in claims 21, 22, 25, 26 and 30-40 are taught erroneously. Response to 7) Applicants have not specifically pointed out in each claim and limitation, why they are erroneous. The disclosure of Ding et al. is relied upon for all that it teaches and therefore, not only the Examples are considered when making an art rejection. 8) Examiner relies of Ding et al. (Pharm Res, 1997) tosupplement the teachings of Ding et al. Response to 8) Examiner agrees that the ratio of cyclosporine to castor oil is 0.074/0.926 or 0.08. Please note that the ratio is 0.08 and not 0.8% as pointed out by Applicants in page 13, paragraph 4 of the after final arguments. 9) Ding et al. patent discloses exemplary compositions, all but one having weight ratios of the cyclosporine to castor oil of 0.08%, and all but one having cyclosporin concentrations of 0.1% or above. The clear teaching is that an optimal weight ratio is 0.8%. Thus Ding et al. teaches away from the present invention. Response to 9) First of all, Examiner points out that the limitations of claim 21 are "cyclosporin in a therapeutically effective amount of less than 0.1 % by weight" and "the weight ratio of the cyclosporin A to the castor oil being less less than 0.08". It is unclear to Examiner how is the 0.8% optimal ratio being obtained. Ding et al. teaches in claim 7, that the cyclosporin is present in the amount of between about 0.05 to and about 0.40%, which clearly encompasses 0.1 %, and castor oil at 0.625-5.0%, e.g., 0.1/5.0 = 0.02 (which is less than 0.08). In addition, the limitation "the weight ratio of the cyclosporin A to the castor oil being less less than 0.08" is taught as within the more preferred ratio of cyclosporin to castor oil of 0.12 and 0.02 (e.g., column 3, lines 17-20). 10) Furthermore, Applicants point out that the Office Action's reasoning regarding surprising results can in no event pertain to claims 37-40 which are drawn to preferred specific embodiments comprising a single concentration of cyclosporin (0.05%) and/or castor oil (1.25%). Any such conclusion can only be improperly reached from a prior knowledge of and a hindsight analysis of the claims in light of the Applicants' own specification. Response to 10) Claim 37 is drawn to claim 21 wherein castor oil is 1.25% by weight, which is encompassed by the teachings of Ding et al. (e.g., claim 7, which encompasses 0.05 % of cyclosporin and 1.25% of castor oil to make a ratio of 0.04). 11) For substantially the same reasons above, the present claims are patentable over Ding et al. Specifically, claims 8 discloses compositions with relatively wide ranges of concentrations of clyclosporin A and castor oil teaching away from the present unexpected advantages. Response to 11). It would have been obvious to one of ordinary skill in the art to at once envisage the embodiments encompassed by the ranges, e.g., in claim 8, which are 0.05-0.4 of cyclosporin (encompassing less than 0.1% and specifically 0.05%) and castor oil between 1.0-5.0% weight (which encompass 1.25% of castor oil).

AF/ IFW

OIPE IAP66 NOV 23 2007 PATENT & TRADEMARK OFFICE

TRANSMITTAL FORM

(to be used for all correspondence after initial filing)

Application Number	10/927,857
Filing Date	August 27, 2004
First Named Inventor	Acheampong et al.
Group Art Unit	1654
Examiner Name	cordero Garcia, Marcela M.
Total Number of Pages in This Submission	6
Attorney Docket Number	D-3111

ENCLOSURES (*check all that apply*)

- [X] Fee Transmittal Form
- [X] Fee Attached
- [ ] Amendment/Reply
- [ ] After Final
- [ ] Affidavits/declaration(s)
- [X] 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
- [X] Appeal Communication to TC *(Appeal Notice, Brief, Reply Brief)*
- [ ] Proprietary Information
- [ ] Status Letter
- [X] Other Enclosure(s) *(please identify below)*

Return Self Addressed Postcard

Remarks

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

Firm Name	Stout, Uxa, Buyan & Mullins, LLP		
Signature			
Printed Name	Carlos A. Fisher		
Date	November 26 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. 26, 2007

Fees Pursuant to the Consolidated Appropriations Act 2005 (H.R. 4818).

FEE TRANSMITTAL For FY 2008

Patent fees are subject to annual revision.

☐ Application claims small entity status. See 37 CFR 1.27

TOTAL AMOUNT OF PAYMENT ($) 970.00

Complete if Known	
Application Number	10/927,857
Filing Date	August 27, 2004
First Named Inventor	Andrew Acheampong
Examiner Name	Cordero Garcia, Marcela M
Art Unit	1654
Attorney Docket No.	D-3111

METHOD OF PAYMENT *(check all that apply)*

☒ Check ☐ Credit Card ☐ Money Order ☐ None ☐ Other (please identify): PLEASE USE CHECK FOR 2 MONTH EXTENSION FEE $460.00, AND THE DEPOSIT ACCOUNT FOR THE APPEAL FEE $510.00.

☒ Deposit Account Deposit Account Number 01-0885 Deposit Account Name Allergan, Inc.

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**

☒ Charge any additional fee(s) associated with this communication ☒ Credit any overpayments

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.

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	310	155	510	255	210	105	
Design	210	105	100	50	130	65	
Plant	210	105	310	155	160	80	
Reissue	310	155	510	255	620	310	
Provisional	210	105	0	0	0	0	

Subtotal (1) 0

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	210	105
Multiple Dependent Claims	370	185

Total Claims ____ -20 or HP = ____ x Fee ($) ____ Fee Paid ($) ____

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

Indep. Claims ____ -3 or HP = ____ X Fee ($) ____ Fee Paid ($) ____

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

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

Subtotal (2) 0

3. APPLICATION SIZE FEE

If the specification and drawings exceed 100 sheets of paper, the application size fee due is $260 ($130 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).

Total Sheets ____ -100 = Extra Sheets ____ /50= Number of each additional 50 or fraction thereof ____(round up to a whole number) x Fee ($) ____ = Fee Paid ($) ____

Subtotal (3) 0

4. OTHER FEE(S)

	Fee Paid ($)
☐ Surcharge - Late filing fee or oath/declaration: $130 fee ($65 small entity discount)	
☐ Non-English Specification: $130 fee (no small entity discount)	
☐ 1-month extension of time: $120 fee ($60 small entity discount)	
☒ 2-month extension of time: $460 fee ($230 small entity discount)	460.00
☐ 3-month extension of time: $1050 fee ($525 small entity discount)	
☐ 4-month extension of time: $1640 fee ($820 small entity discount)	
☐ 5-month extension of time: $2230 fee ($1115 small entity discount)	
☐ Information Disclosure Statement Fee: $180 fee (no small entity discount)	
☒ Notice of Appeal: $510 fee ($255 small entity discount)	510.00
☐ Filing a Brief in Support of Appeal: $510 fee ($255 small entity discount)	
☐ Request for Oral Hearing: $1030 fee ($515 small entity discount)	
☐ Utility Issue Fee: $1440 fee ($720 small entity discount)	
☐ Recording each patent assignment per property (times number of properties): $40 fee (no small entity fee discount)	
☐ Request for Continued Examination: $810 fee ($405 small entity discount)	
☐ Other: ____	

Subtotal (4) 970.00

SUBMITTED BY

Name (Print/Type)	Douglas Fisher	Registration No. (Attorney/Agent)	36,510	Telephone	949-450-1750
Signature				Date	11/16/07

The PTO did not receive the following listed Item(s) A check for $970.00 but we got $460.00

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Appl. No.	: 10/927,857	Confirmation No. 2409
Applicant	: ACHEAMPONG ET AL.	
Filed	: August 27, 2004	
Title	: METHODS OF PROVIDING THERAPEUTIC EFFECTS USING CYCLOSPORIN COMPONENTS	
TC/A.U.	: 1654	
Examiner	: Cordero Garcia, Marcela M.	
Docket No.	: D-3111	
Customer No.	: 33197	

CERTIFICATE OF MAILING OR FACSIMILE TRANSMISSION

I hereby certify that this paper 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 the date shown below.

Date: November 16, 2007

Name: Sharon Waddell

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

PETITION FOR TWO MONTH EXTENSION OF TIME

Dear Sir:

Applicants hereby request a two-month extension of time to respond to the Final Office Action mailed July 2, 2007. A check for $460 is enclosed for the payment of this fee. If any other fee is due in connection with this communication please use Deposit Account 01-0885.

Sincerely yours,

Date: November 16, 2007

Carlos A. Fisher
Reg. No. 36, 510
Stout, Uxa, Buyan & Mullins, LLP
4 Venture, Suite 300
Irvine, California 92618
Telephone: 949-450-1750

11/23/2007 EHAILE1 00000028 10927857
01 FC:1252
460.00 OP

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Appl. No. : 10/927,857 Confirmation No. 2409
Applicant : ACHEAMPONG ET AL.
Filed : August 27, 2004
Title : METHODS OF PROVIDING THERAPEUTIC EFFECTS USING CYCLOSPORIN COMPONENTS

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

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

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

CERTIFICATE OF MAILING OR FACSIMILE TRANSMISSION

I hereby certify that this paper 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 the date shown below.

Date: November 16, 2007
Name: Shawnna Waddell

NOTICE OF APPEAL

11/27/2007 EHAILE1 00000020 010885 10927857
01 FC:1401 510.00 DA

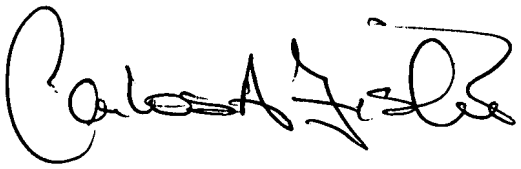
Dear Sir,

In reply to the Advisory Action mailed September 27, 2007, 2007, Applicants hereby appeal from the rejection of claims 1-22, 25-26, and 30-40 pursuant to 35 U.S.C. §103.

Applicants hereby enclose a check in the amount $460.00 in payment of the extension fee associated with a two-month extension of time to reply to the Final Office Action mailed September 27, 2007. Kindly utilize Deposit Account 01-0885 for the payment of

the fee associated with filing the Notice of Appeal and any other fee now due.

Respectfully submitted,



Carlos A. Fisher
Attorney for Applicant
Reg. No. 36, 510
4 Venture, Suite 300
Irvine, CA 92618
(949) 450-1750
Facsimile (494) 450-1764

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application No.	:	10/927,857	Confirmation No. 2409
Applicant	:	Andrew Acheampong	
Filed	:	August 27, 2004	
Title	:	METHODS OF PROVIDING HERAPEUTIC EFFECTS USING CYCLOSPORIN COMPONENTS	
TC/A.U.	:	1654	
Examiner	:	Cordero Garcia, Marcela M.	
Docket No.	:	D-3111	
Customer No.	:	33197	

Mail Stop Appeal Brief - Patent
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

EXPRESS MAIL CERTIFICATE

EXPRESS MAIL MAILING LABEL NO. EV 516292512 US

Date of Deposit: **January 15, 2008**

I hereby certify that the following documents as identified below are being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 CFR 1.10 on the date indicated above and are addressed to the Mail Stop Appeal Brief - Patent, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450:

- ☒ Appeal Brief (30 pages)
- ☒ Stamped, self-addressed postcard
- ☒ Transmittal Form
- ☒ Fee Transmittal Form
- ☐
- ☐
- ☐
- ☐ Other: _____

Each of the 4 above-identified documents are enclosed herewith.

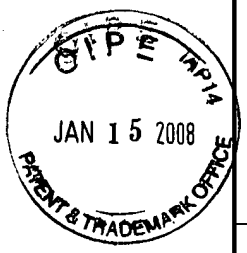
Respectfully submitted,

Date: January 15, 2008

Shawnna Waddell
Assistant to Carlos A. Fisher
Stout, Uxa, Buyan & Mullins, LLP
4 Venture, Suite 300
Irvine, California 92618
Telephone: 949-450-1750

01-17-08

AF/B



TRANSMITTAL FORM

(to be used for all correspondence after initial filing)

Application Number	10/927,857
Filing Date	August 27, 2004
First Named Inventor	Andrew Acheampong
Group Art Unit	1654
Examiner Name	Cordero Garcia, Marcela M.
Total Number of Pages in This Submission: 37	Attorney Docket Number: D-3111

ENCLOSURES (*check all that apply*)

- [X] 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
- [X] Appeal Communication to TC (*Appeal Notice, Brief, Reply Brief*) 30 pages
- [ ] Proprietary Information
- [ ] Status Letter
- [X] Other Enclosure(s) (*please identify below*)

Express Mail Certificate

Self Addressed Postcard

- U.S. Patent 5,424,979

Remarks

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

Firm Name	Stout, Uxa, Buyan & Mullins, LLP		
Signature	Carlos A. Fisher		
Printed Name	Carlos A. Fisher		
Date	January 15, 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	Shawnna Waddell		
Typed or printed name	Shawnna Waddell	Date	Jan. 15 2008

Fees Pursuant to the Consolidated Appropriations Act 2005 (H.R. 4818).

FEE TRANSMITTAL For FY 2008

Patent fees are subject to annual revision.

☐ Application claims small entity status. See 37 CFR 1.27

TOTAL AMOUNT OF PAYMENT ($) 510.00

Complete if Known	
Application Number	10/927,857
Filing Date	August 27, 2004
First Named Inventor	Andrew Acheampong
Examiner Name	Codero Garcia, Marcela M.
Art Unit	1654
Attorney Docket No.	D-3111

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, Inc.

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**

☐ Charge any additional fee(s) associated with this communication ☒ Credit any overpayments

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.

