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

UTILITY PATENT APPLICATION TRANSMITTAL

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

Attorney Docket No.	BAN 102
First Inventor	Nachiappan Chidambaram
Title	Solvent System for Enhancing the Solubility of Pharmaceutical Agents
Express Mail Label No.	EV 487330851 US

APPLICATION ELEMENTS

See MPEP chapter 600 concerning utility patent application contents.

1. ☑ **Fee Transmittal Form** (e.g., PTO/SB/17)
   (Submit an original and a duplicate for fee processing)
2. ☐ **Applicant claims small entity status.** See 37 CFR 1.27.
3. ☑ **Specification** [*Total Pages* 20]
   Both the claims and abstract must start on a new page
   (For information on the preferred arrangement, see MPEP 608.01(a))
4. ☐ **Drawing(s)** (*35 U.S.C. 113*) [*Total Sheets* _____]
5. **Oath or Declaration** [*Total Sheets* _____]
   a. ☐ Newly executed (original or copy)
   b. ☐ A copy from a prior application (37 CFR 1.63(d))
   (for continuation/divisional with Box 18 completed)
   i. ☐ DELETION OF INVENTOR(S)
   Signed statement attached deleting inventor(s) name in the prior application, see 37 CFR 1.63(d)(2) and 1.33(b).
6. ☑ **Application Data Sheet.** See 37 CFR 1.76
7. ☐ **CD-ROM or CD-R** in duplicate, large table or Computer Program *(Appendix)*
   ☐ Landscape Table on CD
8. **Nucleotide and/or Amino Acid Sequence Submission**
   (if applicable, items a. – c. are required)
   a. ☐ Computer Readable Form (CRF)
   b. Specification Sequence Listing on:
      i. ☐ CD-ROM or CD-R (2 copies); or
      ii. ☐ Paper
   c. ☐ Statements verifying identity of above copies

ADDRESS TO:

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

ACCOMPANYING APPLICATION PARTS

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

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

☐ Continuation ☐ Divisional ☐ Continuation-in-part (CIP) of prior application No.: .....

Prior application information: *Examiner* _____ *Art Unit:* _____

19. CORRESPONDENCE ADDRESS

☑ The address associated with Customer Number: **23579** *OR* ☐ Correspondence address below

Name					
Address					
City		State		Zip Code	
Country		Telephone		Email	

Signature		Date	March 3, 2006
Name (Print/Type)	Patrea L. Pabst	Registration No. (Attorney/Agent)	31,284

PTO/SB/17 (01-06)
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U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

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

FEE TRANSMITTAL
For FY 2006

☐ Applicant claims small entity status. See 37 CFR 1.27

TOTAL AMOUNT OF PAYMENT ($) $1750.00

Complete if Known	
Application Number	
Filing Date	March 3, 2006
First Named Inventor	Nachiappan Chidambaram
Examiner Name	
Art Unit	
Attorney Docket No.	BAN 102

METHOD OF PAYMENT (check all that apply)

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

☑ Deposit Account Deposit Account Number: 50-3129 Deposit Account Name: Pabst Patent Group LLP

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) or underpayments of fee(s) under 37 CFR 1.16 and 1.17 ☑ 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 (All the fees below are due upon filing or may be subject to a surcharge.)

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	$1,000.00
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	

2. EXCESS CLAIM FEES

Fee Description	Fee ($)	Small Entity Fee ($)
Each claim over 20 (including Reissues)	50	25
Each independent claim over 3 (including Reissues)	200	100
Multiple dependent claims	360	180

Total Claims		Extra Claims		Fee ($)		Fee Paid ($)
31	- 20 or HP =	11	x	$50	=	$550

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

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

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

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

3. APPLICATION SIZE FEE

If the specification and drawings exceed 100 sheets of paper (excluding electronically filed sequence or computer listings under 37 CFR 1.52(e)), 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		Extra Sheets		Number of each additional 50 or fraction thereof		Fee ($)		Fee Paid ($)
	- 100 =		/ 50 =		(round up to a whole number) x		=	

4. OTHER FEE(S)

Non-English Specification, $130 fee (no small entity discount) — Fees Paid ($)