FEE CALCULATION

1. BASIC FILING, SEARCH, AND EXAMINATION FEES

	FILING FEES		SEARCH FEES		EXAMINATION FEES		
Application Type	**Fee ($)**	**Small Entity Fee ($)**	**Fee ($)**	**Small Entity Fee ($)**	**Fee ($)**	**Small Entity Fee ($)**	**Fees Paid ($)**
Utility	310	155	510	255	210	105	
Design	210	105	100	50	130	65	
Plant	210	105	310	155	160	80	
Reissue	310	155	510	255	620	310	
Provisional	210	105	0	0	0	0	

Subtotal (1) **0**

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	210	105
Multiple Dependent Claims	370	185

Total Claims	Extra Claims	Fee ($)	Fee Paid ($)
____ -20 or HP =	____	x ____	____

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

Indep. Claims	Extra Claims	Fee ($)	Fee Paid ($)
____ -3 or HP =	____	X ____	____

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

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

Subtotal (2) **0**

3. APPLICATION SIZE FEE

If the specification and drawings exceed 100 sheets of paper, the application size fee due is $260 ($130 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).

Total Sheets	Extra Sheets	Number of each additional 50 or fraction thereof	Fee ($)	Fee Paid ($)
____ -100 =	____	/50= ____(round up to a whole number)	x ____	=

Subtotal (3) **0**

4. OTHER FEE(S)

	Fee Paid ($)
☐ Surcharge - Late filing fee or oath/declaration: $130 fee ($65 small entity discount)	
☐ Non-English Specification: $130 fee (no small entity discount)	
☐ 1-month extension of time: $120 fee ($60 small entity discount)	
☐ 2-month extension of time: $460 fee ($230 small entity discount)	
☐ 3-month extension of time: $1050 fee ($525 small entity discount)	
☐ 4-month extension of time: $1640 fee ($820 small entity discount)	
☐ 5-month extension of time: $2230 fee ($1115 small entity discount)	
☐ Information Disclosure Statement Fee: $180 fee (no small entity discount)	
☐ Notice of Appeal: $510 fee ($255 small entity discount)	
☒ Filing a Brief in Support of Appeal: $510 fee ($255 small entity discount)	510.00
☐ Request for Oral Hearing: $1030 fee ($515 small entity discount)	
☐ Utility Issue Fee: $1440 fee ($720 small entity discount)	
☐ Recording each patent assignment per property (times number of properties): $40 fee (no small entity fee discount)	
☐ Request for Continued Examination: $810 fee ($405 small entity discount)	
☐ Other: ____	
Subtotal (4)	**510.00**

SUBMITTED BY

Name (Print/Type)	Carlos A. Fisher	*Registration No. (Attorney/Agent)*	36,510	*Telephone*	949-450-1750
Signature	Carlos A. Fisher			*Date*	January 15, 2008

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Appl. No.	: 10/927,857	Confirmation No.	2409
Appellant	: ACHEAMPONG ET AL.		
Filed	: August 27, 2004		
Title	: METHODS OF PROVIDING THERAPEUTIC EFFECTS USING CYCLOSPORIN COMPONENTS		
TC/A.U.	: 1654		
Examiner	: Cordero Garcia, Marcela M.		
Docket No.	: D-3111		
Customer No.	: 33197		

CERTIFICATE OF EXPRESS MAILING

I hereby certify that this paper is being sent by Express Mail bearing Label No. EV516292512 US to Box Appeal Brief-Patents, Commissioner for Patents, P.O. Box1450, Alexandria, VA 22313-1450 on the date shown below.

Date: January 15, 2008

Name: Shawnna Waddell

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

APPEAL BRIEF

01/18/2008 SDENBOB3 00000001 010885 10927857
01 FC:1402 510.00 DA

TABLE OF CONTENTS

REAL PARTY IN INTEREST

The inventors Andrew Acheampong, Diane Tang-Liu, James N. Chang, and David F. Power assigned their entire interest in this patent application to Allergan, Inc. via an assignment document signed by the inventors on August 12, 2004 and recorded at reel 0157490, frame 0698 on August 27, 2004. Allergan, Inc., is therefore the owner of this patent application and the real party in interest in this appeal.

RELATED APPEALS AND INTERFERENCES

There are no related appeals or interferences.

STATUS OF CLAIMS

Claims 1 – 20 are withdrawn.

Claims 23-24 and 27-29 have been cancelled.

Claims 21-22, 25-26, and 30-40 are pending, have been rejected, and are under appeal.

STATUS OF AMENDMENTS

No amendment of any claim has been filed after the date of final rejection.

SUMMARY OF CLAIMED SUBJECT MATTER

Independent claim 21 is drawn to a therapeutically effective composition for treating an eye of a human or animal comprising an emulsion comprising water, castor oil, and cyclosporin A in a therapeutically effective amount of less than 0.1% by weight, the weight ratio of the cyclosporin A to the castor oil being less than 0.08. Support for this claim can be found in the specification, e.g., at Example 1, beginning on page 25 and page 8, lines 2-12.

Dependent claim 22 is drawn to the composition of claim 21 wherein the composition is formed as to result in substantially no detectable concentration of cyclosporin A in a patient's blood when an amount of the composition effective to treat dry eye syndrome is administered to the patient's eye. Support for this claim can be found where indicated for claim 21 and in the specification at, e.g., page 9, line 6 to page 10, line 13.

Dependent claim 25 is drawn to the composition of claim 21 wherein the composition is in the form of an emulsion. Support for this claim can be found where indicated for claim 21 and in the specification at, e.g., page 23, lines 16-19.

Dependent claim 26 is drawn to the composition of claim 21 wherein the castor oil is present in an amount greater than 0.625% by weight of the composition. Support for this claim can be found where indicated for claim 21 and in the specification at, e.g., page 16, lines 1-7.

Dependent claim 30 is drawn to the composition of claim 21 having a make-up so that when the composition is topically 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 A. Support for this claim can be found where indicated for claim 21 and in the specification at, e.g., page 8, lines 13-23 and page 9, line 6 to page 10, line 13.

Dependent claim 31 is drawn to the composition of claim 21 wherein the composition comprises an effective amount of an emulsifier component. Support for this claim can be found where indicated for claim 21 and in the specification at, e.g., page 17, lines 20-27.

Dependent claim 32 is drawn to the composition of claim 21 wherein the composition comprises an effective amount of a tonicity component. Support for this claim can be found where indicated for claim 21 and in the specification at, e.g., page 20, lines 7-17.

Dependent claim 33 is drawn to the composition of claim 21 wherein the composition comprises an effective amount of an organic tonicity component. Support for this claim can be found where indicated for claim 21 and in the specification at, e.g., page 20, lines 7-17.

Dependent claim 34 is drawn to the composition of claim 21 wherein the composition comprises a polyelectrolytic component in an amount effective in stabilizing the composition. Support for this claim can be found where indicated for claim 21 and in the specification at, e.g., the paragraph bridging pages 19 and 20.

Dependent claim 35 is drawn to 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. Support for this claim can be found where indicated for claim 21 and in the specification at, e.g., page 7, lines 16-19.

Dependent claim 36 is drawn to 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. Support for this claim can be found where indicated for claim 21 and in the specification at, e.g., page 7, lines 16-19.

Dependent claim 37 is drawn to the composition of claim 21, which includes 1.25%, by

weight of castor oil. Support for this claim can be found where indicated for claim 21 and in the specification at, e.g., Example 1, beginning on page 25.

Dependent claim 38 is drawn to the composition of claim 21 which includes 0.05% by weight of cyclosporin A. Support for this claim can be found where indicated for claim 21 and in the specification at, e.g., Example 1, beginning on page 25.

Dependent claim 39 is drawn to the composition of claim 38 which includes 1.25% by weight of castor oil. Support for this claim can be found where indicated for claim 38 and in the specification at, e.g., Example 1, beginning on page 25.

Independent claim 40 is drawn to a composition for treating an eye of a human or animal comprising an emulsion comprising water, 1.25% by weight of castor oil and 0.05% by weight of cyclosporin A, the weight ratio of the cyclosporin A to the castor oil being 0.04. Support for this claim can be found e.g., Example 1, beginning on page 25 and page 3, lines 4-6.

GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

Presently pending claims 1-22, 25-26, and 30-40 have all been rejected pursuant to 35 U.S.C. §103(a) as being allegedly obvious over Ding et al., U.S. Patent Serial No. 5,474,979.

Claims 21-36 have been rejected under the doctrine of non-statutory obviousness-type double patenting over Ding et al., U.S. Patent Serial No. 5,474,979.

ARGUMENT

Rejections pursuant to 35 USC 103(a)

a) Claims 21, 22, 25-26 and 30-39

Claims 21, 22, 25-26 and 30-39 were rejected as allegedly obvious pursuant to 35 USC §103(a) over U.S. Patent Serial No. 5,474,979, to Ding et al. (the "Ding patent"). Appellants respectfully appeal from the Examiner's 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 see 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 nonobviousness 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

Ding et al., U.S. Patent Serial No. 5,474,979 (hereinafter "Ding") is the sole prior art reference alleged by the Examiner to render the present invention obvious. This reference is directed to stable emulsions for the delivery of poorly water-soluble medications to sensitive tissues. Ding, column 1, lines 4-6. Ding states that oils exacerbate the symptoms of certain ocular surface diseases such as dry eye syndrome, that are otherwise effectively treated using cyclosporin, a poorly water-soluble drug. Ding, et al., column 2, lines 46-49. Additionally, ocular formulations containing cyclosporin dissolved in oil (as in an emulsion) limits the bioavailability of cyclosporin to the target tissue. Ding, column 1, lines 45-53.

Ding discloses an emulsion containing cyclosporin (a poorly water soluble drug), castor oil and polysorbate 80 wherein the weight ratio of cyclosporin to castor oil is below 0.16 and preferably between 0.12 and 0.02. The stated advantage of these ratios is that, when so formulated the emulsion resists crystallization of the cyclosporin upon storage at room temperature for at least 9 months. Ding, column 3, lines 21-25 and lines 58-63. Thus, Ding discloses nothing concerning the limits of these ranges of ratios with respect to either efficacy or comfort.

In Example 1, Ding discloses 5 cyclosporin-containing compositions: these compositions include A) 0.4% cyclosporin A and 5% castor oil, B) 0.2% cyclosporin A and 5% castor oil, C) 0.2% cyclosporin A and 2.5% castor oil, D) 0.1% cyclosporin A and 2.5% castor oil, and E) 0.5% cyclosporin A and 0.625% castor oil. The weight ratios of cyclosporin A to castor oil in all these formulations is 0.08, except in composition B, in which case the ratio is 0.04 and the concentration of cyclosporin A is 0.2% by weight. These compositions were applied to rabbit eyes eight times a day for 7 days and found to cause "slight to mild discomfort" and slight hyperemia in rabbit eyes. Significantly, the compositions of only Examples 1A-1D (each having

a concentration of cyclosporin of 0.1% or greater) were indicated as delivering a "therapeutic level of cyclosporin" in ocular tissues. Ding, column 5, lines 19-22.

Very conspicuously absent from Ding's conclusions concerning the delivery of therapeutic levels of cyclosporin to the tissues of interest was Example 1E, which was not indicated in any way as being therapeutically effective.

The Differences Between the Prior Art and the Claims at Issue

Independent claim 21 is drawn to a therapeutically effective composition for treating an eye of a human or animal comprising an emulsion comprising water, castor oil, and cyclosporin A in a therapeutically effective amount of less than 0.1% by weight, the weight ratio of the cyclosporin A to the castor oil being less than 0.08. Thus, not only must the composition itself be therapeutically effective, but the amount of cyclosporin A must also be therapeutically effective and less than 0.1% by weight.

This latter fact alone is sufficient to demonstrate a non-obvious difference between the present invention and the disclosure of Ding. There is absolutely no indication in Ding that a therapeutically effective dosage of cyclosporin can be achieved at a concentration less than 0.1%. Indeed, the apparent failure of Ding to even test the bioavailablity of composition 1E (at 0.05% cyclosporin having less half or less the amount of cyclosporin A as any other of compositions A-D) demonstrates that Ding et al. could not and did not predict that compositions containing cyclosporin A dosages of less than 0.1% would be therapeutically effective, or alternatively, that composition 1E failed to deliver a therapeutic level of cyclosporin to the ocular tissues of interest. Either possibility must lead to the conclusion that therapeutically effective compositions having less than 0.1% cyclosporin A, as required by claim 21 and its dependent claims were unpredictable at the priority date of the present application.

Furthermore, present claim 21 and its dependent claims require that the ratio of cyclosporin A to castor oil must be less than 0.08%. Although it is true that Ding discloses a range of weight ratios of cyclosporin A to castor oil (less than 0.16 and preferably between 0.12 and 0.02), there is absolutely no indication in Ding that a composition having therapeutically effective dosages of cyclosporin less than 0.1% while simultaneously maintaining a ratio of castor oil to cyclosporin less than 0.08 could be made. Such higher relative concentrations of castor oil are thought to facilitate the resolution of "break-down" of the emulsion in the eye following instillation into the eye. See e.g., Specification at page 4, lines 5-11. Additionally, these relatively higher concentrations of castor oil may improve the cyclosporin's bioavailability when present in the composition in small amounts.

The Level of Ordinary Skill in the Art

Appellants submit that a person of ordinary skill in the art could not have predicted the present invention in light of Ding et al. As stated above, Ding that therapeutically effective compositions have a therapeutically effective amount of cyclosporin A above 0.1% by weight. Not only does Ding fail to indicate that cyclosporin A concentrations below this range would be therapeutically effective, but Ding's conspicuous failure to perform bioavailability testing on composition E, the only composition specifically made by Ding that has an amount of cyclosporin less than 0.1%, indicates that Ding et al. (having at least ordinary skill in the art) did not reasonably expect this composition to contain a therapeutically effective amount of cyclosporin A.

The Examiner has responded that all the embodiments encompassed by Ding et al. "are considered operative." Advisory Action of September 27, 2007, page 2.