Other (e.g., late filing surcharge): _____

SUBMITTED BY

Signature		Registration No. (Attorney/Agent) 31,284	Telephone 404-879-2151
Name (Print/Type)	Patrea L. Pabst		Date March 3, 2006

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants:	Nachiappan Chidambaram and Aqeel Fatmi		
Serial No.:		Express Mail Label No.:	EV 487330851 US
Filed:	March 3, 2006	Date of Deposit:	March 3, 2006
For:	SOLVENT SYSTEM FOR ENHANCING THE SOLUBILITY OF PHARMACEUTICAL AGENTS		

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

EXPRESS MAIL TRANSMITTAL LETTER
FOR PATENT APPLICATION AND CERTIFICATE OF MAILING

Sir:

Pursuant to 35 U.S.C. § 21(a) as amended by Public Law 97-247 and 37 C.F.R. § 1.10, Applicants enclose for filing the attached patent application entitled *"Solvent System for Enhancing the Solubility of Pharmaceutical Agents"*, which claims priority to U.S.S.N. 60/659,679 filed March 8, 2005. The application contains a total of 20 pages, which include 1 page of abstract, 16 pages of specification, 3 pages of claims and a partially executed Declaration for Patent Application. A fully executed Declaration for Patent Application, Assignment of rights in the application from Nachiappan Chidambaram and Aqeel Fatmi to Banner Pharmacaps, Inc., Power of Attorney and Correspondence Address Indication Form, and a Statement Under 37 C.F.R. § 3.73(b) will be submitted shortly.

The Commissioner is hereby authorized to charge Deposit Account No. 50-3129 in the amount of $1,750.00 to cover the application filing fee, search fee, and examination fee for a

large entity. It is believed that this is the proper filing fee for a large entity as the application contains 4 independent claims, a total of 31 claims, and 20 total pages.

This application is not entitled to claim small entity status under 37 C.F.R. § 1.27.

This application is being filed on March 3, 2006 by mailing the application to Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 via the United States Postal Service "Express Mail Post Office to Addressee" service under 37 C.F.R. § 1.10. The Express Mail label number appears in the heading of this paper which is attached to the application papers pursuant to 37 C.F.R. § 1.10(b).

The Commissioner is hereby authorized to charge any additional fees that may be required, or credit any overpayment in connection with this application, to Deposit Account No. 50-3129.

All correspondence concerning this application should be mailed to:

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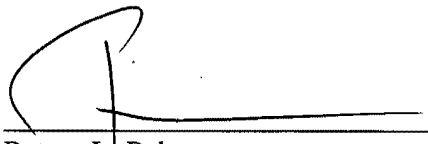
Respectfully submitted,



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Date: March 3, 2006

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CERTIFICATE OF MAILING UNDER 37 C.F.R. § 1.10

I hereby certify that this Express Mail Transmittal Letter for Patent Application and Certificate of Mailing and any documents referred to as attached therein are being deposited with the United States Postal Service on this date, March 3, 2006, in an envelope as "Express Mail Post Office to Addressee" service under 37 C.F.R. § 1.10, Express Mail Label No. EV 487330851 US, addressed to Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

Chandra Russell

Chandra Russell

Date: March 3, 2006

UNITED STATES

UTILITY PATENT APPLICATION

BY

NACHIAPPAN CHIDAMBARAM

AND

AQEEL FATMI

FOR

SOLVENT SYSTEM FOR ENHANCING THE SOLUBILITY OF PHARMACEUTICAL AGENTS

SOLVENT SYSTEM FOR ENHANCING THE SOLUBILITY OF PHARMACEUTICAL AGENTS

FIELD OF THE INVENTION

This invention is in the field of fill materials encapsulated in soft gelatin capsules.

This application claims priority under 35 U.S.C. 119 to U.S.S.N. 60/659,679 filed March 8, 2005.

BACKGROUND OF THE INVENTION

Filled one-piece soft gelatin capsules ("softgels") have been widely used for years to encapsulate consumable materials such as vitamins and pharmaceuticals in a liquid vehicle or carrier. Because softgels have properties which are quite different from two-piece hardshell capsules, softgels are more capable of retaining a liquid fill material.

Not all liquids may be enclosed in a softgel capsule. Liquids containing more than about 20% water by weight are generally not enclosed in softgels, because the water tends to dissolve the gelatin shell. Other solvents such as propylene glycol, glycerin, low molecular weight alcohols, ketones, acids, amines, and esters all tend to degrade or dissolve the gelatin shell to some extent.

Softgels are also somewhat sensitive to pH, and generally require a pH in the encapsulated liquid from about 2.5 to about 7.5. Highly acidic liquids may hydrolyze the gelatin, resulting in leaks, while basic liquids may tan the gelatin, resulting in decreased solubility of the gelatin shell.

Pharmaceutical liquids are usually enclosed in softgels as either viscous solutions or suspensions. Suspensions are pharmaceutically less desirable because they can settle during manufacture, which leads to a less uniform product. In contrast, solutions provide the best liquid form for obtaining optimal "content uniformity" in a batch. Further, solutions typically provide a faster and more uniform absorption of an active agent than do suspensions.

Suitable softgel solutions, however, can be difficult to achieve. One constraint is size. Many pharmaceutical agents require volumes of solvent too large to produce a softgel capsule small enough to be taken by patients. The solvent must also have sufficient solvating power to dissolve a large amount of the pharmaceutical agent to produce a concentrated solution and yet not dissolve, hydrolyze or tan the gelatin shell.

Concentrated solutions of pharmaceutical agents for use in softgel capsules have been described. Most of these systems involve ionizing the free pharmaceutical agent *in situ* to the corresponding salt. For example, U.S. Patent No. 5,360,615 to Yu *et al.* discloses a solvent system for enhancing the solubility of acidic, basic, or amphoteric pharmaceutical agents. The solvent system comprises polyethylene glycol, an ionizing agent, and water. The ionizing agent functions by causing the partial ionization of the free pharmaceutical agent. U.S. Patent No. 6,383,515, U.S. Patent Application Publication No. 2002/0187195, and U.S. Patent Application Publication No. 2001/0007668 to Sawyer *et al.* discloses pharmaceutically acceptable solutions containing a medicament suitable for filling softgel capsules comprising a polymer such as polyethylene glycol and an acid salt of a compound having three or more carbon atoms, such as sodium propionate. The salt helps to ionize the medicament without relying on the use of strong acids or bases. U.S. Patent No. 6,689,382 to Berthel *et al.* describes a pharmaceutical formulation suitable for filling softgel capsules comprising (a) a therapeutically effective amount of a non-steroidal anti-inflammatory drug (NSAID); and (b) a solvent system comprising 40% to 60% by weight a polyoxyethylene ether, 15% to 35% by weight of glycerin and 15% to 35% by weight water. In cases where the NSAID has a carboxyl or an acidic functional group, the solvent system also includes hydroxide ions. U.S. Patent No. 5,505,961 to Shelley *et al.* describes a method for increasing the solubility of acetaminophen alone or in combination with other pharmaceutically active agents to form a clear solution for encapsulation into a softgel capsule. The method comprises solubilizing acetaminophen in a

mixture of propylene glycol, polyethylene glycol, water, polyvinylpyrrolidone and sodium or potassium acetate.

The previously described methods all involve the conversion of the free pharmaceutical agent to the corresponding salt. In cases where the free pharmaceutical agent is acidic, the resulting anion can react with the polyethylene glycol in the fill to produce polyethylene glycol esters, thus reducing the amount of available pharmaceutical agent.

There is a need for a solvent system containing a medicament, which can be encapsulated in a softgel capsule, wherein the formation of PEG esters is minimized.

Therefore it is an object of the invention to provide a stable solvent system for pharmaceutical agents, which is suitable for encapsulation in a softgel capsule, wherein the formation of PEG esters is minimized.

BRIEF SUMMARY OF THE INVENTION

Liquid and semi-solid pharmaceutical compositions, which can be administered in liquid form or can be used for preparing capsules, are described herein. The composition comprises the salt of one or more active agents, and 0.2-1.0 mole equivalents of a de-ionizing agent per mole of active agent. The pH of the composition is adjusted within the range of 2.5 – 7.5. The de-ionizing agent causes partial de-ionization (neutralization) of the salt of the active agent resulting in enhanced bioavailability of salts of weakly acidic, basic or amphoteric active agents as well as decreased amounts of polyethylene glycol (PEG) esters.