With respect, this statement is not consistent with a proper reading of the law, and clearly skews the obviousness analysis. First, *Graham* is concerned with the meaning of a prior art reference (i.e., Ding et al.) to a person of ordinary skill in the art, rather than to the Examiner. *Accord KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. __, 82 U.S.P.Q.2d 1385 (2007) (obviousness is determined from the point of view of a person of ordinary skill in the art at the time the invention was made). Appellants submit that a ordinarily skilled drug formulator would recognize that, for example, a ratio of cyclosporin A to castor oil of "less than 0.16", includes a composition containing no cyclosporin A, as well as compositions containing vanishing small traces of the drug. Such a person would clearly not reasonably expect such trace amounts (or lack) of cyclosporin to constitute a "therapeutically effective amount" of the drug.

Secondly, the Examiner has not explained what is meant by the term "operative" in the sentence quoted above. However, the Examiner cannot mean that every embodiment encompassed by the disclosure of Ding is therapeutically effective, for the reasons presented in the previous paragraph. Nowhere in the lengthy Advisory Action does the Examiner address the material fact that the therapeutic effectiveness of the presently claimed composition and the therapeutic effectiveness of the amount of cyclosporin A in the claimed composition are limitations of the appealed claims, and that this effectiveness is in no way suggested or rendered predictable for the claimed compositions based upon the Ding et el. reference. Thus, whatever the meaning to the term "operable" in the Examiner's Advisory Action comments, a person of ordinary skill in the art would not have believed that all compositions having a ratio of cyclosporin A to castor oil within the range of ratios disclosed by Ding would be therapeutically effective. This is the proper legal inquiry, and to the extent the Examiner's statement contends otherwise, Appellants submit that this is error.

A reference teaches away from an invention when a person of ordinary skill in the art, upon reading a reference, would be led in a direction divergent from the path taken by the

inventor of presently claimed subject matter. See, e.g., *In re Gurley*, 27 F.3d 551,553, 31 U.S.P.Q.2d 1130, ____, (Fed. Cir. 1994). As acknowledged by the Examiner in his remarks in the Advisory Action, Ding discloses that the emulsions described therein are effective to prevent the precipitation of cyclosporin from solution, to prevent the deleterious effects on ocular surface disease caused by oil, and to provide a relatively low level of irritation to sensitive tissues including the eye, upon topical administration.

However, Ding is largely silent as to the range of cyclosporin concentrations conferring therapeutic effectiveness to the emulsions it describes. Only when discussing the compositions of Examples 1A-1D (respectively, 0.4%, 0.2%, 0.2% and 0.1% cyclosporin by weight) is any testing done concerning the delivery of cyclosporin to the eye by these emulsions. Ding, column 5. Thees tests were performed in rabbit eyes and only examined the "bioavailability" of cyclosporin in the disclosed emulsions; the "therapeutic level" of cyclosporin A in tissues of interest was determined, presumably by sacrificing the animals and assaying the amount of drug in dissected ocular tissues. Nevertheless, Ding does not indicate that any testing was performed to determine whether these emulsions were in fact effective in the treatment of dry eye syndrome.

Not one of Examples 1A-1D describles compositions falling within present claim 21 or its dependent claims. Despite the fact that "[t]he formulations of Examples 1-4 [all the formulations] were applied to rabbit eyes eight times a day for seven days and found to cause mild to moderate discomfort to ocular tissue, only the cyclosporin composition having less than 0.1% cyclosporin A by weight (Example 1E) was excluded by Ding et al. from bioavailability testing. This fact would clearly indicate to a person of ordinary skill in the art that Ding et al. did not expect that the composition of Example 1E is therapeutically effective, or Ding was aware that composition 1E did not deliver therapeutic levels of cyclodsporin to the tissues of interest. Accordingly, a person of ordinary skill in the art, upon reading Ding et al, would be led in a

direction divergent from the present formulations having a cyclosporin A concentration of less than 0.1% by weight. Indeed, based at least in part upon this, a finding that an ocular composition containing less than 0.1% cyclosporin A is therapeutically effective is surprising. Accordingly, Ding teaches away from the present invention.

Furthermore, even if Ding did not teach away from the invention of the instant application, given the disclosure (or lack of disclosure) of Ding it is clear that the present invention would have been unpredictable to a person of ordinary skill in the art at the time the invention was made. All Ding discloses is that a composition containing less that 0.1% by weight of cyclosporin A can be made, and is slightly or moderately irritating to the eye. Ding also discloses that, although 5 cyclosporin A-containing compositions were made, Ding decided not to even test the composition containing less than 0.1% cyclosporin A for efficiency of therapeutic delivery.

In order to be predictable, one must have a reasonable expectation of success. The word expect has a meaning defined as "to consider probabable or certain"; Miriam-Webster's Online Dictionary, www.m-w.com/dictionary/expecting (accessed January 11, 2008). However, an event that has no greater than a 50% probability of occurring can not give rise to a reasonable expectation of success. To be probable an event must be more likely to occur than simply based upon a flip of a coin; it must be at least "more possible than not".

In the present case, either a given concentration of cyclosporin is therapeutically effective or it is not. But without further information either option is merely a possibility and cannot give rise to a "reasonable expectation". Without a reasonable expectation of success, the present invention cannot be either predictable or obvious over Ding.

For these reasons, Appellants respectfully submit that the Examiner has erred in rejecting claims 21, 22, 25-26 and 30-39 as allegedly obvious over U.S. Patent Serial No. 5,474,979, and ask the Board to reverse this Examiner's rejection and permit the claims to proceed to issue.

b) Claim 40

Appellants hereby incorporate by reference the arguments made above with respect to claims 21, 22, 25-26 and 30-39 in their argument for the reversal of the rejection of claim 40 under 35 U.S.C. §103(a) as being allegedly obvious over Ding et al. In addition, Appellant have the following comments.

Claim 40 is drawn to a composition for treating an eye of a human or animal comprising an emulsion comprising water, 1.25% by weight of castor oil and 0.05% by weight of cyclosporin A, wherein the weight ratio of the cyclosporin A to the castor oil is 0.04. Claim 40 is thus drawn to a composition having specific concentrations of castor oil and cyclosporin A.

The concentration of cyclosporin A in the composition of claim 40 is 0.05% by weight. This is thus half the concentration of cyclosporin A as is present in the composition of Example 1D of Ding et al., the composition having the lowest concentration of cyclosporin (0.1% by weight) disclosed as being able to deliver therapeutic levels of cyclosporin A to tissues of interest. *See* Ding, column 5, lines 18-22.

Additionally, claim 40 defines a composition that has the same concentration of cyclosporin A (0.5% by weight) as was present in the composition of Example 1E in Ding, conspicuously omitted from the evaluation of therapeutic dosages in Ding. *Id.*

As stated above, Ding's omission of the composition of Example 1E from such evaluation is significant. Appellants submit that a person of ordinary skill in the art is not an automaton; such a person would conclude based on the evidence of record that Ding et al. had a reason for failing to report testing this formulation for therapeutic delivery of cyclosporin. This reason could reasonably be one of two things: either Ding et al. did not believe that a composition containing 0.05% cyclosporin A would delivery therapeutically effective dosages of cyclosporin A to the ocular tissues of interest, or the composition of Example 1E was tested and failed to deliver such dosages.

In either event, Ding et al. would dissuade such a person from attempting to employ a composition containing 0.05% cyclosporin for the treatment of ocular conditions. Thus, Ding teaches away from a composition for treating an eye of a human or animal comprising an emulsion comprising water, 1.25% by weight of castor oil and 0.05% by weight of cyclosporin A.

Thus, the disclosure in the present patent application that Composition II in Example 1, which contains 0.05% cyclosporin A and 1.25% castor oil "provides overall efficacy in treating dry eye disease substantially equal" to Composition 1, containing twice as much cyclosporin A, is clearly a surprising and unpredictable result. Specification, at page 26, lines 23-25.

Furthermore, Ding provides absolutely no reasoning for increasing the concentration of castor oil (relative to the concentration of cyclosporin A) to 1.25%. Thus, nothing in Ding or otherwise in the record indicates to the person of ordinary skill in the art that merely increasing the concentration of castor oil in composition of Example 1E would render effective a composition previously thought to be ineffective for the treatment of ocular surface disease.

For this reason, Appellants contend that the Examiner erred in rejecting claim 40 as being obvious over Ding, and respectfully ask the Board to reverse the rejection of this claim and permit it to proceed to issue.

Non-Statutory Obviousness-Type Double Patenting Rejection

a) Claims 21, 22, 25-26 and 30-36

Claims 21, 22, 25-126 and 30-36 stand rejected pursuant to the judicially created doctrine of obviousness-type double patenting over claims 1-8 of Ding et al., U.S. Patent No. 5,474,979.

While obviousness-type double patenting and §103 rejections may be analogous in the sense that an obviousness analysis is performed "the objects of comparison are very different: Obviousness compares claimed subject matter to the prior art; nonstatutory double patenting compares claims in an earlier patent to claims in a later patent or application." *Geneva Pharmaceuticals, Inc. v. GlaxoSmithKline PLC*, 349 F.3d 1373, 68 USPQ2d 1865 (Fed. Cir. 2003). Furthermore, "when considering whether the invention defined in a claim or 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." MPEP §804(II)(b)(1) *citing General Foods Corp. v. Studiengesellschaft Hohle mbH*, 972 F.2d 1272, 1279, 23 USPQ2d 1839, 1846 (Fed. Cir. 1992).

Claim 1 of Ding is drawn to a pharmaceutical composition comprising a non-irritating emulsion of at least one cyclosporin in admixture with a higher fatty acid glyceride, polysorbate 80 and an emulsion-stabilizing amount of Pemulin® in water. Claims 2-5 are dependant claims. Claim 2 specifies that the cyclosporin comprises cyclosporin A. Claim 3, which depends from claim 2, indicates that the weight ratio of the higher fatty acid glyceride and polysorbate 80 is between about 0.3 and about 30. Claim 4, which depends from claim 3, indicates that the higher fatty acid glyceride comprises castor oil, and that the weight ratio of cyclosporin to castor oil is

below about 0.16. Claim 5 depends from claim 1, and indicates that the higher fatty acid glyceride and polysorbate 80 are present are present in amounts sufficient to prevent crystallization of cyclosporin for a period of up to about 9 months.

Claim 6 of Ding is an independent claim directed to a pharmaceutical emulsion comprising cyclosporin A, castor oil, Pemulin®, glycerine, polysorbate 80 and water in amounts sufficient to prevent crystallization of cyclosporin A for up to 9 months and suitable for topical ocular administration. As such claim 6 adds nothing to claims 1-5, and does not render the present invention obvious for the same reasons. Claim 7 is drawn to the pharmaceutical emulsion of claim 6 in which the cyclosporin A is present in an amount of from about 0.05% to about 0.4% by weight and the castor oil is present in an amount of from about 0.625% to about 5% by weight, the polysorbate 80 is present in about 1% by weight, the Pemulin® is present in an amount of about 0.05% by weight, and the glycerine is present in an amount of about 2.2% by weight.

Claim 8 is an independent claim drawn to a pharmaceutical emulsion consisting of cyclosporin A is present in an amount of from about 0.05% to about 0.4% by weight and the castor oil is present in an amount of from about 0.625% to about 5% by weight, the polysorbate 80 is present in about 1% by weight, the Pemulin® is present in an amount of about 0.05% by weight, and the glycerin is present in an amount of about 2.2% by weight, with a pH of between about 7.2 and 7.6, suitable for application to ocular tissue.

Each of claims 1-8 of Ding is drawn to a "pharmaceutical" emulsion or composition. In order to constitute a "pharmaceutical composition", the composition of claims 1-8 of Ding must be pharmaceutically active, and must define an pharmaceutically effective amount of the only active ingredient, cyclosporin A. However, none of these claims indicates what an "pharmaceutical" dosage of cyclosporin A would be.

Under the doctrine of obviousness-type double patenting only the claims (rather than the specification) may be used to reject pending claims in a double patenting rejection, however, "those portions of the specification which provide support for the patent claims may also be examined and considered when addressing the issue of whether a claim in the application defines an obvious variation of an invention claimed in the patent." *In re Vogel*, 422 F.2d 438, 441-42, 164 USPQ 619, 622 (CCPA 1970). Since the claims do not tell us what a "pharmaceutical" concentration of cyclosporin A is, the Ding patent's disclosure must be consulted to help explain the meaning of this term to a person of ordinary skill in the art at the time the present patent application was filed.

Ding discloses 5 exemplary compositions (Examples 1A-1E) containing cyclosporin A, present in concentrations of 4%, 2%, 2% 0.1% and 0.5% by weight, respectively. Although each composition appeared to cause slight to moderate discomfort when applied to rabbit eyes, only those compositions (Examples 1A-1D) having a cyclosporin A concentration of 0.1% or greater were reported to deliver therapeutic levels of cyclosporin A to tissues of interest. Not only was the composition of Example 1E not reported to have such efficacy, but Ding et al. are conspicuously silent with respect to the therapeutic efficacy of this composition. See Ding, column 4, lines 32-67 and column 5, lines 18-23.

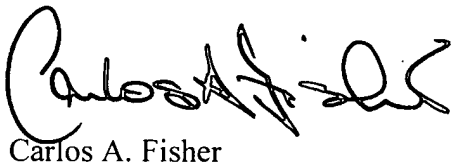
Thus, the specification of Ding, read from the perspective of a person of ordinary skill in the art seeking to define the term "pharmaceutical" as used in the claims, makes clear that a pharmaceutical composition has a cyclosporin A concentration of 0.1% by weight or above. Indeed, such a person would be led by Ding not to believe that a "pharmaceutical composition" is defined by concentrations of cyclosporin less than 0.1%, thus Ding teaches "in a direction divergent from the path taken" by the inventors of presently claimed subject matter. See, e.g., *In re Gurley*, 27 F.3d 551, 553, 31 U.S.P.Q.2d 1130, ___ (Fed. Cir. 1994).