DETAILED DESCRIPTION OF THE INVENTION

I. Composition

A. Fill Materials

1. Drugs to be Formulated

The formulation can contain any therapeutic, diagnostic, prophylactic or nutraceutical agent. Exemplary agents include, but are not limited to, analeptic agents; analgesic agents; anesthetic agents; antiasthmatic agents; antiarthritic

agents; anticancer agents; anticholinergic agents; anticonvulsant agents; antidepressant agents; antidiabetic agents; antidiarrheal agents; antiemetic agents; antihelminthic agents; antihistamines; antihyperlipidemic agents; antihypertensive agents; anti-infective agents; anti-inflammatory agents; antimigraine agents; antineoplastic agents; antiparkinson drugs; antipruritic agents; antipsychotic agents; antipyretic agents; antispasmodic agents; antitubercular agents; antiulcer agents; antiviral agents; anxiolytic agents; appetite suppressants (anorexic agents); attention deficit disorder and attention deficit hyperactivity disorder drugs; cardiovascular agents including calcium channel blockers, antianginal agents, central nervous system ("CNS") agents, beta-blockers and antiarrhythmic agents; central nervous system stimulants; diuretics; genetic materials; hormonolytics; hypnotics; hypoglycemic agents; immunosuppressive agents; muscle relaxants; narcotic antagonists; nicotine; nutritional agents; parasympatholytics; peptide drugs; psychostimulants; sedatives; sialagogues, steroids; smoking cessation agents; sympathomimetics; tranquilizers; vasodilators; beta-agonist; and tocolytic agents.

A first class of drugs is selected based on inclusion in the molecule of a weakly acidic, basic or amphoteric group that can form a salt. Any drug that bears an acidic or a basic functional group, for example, an amine, imine, imidazoyl, guanidine, piperidinyl, pyridinyl, quaternary ammonium, or other basic group, or a carboxylic, phosphoric, phenolic, sulfuric, sulfonic or other acidic group, can react with the de-ionizing agent.

Some specific drugs that bear acidic or basic functional groups and thus may be converted to the corresponding salt for use in the described formulations include, but are not limited to, Acetaminophen, Acetylsalicylic acid, Alendronic acid, Alosetron, Amantadine, Amlopidine, Anagrelide, Argatroban, Atomoxetine, Atrovastatin, Azithromycin dehydrate, Balsalazide, Bromocriptan, Bupropion, Candesartan, Carboplatin, Ceftriaxone, Clavulonic acid, Clindamycin, Cimetadine, Dehydrocholic (acid), Dexmethylphenidate, Diclofenac, Dicyclomine, Diflunisal, Diltiazem, Donepezil, Doxorubicin,

Doxepin, Epirubicin, Etodolic acid, Ethacrynic acid, Fenoprofen, Fluoxetine, Flurbiprofen, Furosemide, Gemfibrozil, Hydroxyzine, Ibuprofen, Imipramine, Indomethacin, Ketoprofen, Levothyroxine, Maprolitline, Meclizine, Methadone, Methylphenidate, Minocycline, Mitoxantone, Moxifloxacin, Mycophenolic acid, Naproxen, Niflumic acid, Ofloxacin, Ondansetron, Pantoprazole, Paroxetine, Pergolide, Pramipexole, Phenytoin, Pravastain, Probenecid, Rabeprazole, Risedronic acid, Retinoic acid, Ropinirole, Selegiline, Sulindac, Tamsulosin, Telmisertan, Terbinafine, Theophyline, Tiludronic Acid, Tinzaparin, Ticarcillin, Tometin, Valproic acid, Salicylic acid, Sevelamer, Ziprasidone, Zoledronic acid, Acetophenazine, Albuterol, Almotriptan, Amitriptyline, Amphetamine, Atracurium, Beclomethasone, Benztropine, Biperiden, Bosentan, Bromodiphenhydramine, Brompheniramine carbinoxamine, Caffeine, Capecitabine, Carbergoline, Cetirizine, Chlocylizine, Chlorpheniramine, Chlorphenoxamine, Chlorpromazine, Citalopram, Clavunate potassium, Ciprofloxacin, Clemastine, Clomiphene, Clonidine, Clopidogrel, Codeine, Cyclizine, Cyclobenzaprine, Cyproheptadine, Delavirdine, Diethylpropion, Divalproex, Desipramine, Dexmethylphenidate, Dexbrompheniramine, Dexchlopheniramine, Dexchlor, Dextroamphetamine, Dexedrine, Dextromethorphan, Fiflunisal, Diphemanil methylsulphate, Diphenhydramine, Dolasetron, Doxylamine, Enoxaparin, Ergotamine, Ertepenem, Eprosartan, Escitalopram, Esomeprazole, Fenoldopam, Fentanyl, Fexofenadine, Flufenamic acid, Fluvastatin, Fluphenazine, Fluticasone, Fosinopril, Frovatriptan, Gabapentin, Galatamine, Gatifloxacin, Gemcitabine, Haloperidol, Hyalurondate, Hydrocodone, Hydroxychloroquine, Hyoscyamine, Imatinib, Imipenem, Ipatropin, Lisinopril, Leuprolide, Levopropoxyphene, Losartan, Meclofenamic acid, Mefanamic acid, Mesalamine, Mepenzolate, Meperidine, Mephentermine, Mesalimine, Mesoridazine, Metaproteranol, Metformin, Methdialazine, Methscopolamine, Methysergide, Metoprolol, Metronidazole, Mibefradil, Montelukast, Morphine, Mometasone, Naratriptan, Nelfinavir, Nortriptylene, Noscapine, Nylindrin, Omeprazole, Orphenadrine, Oseltamivir, Oxybutynin,

Papaverine, Pentazocine, Phendimetrazine, Phentermine, Pioglitazone, Pilocarpine, Prochloroperazine, Pyrilamine, Quetapine, Ranitidine, Rivastigmine, Rosiglitazone, Salmetrol, Sertaline, Sotalol, Sumatriptan, Tazobactam, Tacrolimus, Tamoxifen, Ticlopidine, Topiramate, Tolterodine, Triptorelin, Triplennamine, Triprolidine, Tramadol, Trovofloxacin, Ursodiol, Promazine, Propoxyphene, Propanolol, Pseudoephedrine, Pyrilamine, Quinidine, Oxybate sodium, Sermorelin, Tacrolimus, Tegaseroid, Teriparatide, Tolterodine, Triptorelin pamoate, Scoplolamine, Venlafaxine, Zamivir, Aminocaproic acid, Aminosalicylic acid, Hydromorphone, Isosuprine, Levorphanol, Melhalan, Nalidixic acid, and Para-aminosalicylic acid.

2. Deionizing Agent

The deionizing agent functions by causing partial deionization (neutralization) of the salt of one or more pharmaceutically active agents. When the active agent is the salt of a weak acid and a strong base, the deionizing agent is preferably a hydrogen ion species. When the active agent is the salt of a weak base and a strong acid, the deionizing agent is preferably a hydroxide ion species. The deionizing agent is preferably present in an amount between 0.2 to 1.0 mole equivalents per mole of the pharmaceutically active agent.

Exemplary hydrogen ion species useful as de-ionizing agents described herein, include, but are not limited to, hydrochloric acid, hydrobromic acid, hydroiodic acid, sulfuric acid, fumaric acid, maleic acid, tartaric acid, methane-, ethane-, and benzene sulfonates, citric acid, malic acid, acetic acid, proprionic acid, pyruvic acid, butanoic acid, and lactic acid.

Exemplary hydroxide ion species useful as de-ionizing agents described herein, include, but are not limited to, metal hydroxides such as sodium hydroxide, potassium hydroxide, ammonium hydroxide, calcium hydroxide, aluminum hydroxide, and magnesium hydroxide.

Additional acid or base can be added to adjust the pH of the fill composition. In a preferred embodiment, the pH of the fill composition is from about 2.5 to about 7.5.

3. Excipients

Formulations may be prepared using a pharmaceutically acceptable carrier composed of materials that are considered safe and effective and may be administered to an individual without causing undesirable biological side effects or unwanted interactions. The carrier is all components present in the pharmaceutical formulation other than the active ingredient or ingredients. As generally used herein "carrier" includes, but is not limited to, plasticizers, crystallization inhibitors, wetting agents, bulk filling agents, solubilizers, bioavailability enhancers, solvents, pH-adjusting agents and combinations thereof.