It is therefore clear that a therapeutically active composition comprising water, castor oil, and a therapeutically active amount of cyclodextrin A less than 0.1% by weight cyclosporin A is contrary to the teaching of the claims of Ding et al. and is surprising in light thereof.

Additionally, the fact that a claimed invention may be encompassed by a disclosed generic disclosure does not, without more, render that invention obvious. See e.g., *In re Baird*, 16 F.3d 380, 29 U.S.P.Q.2d 1550 (Fed. Cir. 1994). For example, while claim 4 mentions a range of weight ratios (below about 0.16) of cyclosporin A to castor oil, this range clearly includes a composition wherein the weight ratio is 0 and the composition lacks cyclosporin. Therefore a person of ordinary skill in the art would know based upon this claim that claim 4 contains inoperable embodiments and would not be guided in any way to the therapeutically effective composition of claim 21 and its dependent claims, wherein the therapeutically effective concentration of cyclosporin A is less than 0.1% by weight, and the ratio of cyclosporin A to castor oil is below 0.08.

For these reasons Appellants hereby request that the Board reverse the Examiner's rejection of claims 21, 22, 25-26 and 30-36 over claims 1-8 of Ding et al. and permit the claims to proceed to issue.

Respectfully submitted,



Carlos A. Fisher
Attorney for Appellant
Reg. No. 36, 510
4 Venture, Suite 300
Irvine, CA 92618
(949) 450-1750
Facsimile (494) 450-1764

CLAIM APPENDIX

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

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

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

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

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

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

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

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

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

16. (Withdrawn) The method of claim 1 wherein the composition comprises an

effective amount of a tonicity component.

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

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

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

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

21. (Previously Presented) A therapeutically effective composition for treating an eye of a human or animal comprising an emulsion comprising water, castor oil, and cyclosporin A in a therapeutically effective amount of less than 0.1% by weight, the weight ratio of the cyclosporin A to the castor oil being less than 0.08.

22. (Previously presented) 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 A.

23. (Canceled)

24. (Canceled)

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

26. (Previously Presented) The composition of claim 21 wherein the castor oil is present in an amount greater than 0.625% by weight of the composition.

27. (Canceled)

28. (Canceled)

29. (Canceled)

30. (Previously presented) The composition of claim 21 having a make-up so that when the composition is topically 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 A.

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

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

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

34. (Original) The composition of claim 21 wherein the composition comprises a

polyelectrolytic component in an amount effective in stabilizing the composition.

35. (Original) 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. (Original) 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. (Previously presented) The composition of claim 21 which includes 1.25% by weight of castor oil.

38. (Previously presented) The composition of claim 21 which includes 0.05% by weight of cyclosporin A.

39. (Previously presented) The composition of claim 38 which includes 1.25% by weight of castor oil.

40. (Previously presented) A composition for treating an eye of a human or animal comprising an emulsion comprising water, 1.25% by weight of castor oil and 0.05% by weight of cyclosporin A, the weight ratio of the cyclosporin A to the castor oil being 0.04.

EVIDENCE APPEENDIX

1. Ding et al., U.S. Patent No. 5,474,979.

RELATED PROCEDINGS APPENDIX

None

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.
10/927,857	08/27/2004	Andrew Acheampong	D-3111	2409

33197 7590 02/07/2008

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

EXAMINER	
ART UNIT	PAPER NUMBER

DATE MAILED: 02/07/2008

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

Notification of Non-Compliant Appeal Brief (37 CFR 41.37)	Application No. 10/927,857	Applicant(s) ACHEAMPONG ET AL.	
	Examiner Marcela Cordero Garcia	Art Unit 1654	

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

The Appeal Brief filed on *15 January 2008* is defective for failure to comply with one or more provisions of 37 CFR 41.37.

To avoid dismissal of the appeal, applicant must file anamended brief or other appropriate correction (see MPEP 1205.03) within **ONE MONTH or THIRTY DAYS** from the mailing date of this Notification, whichever is longer. **EXTENSIONS OF THIS TIME PERIOD MAY BE GRANTED UNDER 37 CFR 1.136.**

1. ☐ The brief does not contain the items required under 37 CFR 41.37(c), or the items are not under the proper heading or in the proper order.

2. ☐ The brief does not contain a statement of the status of all claims, (e.g., rejected, allowed, withdrawn, objected to, canceled), or does not identify the appealed claims (37 CFR 41.37(c)(1)(iii)).

3. ☐ At least one amendment has been filed subsequent to the final rejection, and the brief does not contain a statement of the status of each such amendment (37 CFR 41.37(c)(1)(iv)).

4. ☐ (a) The brief does not contain a concise explanation of the subject matter defined in each of the independent claims involved in the appeal, referring to the specification by page and line number and to the drawings, if any, by reference characters; and/or (b) the brief fails to: (1) identify, for each independent claim involved in the appeal and for each dependent claim argued separately, every means plus function and step plus function under 35 U.S.C. 112, sixth paragraph, and/or (2) set forth the structure, material, or acts described in the specification as corresponding to each claimed function with reference to the specification by page and line number, and to the drawings, if any, by reference characters (37 CFR 41.37(c)(1)(v)).

5. ☒ The brief does not contain a concise statement of each ground of rejection presented for review (37 CFR 41.37(c)(1)(vi))

6. ☐ The brief does not present an argument under a separate heading for each ground of rejection on appeal (37 CFR 41.37(c)(1)(vii)).

7. ☐ The brief does not contain a correct copy of the appealed claims as an appendix thereto (37 CFR 41.37(c)(1)(viii)).

8. ☐ The brief does not contain copies of the evidence submitted under 37 CFR 1.130, 1.131, or 1.132 or of any other evidence entered by the examiner **and relied upon by appellant in the appeal**, along with a statement setting forth where in the record that evidence was entered by the examiner, as an appendix thereto (37 CFR 41.37(c)(1)(ix)).

9. ☐ The brief does not contain copies of the decisions rendered by a court or the Board in the proceeding identified in the Related Appeals and Interferences section of the brief as an appendix thereto (37 CFR 41.37(c)(1)(x)).

10. ☒ Other (including any explanation in support of the above items):

5.vi Grounds of Rejection :The claims in the Double Patenting rejection contains claims that have been cancelled. The grounds of rejection to be reviewed on appeal should list the same rejections and claims as those set in the final office action. .

/Everett R. Williams /
Everett R. Williams
Patent Appeals Specialist

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application No.	:	10/927,857	Confirmation No. 2409
Applicant	:	Acheampong et al.	
Filed	:	August 27, 2004	
Title	:	METHODS OF PROVIDING THERAPEUTIC EFFECTS USING CYCLOSPORIN COMPONENTS	
TC/A.U.	:	1654	
Examiner	:	Cordero Garcia, Marcela M	
Docket No.	:	D-3111	
Customer No.	:	33197	

Mail Stop Appeal Brief - Patent
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

EXPRESS MAIL CERTIFICATE

EXPRESS MAIL MAILING LABEL NO. EV 516292614 US

Date of Deposit: **March 7, 2008**

I hereby certify that the following documents as identified below are being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 CFR 1.10 on the date indicated above and are addressed to the Mail Stop Appeal Brief - Patent, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450:

- ☒ Amended Appeal Brief
- ☒ Transmittal Letter
- ☒ Stamped, self-addressed postcard
- ☐
- ☐
- ☐
- ☐
- ☐ Other: _____

Each of the 3 above-identified documents are enclosed herewith.

Respectfully submitted,

Date: March 7, 2008

Shawnna Waddell
Assistant to Carlos A. Fisher
Stout, Uxa, Buyan & Mullins, LLP
4 Venture, Suite 300
Irvine, California 92618
Telephone: 949-450-1750

03-10-08 IFW AF

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Appl. No.	: 10/927,857	Confirmation No.	2409
Appellant	: ACHEAMPONG ET AL.		
Filed	: August 27, 2004		
Title	: METHODS OF PROVIDING THERAPEUTIC EFFECTS USING CYCLOSPORIN COMPONENTS		
TC/A.U.	: 1654		
Examiner	: Cordero Garcia, Marcela M.		
Docket No.	: D-3111		
Customer No.	: 33197		

CERTIFICATE OF EXPRESS MAILING

I hereby certify that this paper is being sent by Express Mail bearing Label No. EV 516292614 US to Box Appeal Brief-Patents, Commissioner for Patents, P.O. Box1450, Alexandria, VA 22313-1450 on the date shown below.

Date: March 7, 2008

Name: Shirley Wade

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

Transmittal Letter

Applicants are submitting the attached Amended Appeal Brief in response to the Notice of Non-Compliant Brief, mailed February 7, 2008. As this reply is being filed within the period set for such reply, no fee is thought due in connection with the submission of this Amended Appeal Brief. However, if applicants are in error in this regard, please use Deposit Account 50-4004 for the payment of any fee now due.

Respectfully submitted,

Carlos A. Fisher

Carlos A. Fisher
Attorney for Appellant

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Appl. No.	: 10/927,857	Confirmation No.	2409
Appellant	: ACHEAMPONG ET AL.		
Filed	: August 27, 2004		
Title	: METHODS OF PROVIDING THERAPEUTIC EFFECTS USING CYCLOSPORIN COMPONENTS		
TC/A.U.	: 1654		
Examiner	: Cordero Garcia, Marcela M.		
Docket No.	: D-3111		
Customer No.	: 33197		

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

CERTIFICATE OF EXPRESS MAILING

I hereby certify that this paper is being sent by Express Mail bearing Label No. EV516292604US to Box Appeal Brief-Patents, Commissioner for Patents, P.O. Box1450, Alexandria, VA 22313-1450 on the date shown below.

Date: March 7, 2008

Name: Sheena Wallace

AMENDED APPEAL BRIEF

Carlos A. Fisher
Attorney for Appellant

TABLE OF CONTENTS

REAL PARTY IN INTEREST

The inventors Andrew Acheampong, Diane Tang-Liu, James N. Chang, and David F. Power assigned their entire interest in this patent application to Allergan, Inc. via an assignment document signed by the inventors on August 12, 2004 and recorded at reel 0157490, frame 0698 on August 27, 2004. Allergan, Inc., is therefore the owner of this patent application and the real party in interest in this appeal.

RELATED APPEALS AND INTERFERENCES

There are no related appeals or interferences.

STATUS OF CLAIMS

Claims 1 – 20 are withdrawn.

Claims 23-24 and 27-29 have been cancelled.

Claims 21-22, 25-26, and 30-40 are pending, have been rejected, and are under appeal.

STATUS OF AMENDMENTS

No amendment of any claim has been filed after the date of final rejection.

SUMMARY OF CLAIMED SUBJECT MATTER

Independent claim 21 is drawn to a therapeutically effective composition for treating an eye of a human or animal comprising an emulsion comprising water, castor oil, and cyclosporin A in a therapeutically effective amount of less than 0.1% by weight, the weight ratio of the cyclosporin A to the castor oil being less than 0.08. Support for this claim can be found in the specification, e.g., at Example 1, beginning on page 25 and page 8, lines 2-12.

Dependent claim 22 is drawn to the composition of claim 21 wherein the composition is formed as to result in substantially no detectable concentration of cyclosporin A in a patient's blood when an amount of the composition effective to treat dry eye syndrome is administered to the patient's eye. Support for this claim can be found where indicated for claim 21 and in the specification at, e.g., page 9, line 6 to page 10, line 13.

Dependent claim 25 is drawn to the composition of claim 21 wherein the composition is in the form of an emulsion. Support for this claim can be found where indicated for claim 21 and in the specification at, e.g., page 23, lines 16-19.

Dependent claim 26 is drawn to the composition of claim 21 wherein the castor oil is present in an amount greater than 0.625% by weight of the composition. Support for this claim can be found where indicated for claim 21 and in the specification at, e.g., page 16, lines 1-7.

Dependent claim 30 is drawn to the composition of claim 21 having a make-up so that when the composition is topically 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 A. Support for this claim can be found where indicated for claim 21 and in the specification at, e.g., page 8, lines 13-23 and page 9, line 6 to page 10, line 13.

Dependent claim 31 is drawn to the composition of claim 21 wherein the composition comprises an effective amount of an emulsifier component. Support for this claim can be found where indicated for claim 21 and in the specification at, e.g., page 17, lines 20-27.

Dependent claim 32 is drawn to the composition of claim 21 wherein the composition comprises an effective amount of a tonicity component. Support for this claim can be found where indicated for claim 21 and in the specification at, e.g., page 20, lines 7-17.

Dependent claim 33 is drawn to the composition of claim 21 wherein the composition comprises an effective amount of an organic tonicity component. Support for this claim can be found where indicated for claim 21 and in the specification at, e.g., page 20, lines 7-17.

Dependent claim 34 is drawn to the composition of claim 21 wherein the composition comprises a polyelectrolytic component in an amount effective in stabilizing the composition. Support for this claim can be found where indicated for claim 21 and in the specification at, e.g., the paragraph bridging pages 19 and 20.

Dependent claim 35 is drawn to 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. Support for this claim can be found where indicated for claim 21 and in the specification at, e.g., page 7, lines 16-19.

Dependent claim 36 is drawn to 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. Support for this claim can be found where indicated for claim 21 and in the specification at, e.g., page 7, lines 16-19.

Dependent claim 37 is drawn to the composition of claim 21, which includes 1.25%, by

weight of castor oil. Support for this claim can be found where indicated for claim 21 and in the specification at, e.g., Example 1, beginning on page 25.

Dependent claim 38 is drawn to the composition of claim 21 which includes 0.05% by weight of cyclosporin A. Support for this claim can be found where indicated for claim 21 and in the specification at, e.g., Example 1, beginning on page 25.

Dependent claim 39 is drawn to the composition of claim 38 which includes 1.25% by weight of castor oil. Support for this claim can be found where indicated for claim 38 and in the specification at, e.g., Example 1, beginning on page 25.