In a preferred embodiment, a mixture of polyethylene glycol and water is used as a solvent for the salt of the active agent and the de-ionizing agent. Polyethylene glycol is present in an amount from about 10% to about 80% by weight. Water is present in an amount from about 1% to 18% by weight. The molecular weight of polyethylene glycol is between 300 and 1500. Other suitable solvents include surfactants and copolymers of polyethylene glycol. Optionally, glycerin, polyvinyl pyrrolidone (PVP) or propylene glycol (PPG) can be added to enhance the solubility of the drug agent.

B. Shell Composition

1. Gelatin

Gelatin is the product of the partial hydrolysis of collagen. Gelatin is classified as either Type A or Type B gelatin. Type A gelatin is derived from the acid hydrolysis of collagen while Type B gelatin is derived from alkaline hydrolysis of collagen. Traditionally, bovine bones and skins have been used as raw materials for manufacturing Type A and Type B gelatin while porcine skins have been used extensively for manufacturing Type A gelatin. In general acid-processed gelatins form stronger gels than lime-processed gelatins of the same average molecular weight.

2. Other Shell Additives

Other suitable shell additives include plasticizers, opacifiers, colorants, humectants, preservatives, flavorings, and buffering salts and acids.

Plasticizers are chemical agents added to gelatin to make the material softer and more flexible. Suitable plasticizers include glycerin, sorbitol solutions which are mixtures of sorbitol and sorbitan, and other polyhydric alcohols such as propylene glycol and maltitol or combinations thereof.

Opacifiers are used to opacify the capsule shell when the encapsulated active agents are light sensitive. Suitable opacifiers include titanium dioxide, zinc oxide, calcium carbonate and combinations thereof.

Colorants can be used to for marketing and product identification/differentiation purposes. Suitable colorants include synthetic and natural dyes and combinations thereof.

Humectants can be used to suppress the water activity of the softgel. Suitable humectants include glycerin and sorbitol, which are often components of the plasticizer composition. Due to the low water activity of dried, properly stored softgels, the greatest risk from microorganisms comes from molds and yeasts. For this reason, preservatives can be incorporated into the capsule shell. Suitable preservatives include alkyl esters of p-hydroxy benzoic acid such as methyl, ethyl, propyl, butyl and heptyl (collectively known as "parabens") or combinations thereof.

Flavorings can be used to mask unpleasant odors and tastes of fill formulations. Suitable flavorings include synthetic and natural flavorings. The use of flavorings can be problematic due to the presence of aldehydes which can cross-link gelatin. As a result, buffering salts and acids can be used in conjunction with flavorings that contain aldehydes in order to inhibit cross-linking of the gelatin.

II. Method of Making

A. Fill Material

The fill material is prepared by mixing the agent (such as a salt of the drug), the deionizing agent, water, and polyethylene glycol at a temperature of 50°C to 70°C. The resulting solution is encapsulated using the appropriate gel mass. The pharmaceutical agent is present in an amount from about 10% to about 50% by weight. The deionizing agent is present in an amount from about 0.2 to 1.0 mole per mole of the pharmaceutical agent. Water is present in an amount from about 1% to about 20% by weight and polyethylene glycol is present in amount from about 10% to about 80% by weight. Optionally, propylene glycol and/or polyvinyl pyrrolidone are present in an amount from about 1% to about 10%.

B. Gel Mass

The main ingredients of the softgel capsule shell are gelatin, plasticizer, and purified water. Typical gel formulations contain (w/w) 40-50% gelatin, 20-30% plasticizer, and 30-40% purified water. Most of the water is subsequently lost during capsule drying. The ingredients are combined to form a molten gelatin mass using either a cold melt or a hot melt process. The prepared gel masses are transferred to preheated, temperature-controlled, jacketed holding tanks where the gel mass is aged at 50-60°C until used for encapsulation.

1. Cold Melt Process

The cold melt process involves mixing gelatin with plasticizer and chilled water and then transferring the mixture to a jacket-heated tank. Typically, gelatin is added to the plasticizer at ambient temperature (18-22°C). The mixture is cooked (57-95°C) under vacuum for 15-30 minutes to a homogeneous, deaerated gel mass. Additional shell additives can be added to the gel mass at any point during the gel manufacturing process or they may be incorporated into the finished gel mass using a high torque mixer.

2. Hot Melt Process

The hot melt process involves adding, under mild agitation, the gelatin to a preheated (60-80°C) mixture of plasticizer and water and stirring the blend until complete melting is achieved. While the hot melt process is faster than the cold melt process, it is less accurately controlled and more susceptible to foaming and dusting.

C. Softgel Capsule

Softgel capsules are typically produced using a rotary die encapsulation process. The gel mass is fed either by gravity or through positive displacement pumping to two heated (48-65°C) metering devices. The metering devices control the flow of gel into cooled (10-18°C), rotating casting drums. Ribbons are formed as the cast gel masses set on contact with the surface of the drums.

The ribbons are fed through a series of guide rolls and between injection wedges and the capsule-forming dies. A food-grade lubricant oil is applied onto the ribbons to reduce their tackiness and facilitate their transfer. Suitable lubricants include mineral oil, medium chain triglycerides, and soybean oil. Fill formulations are fed into the encapsulation machine by gravity. In the preferred embodiment, the softgels contain printing on the surface, optionally identifying the encapsulated agent and/or dosage.

III. Method of Use

The softgels may be used to encapsulate a wide range of pharmaceutically active agents, nutritional agents and personal care products. Softgel capsules may be administered orally to a patient to deliver a pharmaceutically active agent.

Examples

In the following examples, the fill material can be prepared by mixing the salt of one or more pharmaceutically active agents, the deionizing agent, water and polyethylene glycol at a temperature of 50°C to 70°C. The resulting solution can be encapsulated in a softgel capsule using the appropriate gel mass.

Example 1. Naproxen Sodium with Acetic Acid as the Deionizing Agent

Fill Material:

Ingredients	% (by weight)
Naproxen Sodium	25.50
Acetic Acid	3.00
PVP	1.85
PEG 400	62.30
Water	7.40

Example 2. Naproxen Sodium with Citric Acid as the Deionizing Agent

Fill Material:

Ingredients	% (by weight)
Naproxen Sodium	25.50
Citric Acid	4.75
PVP	1.85
PEG 400	60.50
Water	7.40

Example 3. Naproxen Sodium with Hydrochloric Acid as the Deionizing Agent

Fill Material:

Ingredients	% (by weight)
Naproxen Sodium	25.50
Hydrochloric Acid	4.72
PVP	1.85
PEG 400	63.52
Water	7.40

Example 4. Naproxen Sodium with Acetic Acid as the Deionizing Agent

Fill Material:

Ingredients	% (by weight)
Naproxen Sodium	25.50
Acetic Acid	3.00
PVP	1.85
PEG 400	31.15
Water	7.40
PEG 600	31.15

Example 5. Naproxen Sodium with Citric Acid as the Deionizing Agent

Fill Material:

Ingredients	% (by weight)
Naproxen Sodium	25.50
Citric Acid	4075
PVP	1.85
PEG 400	30.25
Water	7.40
PEG 600	30.25

Example 6. Naproxen Sodium with Hydrochloric Acid as the Deionizing Agent

Fill Material:

Ingredients	% (by weight)
Naproxen Sodium	25.50
Hydrochloric Acid	4072
PVP	1.85
PEG 400	30.25
Water	7.40
PEG 600	30.25

Example 7. Naproxen Sodium with Lactic Acid as the Deionizing Agent

Fill Material:

Ingredients	% (by weight)
Naproxen Sodium	27.50
Lactic Acid	5.27
Propylene Glycol	2.00
PEG 400	64.64
Water	0.60

Example 8. Naproxen Sodium with Lactic Acid as the Deionizing Agent

Fill Material:

Ingredients	% (by weight)
Naproxen Sodium	25.00
Lactic Acid	0.24-0.35 M
Propylene glycol	2.00
PEG 600.	q.s.

Example 9. Naproxen Sodium with Lactic Acid as the Deionizing Agent

Fill Material:

Ingredients	% (by weight)
Naproxen Sodium	25.00
Lactic Acid	5.00
Propylene glycol	2.00
PEG 600	61.2
PEG 1000	6.80

describing particular embodiments only, and is not intended to limit the scope of the present invention which will be limited only by the appended claims.