Independent claim 40 is drawn to a composition for treating an eye of a human or animal comprising an emulsion comprising water, 1.25% by weight of castor oil and 0.05% by weight of cyclosporin A, the weight ratio of the cyclosporin A to the castor oil being 0.04. Support for this claim can be found e.g., Example 1, beginning on page 25 and page 3, lines 4-6.

GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

Presently pending claims 1-22, 25-26, and 30-40 have all been rejected pursuant to 35 U.S.C. §103(a) as being allegedly obvious over Ding et al., U.S. Patent Serial No. 5,474,979.

Claims 21,22, 25, 26, and 30-36 have been rejected under the doctrine of non-statutory obviousness-type double patenting over Ding et al., U.S. Patent Serial No. 5,474,979.

ARGUMENT

Rejections pursuant to 35 USC 103(a)

a) Claims 21, 22, 25-26 and 30-39

Claims 21, 22, 25-26 and 30-39 were rejected as allegedly obvious pursuant to 35 USC §103(a) over U.S. Patent Serial No. 5,474,979, to Ding et al. (the "Ding patent"). Appellants respectfully appeal from the Examiner's 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 see 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 nonobviousness 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

Ding et al., U.S. Patent Serial No. 5,474,979 (hereinafter "Ding") is the sole prior art reference alleged by the Examiner to render the present invention obvious. This reference is directed to stable emulsions for the delivery of poorly water-soluble medications to sensitive tissues. Ding, column 1, lines 4-6. Ding states that oils exacerbate the symptoms of certain ocular surface diseases such as dry eye syndrome, that are otherwise effectively treated using cyclosporin, a poorly water-soluble drug. Ding, et al., column 2, lines 46-49. Additionally, ocular formulations containing cyclosporin dissolved in oil (as in an emulsion) limits the bioavailability of cyclosporin to the target tissue. Ding, column 1, lines 45-53.

Ding discloses an emulsion containing cyclosporin (a poorly water soluble drug), castor oil and polysorbate 80 wherein the weight ratio of cyclosporin to castor oil is below 0.16 and preferably between 0.12 and 0.02. The stated advantage of these ratios is that, when so formulated the emulsion resists crystallization of the cyclosporin upon storage at room temperature for at least 9 months. Ding, column 3, lines 21-25 and lines 58-63. Thus, Ding discloses nothing concerning the limits of these ranges of ratios with respect to either efficacy or comfort.

In Example 1, Ding discloses 5 cyclosporin-containing compositions: these compositions include A) 0.4% cyclosporin A and 5% castor oil, B) 0.2% cyclosporin A and 5% castor oil, C) 0.2% cyclosporin A and 2.5% castor oil, D) 0.1% cyclosporin A and 2.5% castor oil, and E) 0.5% cyclosporin A and 0.625% castor oil. The weight ratios of cyclosporin A to castor oil in all these formulations is 0.08, except in composition B, in which case the ratio is 0.04 and the concentration of cyclosporin A is 0.2% by weight. These compositions were applied to rabbit eyes eight times a day for 7 days and found to cause "slight to mild discomfort" and slight hyperemia in rabbit eyes. Significantly, the compositions of only Examples 1A-1D (each having

a concentration of cyclosporin of 0.1% or greater) were indicated as delivering a "therapeutic level of cyclosporin" in ocular tissues. Ding, column 5, lines 19-22.

Very conspicuously absent from Ding's conclusions concerning the delivery of therapeutic levels of cyclosporin to the tissues of interest was Example 1E, which was not indicated in any way as being therapeutically effective.

The Differences Between the Prior Art and the Claims at Issue

Independent claim 21 is drawn to a therapeutically effective composition for treating an eye of a human or animal comprising an emulsion comprising water, castor oil, and cyclosporin A in a therapeutically effective amount of less than 0.1% by weight, the weight ratio of the cyclosporin A to the castor oil being less than 0.08. Thus, not only must the composition itself be therapeutically effective, but the amount of cyclosporin A must also be therapeutically effective and less than 0.1% by weight.

This latter fact alone is sufficient to demonstrate a non-obvious difference between the present invention and the disclosure of Ding. There is absolutely no indication in Ding that a therapeutically effective dosage of cyclosporin can be achieved at a concentration less than 0.1%. Indeed, the apparent failure of Ding to even test the bioavailablity of composition 1E (at 0.05% cyclosporin having less half or less the amount of cyclosporin A as any other of compositions A-D) demonstrates that Ding et al. could not and did not predict that compositions containing cyclosporin A dosages of less than 0.1% would be therapeutically effective, or alternatively, that composition 1E failed to deliver a therapeutic level of cyclosporin to the ocular tissues of interest. Either possibility must lead to the conclusion that therapeutically effective compositions having less than 0.1% cyclosporin A, as required by claim 21 and its dependent claims were unpredictable at the priority date of the present application.

Furthermore, present claim 21 and its dependent claims require that the ratio of cyclosporin A to castor oil must be less than 0.08%. Although it is true that Ding discloses a range of weight ratios of cyclosporin A to castor oil (less than 0.16 and preferably between 0.12 and 0.02), there is absolutely no indication in Ding that a composition having therapeutically effective dosages of cyclosporin less than 0.1% while simultaneously maintaining a ratio of castor oil to cyclosporin less than 0.08 could be made. Such higher relative concentrations of castor oil are thought to facilitate the resolution of "break-down" of the emulsion in the eye following instillation into the eye. See e.g., Specification at page 4, lines 5-11. Additionally, these relatively higher concentrations of castor oil may improve the cyclosporin's bioavailability when present in the composition in small amounts.

The Level of Ordinary Skill in the Art

Appellants submit that a person of ordinary skill in the art could not have predicted the present invention in light of Ding et al. As stated above, Ding that therapeutically effective compositions have a therapeutically effective amount of cyclosporin A above 0.1% by weight. Not only does Ding fail to indicate that cyclosporin A concentrations below this range would be therapeutically effective, but Ding's conspicuous failure to perform bioavailability testing on composition E, the only composition specifically made by Ding that has an amount of cyclosporin less than 0.1%, indicates that Ding et al. (having at least ordinary skill in the art) did not reasonably expect this composition to contain a therapeutically effective amount of cyclosporin A.

The Examiner has responded that all the embodiments encompassed by Ding et al. "are considered operative." Advisory Action of September 27, 2007, page 2.

With respect, this statement is not consistent with a proper reading of the law, and clearly skews the obviousness analysis. First, *Graham* is concerned with the meaning of a prior art reference (i.e., Ding et al.) to a person of ordinary skill in the art, rather than to the Examiner. *Accord KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. __, 82 U.S.P.Q.2d 1385 (2007) (obviousness is determined from the point of view of a person of ordinary skill in the art at the time the invention was made). Appellants submit that a ordinarily skilled drug formulator would recognize that, for example, a ratio of cyclosporin A to castor oil of "less than 0.16", includes a composition containing no cyclosporin A, as well as compositions containing vanishing small traces of the drug. Such a person would clearly not reasonably expect such trace amounts (or lack) of cyclosporin to constitute a "therapeutically effective amount" of the drug.

Secondly, the Examiner has not explained what is meant by the term "operative" in the sentence quoted above. However, the Examiner cannot mean that every embodiment encompassed by the disclosure of Ding is therapeutically effective, for the reasons presented in the previous paragraph. Nowhere in the lengthy Advisory Action does the Examiner address the material fact that the therapeutic effectiveness of the presently claimed composition and the therapeutic effectiveness of the amount of cyclosporin A in the claimed composition are limitations of the appealed claims, and that this effectiveness is in no way suggested or rendered predictable for the claimed compositions based upon the Ding et el. reference. Thus, whatever the meaning to the term "operable" in the Examiner's Advisory Action comments, a person of ordinary skill in the art would not have believed that all compositions having a ratio of cyclosporin A to castor oil within the range of ratios disclosed by Ding would be therapeutically effective. This is the proper legal inquiry, and to the extent the Examiner's statement contends otherwise, Appellants submit that this is error.

A reference teaches away from an invention when a person of ordinary skill in the art, upon reading a reference, would be led in a direction divergent from the path taken by the

inventor of presently claimed subject matter. See, e.g., *In re Gurley*, 27 F.3d 551,553, 31 U.S.P.Q.2d 1130, ____, (Fed. Cir. 1994). As acknowledged by the Examiner in his remarks in the Advisory Action, Ding discloses that the emulsions described therein are effective to prevent the precipitation of cyclosporin from solution, to prevent the deleterious effects on ocular surface disease caused by oil, and to provide a relatively low level of irritation to sensitive tissues including the eye, upon topical administration.

However, Ding is largely silent as to the range of cyclosporin concentrations conferring therapeutic effectiveness to the emulsions it describes. Only when discussing the compositions of Examples 1A-1D (respectively, 0.4%, 0.2%, 0.2% and 0.1% cyclosporin by weight) is any testing done concerning the delivery of cyclosporin to the eye by these emulsions. Ding, column 5. Thees tests were performed in rabbit eyes and only examined the "bioavailability" of cyclosporin in the disclosed emulsions; the "therapeutic level" of cyclosporin A in tissues of interest was determined, presumably by sacrificing the animals and assaying the amount of drug in dissected ocular tissues. Nevertheless, Ding does not indicate that any testing was performed to determine whether these emulsions were in fact effective in the treatment of dry eye syndrome.

Not one of Examples 1A-1D describles compositions falling within present claim 21 or its dependent claims. Despite the fact that "[t]he formulations of Examples 1-4 [all the formulations] were applied to rabbit eyes eight times a day for seven days and found to cause mild to moderate discomfort to ocular tissue, only the cyclosporin composition having less than 0.1% cyclosporin A by weight (Example 1E) was excluded by Ding et al. from bioavailability testing. This fact would clearly indicate to a person of ordinary skill in the art that Ding et al. did not expect that the composition of Example 1E is therapeutically effective, or Ding was aware that composition 1E did not deliver therapeutic levels of cyclodsporin to the tissues of interest. Accordingly, a person of ordinary skill in the art, upon reading Ding et al, would be led in a

direction divergent from the present formulations having a cyclosporin A concentration of less than 0.1% by weight. Indeed, based at least in part upon this, a finding that an ocular composition containing less than 0.1% cyclosporin A is therapeutically effective is surprising. Accordingly, Ding teaches away from the present invention.

Furthermore, even if Ding did not teach away from the invention of the instant application, given the disclosure (or lack of disclosure) of Ding it is clear that the present invention would have been unpredictable to a person of ordinary skill in the art at the time the invention was made. All Ding discloses is that a composition containing less that 0.1% by weight of cyclosporin A can be made, and is slightly or moderately irritating to the eye. Ding also discloses that, although 5 cyclosporin A-containing compositions were made, Ding decided not to even test the composition containing less than 0.1% cyclosporin A for efficiency of therapeutic delivery.

In order to be predictable, one must have a reasonable expectation of success. The word expect has a meaning defined as "to consider probabable or certain"; Miriam-Webster's Online Dictionary, www.m-w.com/dictionary/expecting (accessed January 11, 2008). However, an event that has no greater than a 50% probability of occurring can not give rise to a reasonable expectation of success. To be probable an event must be more likely to occur than simply based upon a flip of a coin; it must be at least "more possible than not".

In the present case, either a given concentration of cyclosporin is therapeutically effective or it is not. But without further information either option is merely a possibility and cannot give rise to a "reasonable expectation". Without a reasonable expectation of success, the present invention cannot be either predictable or obvious over Ding.

For these reasons, Appellants respectfully submit that the Examiner has erred in rejecting claims 21, 22, 25-26 and 30-39 as allegedly obvious over U.S. Patent Serial No. 5,474,979, and ask the Board to reverse this Examiner's rejection and permit the claims to proceed to issue.

b) Claim 40

Appellants hereby incorporate by reference the arguments made above with respect to claims 21, 22, 25-26 and 30-39 in their argument for the reversal of the rejection of claim 40 under 35 U.S.C. §103(a) as being allegedly obvious over Ding et al. In addition, Appellant have the following comments.

Claim 40 is drawn to a composition for treating an eye of a human or animal comprising an emulsion comprising water, 1.25% by weight of castor oil and 0.05% by weight of cyclosporin A, wherein the weight ratio of the cyclosporin A to the castor oil is 0.04. Claim 40 is thus drawn to a composition having specific concentrations of castor oil and cyclosporin A.

The concentration of cyclosporin A in the composition of claim 40 is 0.05% by weight. This is thus half the concentration of cyclosporin A as is present in the composition of Example 1D of Ding et al., the composition having the lowest concentration of cyclosporin (0.1% by weight) disclosed as being able to deliver therapeutic levels of cyclosporin A to tissues of interest. *See* Ding, column 5, lines 18-22.

Additionally, claim 40 defines a composition that has the same concentration of cyclosporin A (0.5% by weight) as was present in the composition of Example 1E in Ding, conspicuously omitted from the evaluation of therapeutic dosages in Ding. *Id.*

As stated above, Ding's omission of the composition of Example 1E from such evaluation is significant. Appellants submit that a person of ordinary skill in the art is not an automaton; such a person would conclude based on the evidence of record that Ding et al. had a reason for failing to report testing this formulation for therapeutic delivery of cyclosporin. This reason could reasonably be one of two things: either Ding et al. did not believe that a composition containing 0.05% cyclosporin A would delivery therapeutically effective dosages of cyclosporin A to the ocular tissues of interest, or the composition of Example 1E was tested and failed to deliver such dosages.

In either event, Ding et al. would dissuade such a person from attempting to employ a composition containing 0.05% cyclosporin for the treatment of ocular conditions. Thus, Ding teaches away from a composition for treating an eye of a human or animal comprising an emulsion comprising water, 1.25% by weight of castor oil and 0.05% by weight of cyclosporin A.

Thus, the disclosure in the present patent application that Composition II in Example 1, which contains 0.05% cyclosporin A and 1.25% castor oil "provides overall efficacy in treating dry eye disease substantially equal" to Composition 1, containing twice as much cyclosporin A, is clearly a surprising and unpredictable result. Specification, at page 26, lines 23-25.

Furthermore, Ding provides absolutely no reasoning for increasing the concentration of castor oil (relative to the concentration of cyclosporin A) to 1.25%. Thus, nothing in Ding or otherwise in the record indicates to the person of ordinary skill in the art that merely increasing the concentration of castor oil in composition of Example 1E would render effective a composition previously thought to be ineffective for the treatment of ocular surface disease.

For this reason, Appellants contend that the Examiner erred in rejecting claim 40 as being obvious over Ding, and respectfully ask the Board to reverse the rejection of this claim and permit it to proceed to issue.

Non-Statutory Obviousness-Type Double Patenting Rejection

a) Claims 21, 22, 25-26 and 30-36

Claims 21, 22, 25-126 and 30-36 stand rejected pursuant to the judicially created doctrine of obviousness-type double patenting over claims 1-8 of Ding et al., U.S. Patent No. 5,474,979.

While obviousness-type double patenting and §103 rejections may be analogous in the sense that an obviousness analysis is performed "the objects of comparison are very different: Obviousness compares claimed subject matter to the prior art; nonstatutory double patenting compares claims in an earlier patent to claims in a later patent or application." *Geneva Pharmaceuticals, Inc. v. GlaxoSmithKline PLC*, 349 F.3d 1373, 68 USPQ2d 1865 (Fed. Cir. 2003). Furthermore, "when considering whether the invention defined in a claim or 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." MPEP §804(II)(b)(1) *citing General Foods Corp. v. Studiengesellschaft Hohle mbH*, 972 F.2d 1272, 1279, 23 USPQ2d 1839, 1846 (Fed. Cir. 1992).

Claim 1 of Ding is drawn to a pharmaceutical composition comprising a non-irritating emulsion of at least one cyclosporin in admixture with a higher fatty acid glyceride, polysorbate 80 and an emulsion-stabilizing amount of Pemulin® in water. Claims 2-5 are dependant claims. Claim 2 specifies that the cyclosporin comprises cyclosporin A. Claim 3, which depends from claim 2, indicates that the weight ratio of the higher fatty acid glyceride and polysorbate 80 is between about 0.3 and about 30. Claim 4, which depends from claim 3, indicates that the higher fatty acid glyceride comprises castor oil, and that the weight ratio of cyclosporin to castor oil is

below about 0.16. Claim 5 depends from claim 1, and indicates that the higher fatty acid glyceride and polysorbate 80 are present are present in amounts sufficient to prevent crystallization of cyclosporin for a period of up to about 9 months.

Claim 6 of Ding is an independent claim directed to a pharmaceutical emulsion comprising cyclosporin A, castor oil, Pemulin®, glycerine, polysorbate 80 and water in amounts sufficient to prevent crystallization of cyclosporin A for up to 9 months and suitable for topical ocular administration. As such claim 6 adds nothing to claims 1-5, and does not render the present invention obvious for the same reasons. Claim 7 is drawn to the pharmaceutical emulsion of claim 6 in which the cyclosporin A is present in an amount of from about 0.05% to about 0.4% by weight and the castor oil is present in an amount of from about 0.625% to about 5% by weight, the polysorbate 80 is present in about 1% by weight, the Pemulin® is present in an amount of about 0.05% by weight, and the glycerine is present in an amount of about 2.2% by weight.

Claim 8 is an independent claim drawn to a pharmaceutical emulsion consisting of cyclosporin A is present in an amount of from about 0.05% to about 0.4% by weight and the castor oil is present in an amount of from about 0.625% to about 5% by weight, the polysorbate 80 is present in about 1% by weight, the Pemulin® is present in an amount of about 0.05% by weight, and the glycerin is present in an amount of about 2.2% by weight, with a pH of between about 7.2 and 7.6, suitable for application to ocular tissue.

Each of claims 1-8 of Ding is drawn to a "pharmaceutical" emulsion or composition. In order to constitute a "pharmaceutical composition", the composition of claims 1-8 of Ding must be pharmaceutically active, and must define an pharmaceutically effective amount of the only active ingredient, cyclosporin A. However, none of these claims indicates what an "pharmaceutical" dosage of cyclosporin A would be.

Under the doctrine of obviousness-type double patenting only the claims (rather than the specification) may be used to reject pending claims in a double patenting rejection, however, "those portions of the specification which provide support for the patent claims may also be examined and considered when addressing the issue of whether a claim in the application defines an obvious variation of an invention claimed in the patent." *In re Vogel*, 422 F.2d 438, 441-42, 164 USPQ 619, 622 (CCPA 1970). Since the claims do not tell us what a "pharmaceutical" concentration of cyclosporin A is, the Ding patent's disclosure must be consulted to help explain the meaning of this term to a person of ordinary skill in the art at the time the present patent application was filed.

Ding discloses 5 exemplary compositions (Examples 1A-1E) containing cyclosporin A, present in concentrations of 4%, 2%, 2% 0.1% and 0.5% by weight, respectively. Although each composition appeared to cause slight to moderate discomfort when applied to rabbit eyes, only those compositions (Examples 1A-1D) having a cyclosporin A concentration of 0.1% or greater were reported to deliver therapeutic levels of cyclosporin A to tissues of interest. Not only was the composition of Example 1E not reported to have such efficacy, but Ding et al. are conspicuously silent with respect to the therapeutic efficacy of this composition. See Ding, column 4, lines 32-67 and column 5, lines 18-23.

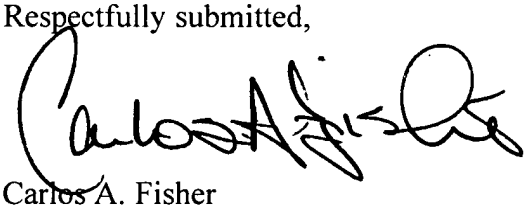
Thus, the specification of Ding, read from the perspective of a person of ordinary skill in the art seeking to define the term "pharmaceutical" as used in the claims, makes clear that a pharmaceutical composition has a cyclosporin A concentration of 0.1% by weight or above. Indeed, such a person would be led by Ding not to believe that a "pharmaceutical composition" is defined by concentrations of cyclosporin less than 0.1%, thus Ding teaches "in a direction divergent from the path taken" by the inventors of presently claimed subject matter. See, e.g., *In re Gurley*, 27 F.3d 551, 553, 31 U.S.P.Q.2d 1130, ___ (Fed. Cir. 1994).

It is therefore clear that a therapeutically active composition comprising water, castor oil, and a therapeutically active amount of cyclodextrin A less than 0.1% by weight cyclosporin A is contrary to the teaching of the claims of Ding et al. and is surprising in light thereof.

Additionally, the fact that a claimed invention may be encompassed by a disclosed generic disclosure does not, without more, render that invention obvious. See e.g., *In re Baird*, 16 F.3d 380, 29 U.S.P.Q.2d 1550 (Fed. Cir. 1994). For example, while claim 4 mentions a range of weight ratios (below about 0.16) of cyclosporin A to castor oil, this range clearly includes a composition wherein the weight ratio is 0 and the composition lacks cyclosporin. Therefore a person of ordinary skill in the art would know based upon this claim that claim 4 contains inoperable embodiments and would not be guided in any way to the therapeutically effective composition of claim 21 and its dependent claims, wherein the therapeutically effective concentration of cyclosporin A is less than 0.1% by weight, and the ratio of cyclosporin A to castor oil is below 0.08.

For these reasons Appellants hereby request that the Board reverse the Examiner's rejection of claims 21, 22, 25-26 and 30-36 over claims 1-8 of Ding et al. and permit the claims to proceed to issue.

Respectfully submitted,



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

CLAIM APPENDIX

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

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

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

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

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

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

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

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

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

16. (Withdrawn) The method of claim 1 wherein the composition comprises an

effective amount of a tonicity component.

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

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

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

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

21. (Previously Presented) A therapeutically effective composition for treating an eye of a human or animal comprising an emulsion comprising water, castor oil, and cyclosporin A in a therapeutically effective amount of less than 0.1% by weight, the weight ratio of the cyclosporin A to the castor oil being less than 0.08.

22. (Previously presented) 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 A.

23. (Canceled)

24. (Canceled)

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

26. (Previously Presented) The composition of claim 21 wherein the castor oil is present in an amount greater than 0.625% by weight of the composition.

27. (Canceled)

28. (Canceled)

29. (Canceled)

30. (Previously presented) The composition of claim 21 having a make-up so that when the composition is topically 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 A.

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

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

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

34. (Original) The composition of claim 21 wherein the composition comprises a

polyelectrolytic component in an amount effective in stabilizing the composition.

35. (Original) 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. (Original) 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. (Previously presented) The composition of claim 21 which includes 1.25% by weight of castor oil.

38. (Previously presented) The composition of claim 21 which includes 0.05% by weight of cyclosporin A.

39. (Previously presented) The composition of claim 38 which includes 1.25% by weight of castor oil.

40. (Previously presented) A composition for treating an eye of a human or animal comprising an emulsion comprising water, 1.25% by weight of castor oil and 0.05% by weight of cyclosporin A, the weight ratio of the cyclosporin A to the castor oil being 0.04.

EVIDENCE APPEENDIX

1. Ding et al., U.S. Patent No. 5,474,979.

RELATED PROCEDINGS APPENDIX

None

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	PATENT NUMBER	GROUP ART UNIT	FILE WRAPPER LOCATION
10/927,857		1654	16M1

Correspondence Address / Fee Address Change

The following fields have been set to Customer Number 51957 on 04/17/2008

- Correspondence Address
- Maintenance Fee Address

The address of record for Customer Number 51957 is:
ALLERGAN, INC.
2525 DUPONT DRIVE, T2-7H
IRVINE,CA 92612-1599

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.
10/927,857	08/27/2004	Andrew Acheampong	D-3111	2409

51957 7590 05/28/2008

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
05/28/2008	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.

UNITED STATES PATENT AND TRADEMARK OFFICE

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

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 10/927,857
Filing Date: August 27, 2004
Appellant(s): ACHEAMPONG ET AL.

Carlos A. Fisher
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed 7 March 2008 appealing from the Office action mailed 2 July 2008.

(1) Real Party in Interest

A statement identifying by name the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The statement of the status of claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The appellant's statement of the grounds of rejection to be reviewed on appeal is correct.

(7) Claims Appendix

The copy of the appealed claims contained in the Appendix to the brief is correct.

(8) Evidence Relied Upon

1. Ding et al. U.S. Patent No. 5,474,979

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

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 1-22, 25-26, 30-40 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 12/27/04).

Ding et al. teach a composition for treating an eye of a human or animal comprising an emulsion comprising water, a hydrophobic component, and cyclosporine component (cyclosporin A, column 3, lines 30-37) in a therapeutically effective amount of less than 0.1% by weight, the weight ratio of the cyclosporin A (See, e.g., Example 1D) to the hydrophobic component (castor oil, a vegetable oil) is 0.08. (see, e.g., Example 1D). Ding et al. also teach that the weight ratio of the cyclosporin component to the hydrophobic component may be preferably varied between 0.12 and 0.02 (see, e.g., column 3, lines 19-20). Example 1E teaches 0.05 % of cyclosporin A; 0.625%

castor oil and a ratio of cyclosporin A to castor oil being 0.08. 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 21) 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 instant claim 21 "the weight ratio of the cyclosporin A to the castor oil being less than 0.08" and the limitation of claim 40: wherein the weight ratio of cyclosporin to castor oil is 0.04. 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. (e.g., Examples 1D and 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). The skilled artisan would have been motivated to do so because such ranges were taught in the Ding patent and it would have been obvious to use all the proportions taught therein. 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) and because optimizing the ratio of cyclosporine/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). Please note that the limitation of claim 22 and claim 30: "wherein the blood of the human has substantially no detectable concentration of the cyclosporin component after application of the composition" would necessarily

read upon a composition with the instantly claimed limitations as taught above. The limitation “emulsion" of claim 25: is taught, e.g., in column 3, lines 21-27 and 57-67; the limitation “wherein the castor oil is present in an amount greater than 0.625 % by weight of the composition" of claim 26 is taught, e.g., in Example 1D (1.25% of castor oil); the limitation “topically administered” of claim 30 is taught by Ding et al.’s claim 8; the limitation “comprising an effective amount of an emulsifier component” of claim 31 is taught in column 3, lines 38-40; the limitations drawn to a “tonicity component” and "organic tonicity component" in claims 32-33 are taught in column 4, lines 12-19; the limitation “polyelectrolytic component in an amount effective in stabilizing the composition” of claim 34 is taught in column 3, lines 64-67 and column 4, lines 1-12; the limitations of claims 35-36: “wherein the pH ranges about 7.0 to about 8.0” and "about 7.2 to about 7.6" are taught, e.g., in Examples 1A-E, column 4, line 43. The limitation of claims 37 and 39: “1.25% by weight of castor oil" is taught e.g., in Example 1D, the limitation “0.05% of cyclosporin A" is taught, e.g., in Example 1E, the limitation of claim 40: "1.25% of castor oil" is taught in Example 1D and 0.05 % by weight of cyclosporin A” is taught in Example 1E. The limitation of claim 40: "wherein the weight ratio of the cyclosporin A to the castor oil being 0.04" is taught, e.g. in Example 1B and is also within the ranges claimed by Ding et al. (e.g., column 3, lines 15-20). The adjustment of particular conventional working conditions (e.g., optimizing the compositions by using the proportions taught by the Ding et al. reference) 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., ratios of all the components in the pharmaceutical composition), 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 highest yield of the highest purity product 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.

(10) Response to Argument

Applicant's arguments have been carefully considered by Examiner, but not deemed persuasive for the following reasons:

Rejections pursuant to 35 USC 103(a)

a) Claims 21, 22, 25-26 and 30-39

i) The Scope and Content of the Prior Art section:

First of all, in the page 12 of the Appeal Brief, last paragraph, Examiner would like to point out the typographical error in line 4 of the last paragraph: Example 1D contains 0.05% of cyclosporin A instead of 0.5% as indicated. With regards to the statement that "Ding discloses nothing concerning the limits of these range of ratios with respect to either efficacy of comfort" (page 12, second paragraph), Examiner points out that claim 8 of Ding is drawn to a pharmaceutical emulsion for topical application to ocular tissue and that encompasses compositions within the claimed ranges. Such pharmaceutical compositions including Examples 1A-D have therapeutic activity in treating dry eye (e.g., column 5, lines 15-25) and are therefore "therapeutically effective" (e.g., column 5, lines 23-25). Additionally, such compositions are mentioned to cause "only slight to mild discomfort and slight hyperemia in the rabbit eyes" (column 5, lines 15-18). The disclosure of Ding et al. also teaches that the pharmaceutical compositions are "nonirritating with high comfort level and low irritation potential suitable for delivery to sensitive areas such as ocular tissues" (column 3, lines 6-10) Please also note that the composition of Example 1E was used in applications to rabbit's eyes (column 5, lines 15-17) since the formulations in Examples 1-4 were used. Additionally, the

instantly claimed ranges are encompassed by claim 8 of Ding et al., which is drawn to pharmaceutical compositions which one of skill in the art would have been motivated to make for their therapeutic effectiveness.

ii) The Differences Between the Prior Art and the Claims at Issue

Applicant argues that there is absolutely no indication in Ding et al. that a therapeutically effective dosage of cyclosporin can be achieved at a concentration less than 0.1% and that the apparent failure of Ding to even test the bioavailability of composition 1E at 0.05% cyclosporin demonstrates that Ding et al. could not and did not predict that compositions containing cyclosporin A dosages of less than 0.1% would be therapeutically effective, or alternatively, that composition 1E failed to deliver a therapeutic level of cyclosporine to the ocular tissues of interest. This is not find persuasive as Ding et al. teach pharmaceutical compositions for topical eye administration encompassing such ranges (e.g., claim 8 of Ding et al) and because the conclusory statement "that Ding et al. could not and did not predict that compositions containing cyclosporin A dosages of less than 0.1% would be therapeutically effective, or alternatively, that composition 1E failed to deliver a therapeutic level of cyclosporin to the ocular tissues of interest" is provided without any evidenciary support. MPEP 2164.05 states:

> "Applicant may submit factual affidavits under 37 CFR 1.132 or cite references to show what one skilled in the art knew at the time of filing the application. A declaration or affidavit is, itself, evidence that must be considered. The weight to give a declaration or affidavit will depend upon the amount of factual evidence

the declaration or affidavit contains to support the conclusion of enablement. In re Buchner, 929 F.2d 660, 661, 18USPQ2d 1331, 1332 (Fed. Cir. 1991) ("expert's opinion on the ultimate legal conclusion must be supported by something more than a conclusory statement"); cf. In re Alton, 76F.3d 1168, 1174, 37 USPQ2d 1578, 1583 (Fed. Cir. 1996) (declarations relating to the written description requirement should have been considered)."

Please also note that the composition of Example 1E was used in applications to rabbit's eyes (column 5, lines 15-17) since the formulations in Examples 1-4 were used. It is clear that application of such compositions to the eye indicates that the pharmaceutical composition is expected to be therapeutically effective with respect to e.g., dry eye (column 5, line 25) and because it would not be made into a pharmaceutical composition without having a bioactive function.

Additionally the arguments directed to "less than 0.08" as not being taught by Ding et al. have been considered but have not been found persuasive as the Ding et al. patent teaches ranges between 0.12 and 0.02, which encompass "less than 0.08".

iii) The Level of Ordinary Skill in the Art

Applicant's arguments have been carefully considered but not deemed persuasive for the reasons set forth above. Additionally, the Ding et al. reference does not teach away from the instant invention. The statement that "a person of ordinary skill in the art could not have predicted the present invention in the light of Ding et al." because not only does Ding fail to indicate that cyclosporin A concentrations below this range would be therapeutically effective, but Ding's conspicuous failure to perform

bioavailability testing on composition E, the only composition specifically made by Ding that has an amount of cyclosporin less than 0.1% indicates that Ding et al. (having at least ordinary skill in the art) did not reasonably expect this composition to contain a therapeutically effective amount of cyclosporine A" (page 14, paragraph 2). However, this is a conclusory statement which has not been supported by evidence. (See MPEP 2164.05). Please also note that the composition of Example 1E was used in applications to rabbit's eyes (column 5, lines 15-17) since the formulations in Examples 1-4 were used. It is clear that application of such compositions to the eye indicates that the pharmaceutical composition is expected to be therapeutically effective with respect to e.g., dry eye (column 5, line 25) and because it would not be made into a pharmaceutical composition without having a bioactive function.

With regards to the arguments in pages 15-17 of the Appeal Brief, Examiner has carefully considered applicant's arguments but does not find them persuasive because the Ding et al. patent teaches pharmaceutical compositions which would reasonably be expected to be therapeutically effective in light of the disclosure of Ding teaching that "The formulations in Examples 1-4 (note this would include Example 1E) were applied to rabbit eyes eight times a day..." (column 5, lines 15-17; see also claim 8). It is clear that application of such compositions to the eye indicates that the pharmaceutical composition is expected to be therapeutically effective with respect to e.g., dry eye (column 5, line 25) and because it would not be made into a pharmaceutical composition without having a bioactive function.

b) Claim 40

Applicant's arguments set forth in pages 18-19 of the Appeal Brief have been carefully considered but not deemed persuasive for the reasons of record and because it would be obvious to use the proportions taught by the Ding et al. reference which include the instantly claimed ranges in pharmaceutical compositions which therefore would be reasonably expected to have the bioactivity taught by the Ding et al. patent.

The arguments indicating that Ding teaches away from a composition for treating an eye of a human or animal comprising an emulsion comprising water, 1.25% of castor oil and 0.05% by weight of cyclosporin A is not deemed persuasive because the "reasonable beliefs" assumed to be held by Ding et al. were not supported by any evidence and therefore are mere conclusory statements. Additionally, the range 0.04 is taught both in Examples and in the acceptable proportion ranges for the pharmaceutical compositions for eye treatment. Applicant's arguments stating that a comparison of a composition with 0.1 % cyclosporin, 1.25 % castor oil and 0.08 cyclosporin/ castor oil (corresponding to Example 1D in Ding et al.) and 0.05% cyclosporin, 1.25% castor oil and 0.04 cyclosporin/ castor oil (page 26 of application's disclosure) provide overall efficacy in treating dry eye that is substantially equal and therefore it is a clearly surprising and unexpected result, have been considered but not deemed persuasive because substantially equal is not defined via any specific detection measurements and therefore it is not clear what "substantially equal" is and therefore the extent of the effect measured is not well determined or evidenced. Additionally, the similar eye irritations in the use of both compositions is not an unexpected result as it is taught by Ding et al. at column 3, lines 6-10 which teaches "nonirritating pharmaceutical compositions with high

comfort level and low irritation potential suitable for delivery to sensitive areas such as ocular tissues" and at column 5, lines 14-17: “The formulations in Examples 1-4 were applied to rabbit eyes eight times a day for seven days and were found to cause only slight to mild discomfort and slight hyperemia in the rabbit eyes”.

Non-Statutory Obviousness-Type Double Patenting Rejection

a) Claims 21, 22, 25-26 and 30-36

Applicant argues in pages 22-23 that the disclosure of Ding is require for a person of ordinary skill in the art to see what the term "pharmaceutical" means, and that the specification of Ding teaches that a pharmaceutical composition has a cyclosporin A concentration of 0.1% by weight or above. Examiner has carefully considered this argument but it is not deemed persuasive because claim 8 of Ding is drawn to a “pharmaceutical emulsion consisting of between about 0.05% and about 0.40% by weight, cyclosporin A” (which clearly includes 0.05% and is not limited to 0.1 % or more as Applicant argues).

Additionally, the arguments regarding that a claimed invention may be encompassed by a generic disclosure does not, without more, render that invention obvious, and that the weight ratio of cyclosporin/castor oil would encompass 0 wherein cyclosporin is zero and therefore non-therapeutic have been carefully considered but not deemed persuasive because the Ding patent is also drawn to a genus which encompasses the instantly claimed subgenus of claim 21 and the instantly claimed species of claim 40. One skilled in the art would have been motivated to make therefore

pharmaceutical compositions which were previously taught by Ding to be “nonirritating with high comfort level and low irritation potential suitable for delivery to sensitive areas such as ocular tissues" (column 3, lines 6-10) including those with 0.05% cyclosporin A (as in Example 1E) since such compositions were applied to rabbits for their therapeutic use as set forth above, and since it would have been obvious to one of ordinary skill in the art to have used the proportions taught by Ding et al.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

/Marcela M Cordero Garcia/

Primary Examiner, Art Unit 1654

Conferees:

/Andrew D Kosar/
Primary Examiner, Art Unit 1654
Acting SPE

/Robert A. Wax/
Robert A. Wax
TQAS Appeals Specialist
Technology Center 1600

MMCG 05/08

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.
10/927,857	08/27/2004	Andrew Acheampong	D-3111	2409

51957 7590 06/12/2008

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

EXAMINER	
ART UNIT	PAPER NUMBER

DATE MAILED: 06/12/2008

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

UNITED STATES DEPARTMENT OF COMMERCE
U.S. Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450

APPLICATION NO./ CONTROL NO.	FILING DATE	FIRST NAMED INVENTOR / PATENT IN REEXAMINATION	ATTORNEY DOCKET NO.
10927857	8/27/04	ACHEAMPONG ET AL.	D-3111

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

EXAMINER
MARCELA M. CORDERO GARCIA

ART UNIT	PAPER
1654	20080605

DATE MAILED:

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

Commissioner for Patents

The Examiner's Answer mailed on 5/28/08 is missing Heading 11)Related Proceedings Appendix is missing. This section should read: 11)Related Prceedings Appendix. None.
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

/Marcela M Cordero Garcia/
Examiner, Art Unit 1654

PTO-90C (Rev.04-03)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Appl. No.	: 10/927,857	Confirmation No.	2409
Appellant	: ACHEAMPONG ET AL.		
Filed	: August 27, 2004		
Title	: METHODS OF PROVIDING THERAPEUTIC EFFECTS USING CYCLOSPORIN COMPONENTS		
TC/A.U.	: 1654		
Examiner	: Cordero Garcia, Marcela M.		
Docket No.	: D-3111		
Customer No.	: 33197		

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

REPLY BRIEF

Carlos A. Fisher
Stout, Uxa, Buyan & Mullins LLP

For Appellant

Appellants are in receipt of the Examiner's Answer mailed May 28, 2008, and have the following comments.

The Examiner has added no new Grounds of Rejection. The sole basis for rejection of 1-22, 25-26 and 30-40 remains the allegation that the claims are obvious under 35 USC §103(a) in view of Ding et al., U.S. Patent No. 5,474,979.

Reply to Examiner's Response to Argument

The Examiner points out the typographical error in line 4 of page 12 of the Appeal Brief, wherein Example 1D is said to contain 0.5% cyclosporin A rather than the correct amount of 0.05% (w/v). Applicants appreciate the Examiner's courtesy in this regard, and hope that the error has not caused any undue hardship.

The Examiner responds to the detailed arguments made by the Appellants, as follows:

Claims 21, 22, 25-26 and 30-39

1) The Examiner attempts to rebut the Applicants' statement on page 12, second paragraph of the Office action that Ding does not disclose the limits of this range of ratios with respect to efficacy or comfort. Thus, the Examiner states that "claim 8 of Ding is drawn to a pharmaceutical emulsion for topical application to ocular tissue and that [sic] encompasses compositions within the claimed ranges." Reply Brief at page 7,

Paragraph 10(a)(i). The range of ratios of cyclosporin A to castor oil contained in claims 21, 22, 25-26 and 30-39 is "less than 0.08". *See* claim 21.

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 cyclosporin A to castor oil; however, if ratios are to be calculated from these ingredients, 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 Examiner's statement fails to consider either the pending claims or the prior art (Ding) as a whole, as dictated e.g., by the Manual of Patent Examining Procedure at Section 2141.02. For example, claim 21 is drawn to a therapeutically effective composition containing cyclosporin A in a therapeutically effective amount of less than 0.1% by weight, the weight ratio of the cyclosporin A to the castor oil being less than 0.08. Thus, not only must the composition itself be therapeutically effective, but the amount of cyclosporin A must also be therapeutically effective and less than 0.1% by weight. Claim 8 says nothing about therapeutic effectiveness at all claimed concentrations, nor is it reasonable 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 nonenabled).

2) The Examiner, citing Ding, col. 5, lines 15-25, alleges that the compositions of Examples 1A-1D of Ding have therapeutic activity in treating dry eye and are therefore therapeutically effective. However, Applicants note that none of Examples 1A-1D fall within the present claims. None of these compositions contain cyclosporin at a concentration below 0.1% by weight. Only Example 1B has a ratio of cyclosporin A to castor oil below 0.08 - however, this composition (1B) contains 0.2% cyclosporin A. To establish *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art. *In re Royka*, 490 F.2d 981, 180 USPQ 580 CCPA 1974). This clearly not the case with Examples 1A-1D of Ding.

The Examiner again states "the instantly claimed ranges [of ratios] are encompassed by claim 8 of Ding et al." Ding, pages 7-8, Paragraph 10(a)(i). However, this is respectfully not true. It is true that if ratios of cyclosporin A to castor oil (unmentioned in claim 8) were to be calculated, there is overlap between the range of ratios so obtained (about 0.01 to about 0.64), and the range or ratios present in the pending instant claims ("less than 0.08").

3. However, equally importantly of course, the pending claims contain other limitations (for example, the requirement that the invention be a therapeutically effective composition containing less than 0.1% cyclosporin A). Furthermore, the

Examiner fails to adequately address the fact the Example 1E, which is the only composition in Ding that contains less than 0.1% cyclosporin A, is not listed at all by Ding in column 5, lines 15-25 as a therapeutically effective composition.

With respect, Ding's clearly intentional omission of Example 1E from mention when discussing the results of animal testing of the cyclosporin A compositions cannot simply be ignored, particularly when Examples 1A-1D are mentioned three times in col. 5. It is a matter of black letter law that even a *prima facie* case of obviousness can "be rebutted by showing that the art, in any material respect, teaches away from the claimed invention." MPEP 2144.05, citing *In re Geisler*, 116 F.3d 1465, 1471, 43 USPQ2d 1362, 1366 (Fed. Cir. 1997). In the present case, Applicants submit that a person of ordinary skill in the art would note Ding's intentional failure to mention the composition of Example 1E when mentioning therapeutic efficacy and interpret this omission as a purposeful teaching away from using less than 0.1% cyclosporin to make a therapeutically effective composition.

The Examiner states that this argument is not persuasive because Ding et al. allegedly teaches pharmaceutical compositions for topical eye administration encompassing (actually overlapping) the range "less than 0.1% cyclosporin". *See Examiner's Answer*, page 8, Paragraph 10(a)(ii). However, as stated above, 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). Therefore, while claim 8 of Ding may disclose wide ranges which include

concentrations of cyclosporin below 0.1 within their purview, there is no justification for assuming that all of the compositions included within claim 8's scope are therapeutically effective, as required of the present claims.

The Examiner characterizes as "conclusory" the Applicant's statement in the Appeal Brief that Ding could not and did not predict that compositions containing cyclosporin A of less than 0.1% would be therapeutically effective. Actually, it is simply factually accurate that Ding did not make this prediction; the Examiner has not pointed to one location in the specification of Ding in which such prediction is made.

The statement that Ding "could not" make such prediction is indeed the result of concluding that the omission of Example 1E was not an oversight, but was intended by Ding; the utter reasonableness of this conclusion is evident from the mention by Ding three times of "Examples 1A-1D" (and thus the lack of mention of Example 1E) in column 5 when discussion the therapeutic effectiveness of higher concentrations of cyclosporin A. The Examiner states that the composition of Example 1E was used in applications to rabbit eyes (Examiner's Answer page 9 and page 10). This is true, and only bolsters the reasonableness of the Applicants' position that a person of reasonable skill in the art would conclude that the rabbit results using the Example 1E composition were somehow unfavorable since they were not reported. With respect, the Examiner's interpretation that because this composition was applied it "is expected to be therapeutically effective" is entirely without basis. The person of ordinary skill in the art

is aware that animal tests of this sort are performed to determine a range of effective concentrations, not because every concentration is "expected" to be effective.

Contrary to the Examiner's position on page 8 of the Examiner's Answer, the fact that a person of ordinary skill in the art would reasonably reach the conclusion that a prior art reference teaches away from a claimed invention does not require evidentiary support. No evidence is needed to "show what one of ordinary skill knew at the time of filing" when the question is what a prior art reference teaches.

Applicants again submit that "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." Ding, like any prior art reference, must be considered for all it teaches, particularly when, as here, it teaches away from the claimed invention. *See e.g.,* MPEP §2141. Respectfully, to ignore this obvious teaching away is reversible error.

Claim 40

a) The Examiner finds the Applicant's arguments concerning the patentability of claim 40 unpersuasive. Applicants incorporate by reference the remarks made in the Appeal Brief and above, and add the following additional comments.

The Examiner again questions Applicant's whether Ding teaches away from a therapeutically effective composition containing less than 0.1% cyclosporin A. Applicants maintain that the reasonableness of a person of ordinary skill in the art reaching such a conclusion is evidenced by the Ding reference itself, as argued above. On page 11 of the Examiner's Answer the Examiner attempts to argue obviousness of claim 40 from the fact that a ratio of cyclosporin A to castor oil of 0.04 an be found in Example 1B (0.3% cyclosporin A to 5.0% castor oil). However, of course, this composition contains six times the maximum amount of cyclosporin A permitted by claim 40. Therefore, the Examiner is not comparing the claimed invention as a whole to Ding - rather the Examiner is attempting to argue in a piecemeal fashion.

The Examiner does not find the surprising the fact that the present specification discloses that a composition containing half the amount of cyclosporin A (0.5%) as the composition of Example 1D of Ding (0.15) would have substantially equal therapeutic efficacy. However, this fact is surprising for at least two reasons. First, it is surprising in light of the disclosure of Ding that a composition having less than 0.1% (much less one having the same amount of the active agent as the composition of Example 1E) would have therapeutic efficacy at all. Secondly, the fact that the efficacies would be substantially equal is also surprising since the concentrations of active ingredient in the composition having the lower concentration is 50% that of the higher. "Substantial" is defined in the Merriam-Webster on-line dictionary as "being

largely but not wholly that which is specified". "Half" is by any person's measure not "largely" equal.

Obviousness Type-Double Patenting

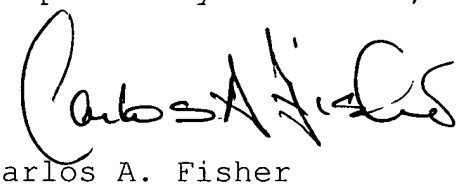
Applicants incorporate by reference the arguments made herein regarding the non-obviousness of the present invention and those made in the Appeal Brief, particularly on pages 20-23 thereof.

CONCLUSION

For the reasons stated in the Appeal Brief (such statements being hereby incorporated by reference herein) and in the present Reply Brief, Appellants hereby respectfully ask the Board to reverse the Examiner's rejection of the presently pending claims and permit Claims 21, 22, 25-26 and 30-39 to proceed to issue.

Applicants hereby request a two month Extension of Time and include a check in the amount of the corresponding extension fee. If the Appellants have overlooked any other fee, kindly use Deposit Account 21-0890 for the payment of any such fee now due.

Respectfully submitted,



Carlos A. Fisher
Attorney for Appellant
Reg. No. 36,510

09/22/08

IFW AF

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of Acheampong, et al.	Group Art Unit: 1654
Serial No.10/927,857 Conf. No. 2409	Examiner: Cordero Garcia, M.
Filed: August 27, 2004	
For: METHODS OF PROVIDING THERAPEUTIC EFFECTS USING CYCLOSPORIN COMPONENTS	

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

EXPRESS MAIL CERTIFICATE

EXPRESS MAIL MAILING LABEL NO. EV 516292781 US

Date of Deposit: **September 18, 2008**

I hereby certify that the following documents as identified below are being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 CFR 1.10 on the date indicated above and are addressed to the Mail Stop Appeal Brief-Patent, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450:

- ☒ Reply Brief
- ☒ 2 Month Extension of Time
- ☒ Stamped, self-addressed postcard
- ☒ Other: Fee Transmittal
  Check in the amount of $460.00

Each of the 4 above-identified documents are enclosed herewith.

Respectfully submitted,

Date: 9/18/2008

Janet McGhee
Assistant to Carlos A. Fisher
Stout, Uxa, Buyan & Mullins, LLP
4 Venture, Suite 300
Irvine, California 92618

Fees Pursuant to the Consolidated Appropriations Act 2005 (H.R. 4818).

FEE TRANSMITTAL For FY 2008

Patent fees are subject to annual revision.

☐ Application claims small entity status. See 37 CFR 1.27

TOTAL AMOUNT OF PAYMENT ($) 460.

Complete if Known	
Application Number	10/927,857
Filing Date	8/27/2004
First Named Inventor	Acheampong
Examiner Name	Cordero Garcia, M.M.
Art Unit	1654
Attorney Docket No.	D-3111

METHOD OF PAYMENT *(check all that apply)*

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

☒ Deposit Account Deposit Account Number 21-0890 Deposit Account Name Carlos A. Fisher

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**

☒ Charge any additional fee(s) associated with this communication ☒ Credit any overpayments

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.

FEE CALCULATION

1. BASIC FILING, SEARCH, AND EXAMINATION FEES

	FILING FEES		SEARCH FEES		EXAMINATION FEES		
Application Type	**Fee ($)**	**Small Entity Fee ($)**	**Fee ($)**	**Small Entity Fee ($)**	**Fee ($)**	**Small Entity Fee ($)**	**Fees Paid ($)**
Utility	310	155	510	255	210	105	
Design	210	105	100	50	130	65	
Plant	210	105	310	155	160	80	
Reissue	310	155	510	255	620	310	
Provisional	210	105	0	0	0	0	

Subtotal (1) 0

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	210	105
Multiple Dependent Claims	370	185

Total Claims	Extra Claims	Fee ($)	Fee Paid ($)
____ -20 or HP =	____	x ____	____

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

Indep. Claims	Extra Claims	Fee ($)	Fee Paid ($)
____ -3 or HP =	____	X ____	____

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

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

Subtotal (2) 0

3. APPLICATION SIZE FEE

If the specification and drawings exceed 100 sheets of paper, the application size fee due is $260 ($130 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).

Total Sheets	Extra Sheets	Number of each additional 50 or fraction thereof	Fee ($)	Fee Paid ($)
____ -100 =	____	/50= ____(round up to a whole number)	x ____ =	

Subtotal (3) 0

4. OTHER FEE(S)

	Fee Paid ($)
☐ Surcharge - Late filing fee or oath/declaration: $130 fee ($65 small entity discount)	
☐ Non-English Specification: $130 fee (no small entity discount)	
☐ 1-month extension of time: $120 fee ($60 small entity discount)	
☒ 2-month extension of time: $460 fee ($230 small entity discount)	460
☐ 3-month extension of time: $1050 fee ($525 small entity discount)	
☐ 4-month extension of time: $1640 fee ($820 small entity discount)	
☐ 5-month extension of time: $2230 fee ($1115 small entity discount)	
☐ Information Disclosure Statement Fee: $180 fee (no small entity discount)	
☐ Notice of Appeal: $510 fee ($255 small entity discount)	
☐ Filing a Brief in Support of Appeal: $510 fee ($255 small entity discount)	
☐ Request for Oral Hearing: $1030 fee ($515 small entity discount)	
☐ Utility Issue Fee: $1440 fee ($720 small entity discount)	
☐ Recording each patent assignment per property (times number of properties): $40 fee (no small entity fee discount)	
☐ Request for Continued Examination: $810 fee ($405 small entity discount)	
☐ Other: ____	

Subtotal (4) 460

SUBMITTED BY

Name (Print/Type)	Carlos A. Fisher	*Registration No. (Attorney/Agent)*	36,510	*Telephone*	949-450-1750
Signature	Carlos A. Fisher			*Date*	9/18/2008

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Appl. No.	: 10/927,857	Confirmation No.	2409
Appellant	: ACHEAMPONG ET AL.		
Filed	: August 27, 2004		
Title	: METHODS OF PROVIDING THERAPEUTIC EFFECTS USING CYCLOSPORIN COMPONENTS		
TC/A.U.	: 1654		
Examiner	: Cordero Garcia, Marcela M.		
Docket No.	: D-3111		
Customer No.	: 33197		

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

REQUEST FOR EXTENSION OF TIME

Sir:

Applicant requests a two-month extension of time. Enclosed herewith is a check in the amount of $460 for the required fee.

Please charge any deficiency or credit any overpayment to Deposit Account No. 21-0890.

09/22/2008 HDEMESS1 00000064 10927857
01 FC:1252 460.00 OP

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

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.
10/927,857	08/27/2004	Andrew Acheampong	D-3111	2409

51957 7590 12/10/2008

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
12/10/2008	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.

UNITED STATES DEPARTMENT OF COMMERCE
U.S. Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450

APPLICATION NO./ CONTROL NO.	FILING DATE	FIRST NAMED INVENTOR / PATENT IN REEXAMINATION	ATTORNEY DOCKET NO.
10927857	8/27/04	ACHEAMPONG ET AL.	D-3111

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

EXAMINER
MARCELA M. CORDERO GARCIA

ART UNIT	PAPER
1654	20081202

DATE MAILED:

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

Commissioner for Patents

The reply brief filed 18 September 2008 is noted and has been entered in the file. The application has been forwarded to the Board of Patent Appeals and Interferences for decision on the appeal.

/Marcela M Cordero Garcia/
Examiner, Art Unit 1654

PTO-90C (Rev.04-03)

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.
10/927,857	08/27/2004	Andrew Acheampong	D-3111	2409

51957 7590 03/19/2009

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
03/19/2009	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.

United States Patent and Trademark Office

Under Secretary of Commerce for Intellectual Property and
Director of the United States Patent and Trademark Office
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

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

Appeal No: 2009-5649
Application: 10/927,857
Appellant: Andrew Acheampong et al.

Board of Patent Appeals and Interferences
Docketing Notice

Application 10/927,857 was received from the Technology Center at the Board on December 17, 2008 and has been assigned Appeal No: 2009-5649.

A review of the file indicates that the following documents have been filed by appellant:

Appeal Brief filed on:	March 07, 2008
Reply Brief filed on:	September 18, 2008
Request for Hearing filed on:	NONE

In all future communications regarding this appeal, please include both the application number and the appeal number.

The mailing address for the Board is:

BOARD OF PATENT APPEALS AND INTERFERENCES
UNITED STATES PATENT AND TRADEMARK OFFICE
P.O. BOX 1450
ALEXANDRIA, VIRGINIA 22313-1450

The facsimile number of the Board is 571-273-0052. Because of the heightened security in the Washington D.C. area, facsimile communications are recommended. Telephone inquiries can be made by calling 571-272-9797 and should be directed to a Program and Resource Administrator.

By order of the Board of Patent Appeals and Interferences