Unless defined otherwise, all technical and scientific terms used herein have the same meanings as commonly understood by one of skill in the art to which the disclosed invention belongs. Although any methods and materials similar or equivalent to those described herein can be used in the practice or testing of the present invention, the preferred methods, devices, and materials are as described. Publications cited herein and the materials for which they are cited are specifically incorporated by reference. Nothing herein is to be construed as an admission that the invention is not entitled to antedate such disclosure by virtue of prior invention.

Those skilled in the art will recognize, or be able to ascertain using no more than routine experimentation, many equivalents to the specific embodiments of the invention described herein. Such equivalents are intended to be encompassed by the following claims.

Example 10. Naproxen Sodium with Lactic Acid as the Deionizing Agent

Fill Material:

Ingredients	% (by weight)
Naproxen Sodium	25.00
Lactic acid	5.00
Propylene glycol	2.00
PEG 600	51.00
PEG 1000	17.00

Example 11. Naproxen Sodium with Lactic Acid as the Deionizing Agent

Fill Material:

Ingredients	% (by weight)
Naproxen Sodium	25.00
Lactic Acid	5.00
Propylene glycol	2.00
PEG 600	34.00
PEG 1000	34.00

Example 12. Naproxen Sodium with Lactic Acid as the Deionizing Agent

Fill Material:

Ingredients	% (by weight)
Naproxen Sodium	25.00
Lactic acid	5.00
Propylene glycol	2.00
PEG 600	17.00
PEG 1000	51.00

It is understood that the disclosed invention is not limited to the particular methodology, protocols, and reagents described as these may vary. It is also to be understood that the terminology used herein is for the purpose of

We claim:

1. A pharmaceutical composition comprising

(a) a salt of one or more pharmaceutically active agents; and

(b) a deionizing agent.

2. The composition of claim 1 wherein the pharmaceutically active agent is selected from the group consisting of therapeutically active agents, diagnostic agents, and prophylactic agents.

3. The composition of claim 1 wherein the deionizing agent is present in an amount from about 0.2 to 1.0 mole equivalents per mole of the pharmaceutically active agent(s).

4. The composition of claim 1 wherein the deionizing agent is selected from the group consisting of hydrogen ion and hydroxide ion.

5. The composition of claim 1 further comprising polyethylene glycol.

6. The composition of claim 5 wherein polyethylene glycol is present in an amount from about 10% to about 80% by weight

7. The composition of claim 5 wherein polyethylene glycol is one or more polyethylene glycols with a molecular weight between 300 and 1500.

8. The composition of claim 1 further comprising water.

9. The composition of claim 8 wherein water is present in an amount from about 1% to about 18% by weight.

10. The composition of claim 1 further comprising one or more excipients.

11. The composition of claim 7 wherein the excipients are selected from the group consisting of plasticizers, crystallization inhibitors, wetting agents, bulk filling agents, solubilizers, bioavailability enhancers, solvents, pH-adjusting agents, dyes, preservatives, solvents, surfactants, and combinations thereof.

12. The composition of claim 11 wherein the solubilizer is selected from the group consisting of glycerin, polyvinylpyrrolidone, propylene glycol and combinations thereof.

13. The composition of claim 12 wherein the solubilizer is present in amount from about 1% to about 10% by weight.

14. A method of making a pharmaceutical composition comprising

a salt of one or more pharmaceutically active agents; and

a deionizing agent comprising

(a) mixing the salt of one or more pharmaceutically active agents, and the deionizing agent at an appropriate temperature; and

(b) encapsulating the mixture in a softgel capsule.

15. The method of claim 14 further comprising polyethylene glycol.

16. The method of claim 14 further comprising water.

17. The method of claim 14 wherein the appropriate temperature is from about 50°C to about 70°C.

18. A method of using a pharmaceutical composition comprising

(a) a salt of one or more pharmaceutically active agents; and

(b) a deionizing agent

comprising administering to a patient in need thereof the salt of one or more pharmaceutically active agents.

19. A softgel capsule comprising a fill material wherein the fill material comprises

(a) a salt of one or more pharmaceutically active agents; and

(b) a deionizing agent.

20. The capsule of claim 19 wherein the pharmaceutically active agent is selected from the group consisting of therapeutically active agents, diagnostic agents, and prophylactic agents.

21. The capsule of claim 19 wherein the deionizing agent is present in an amount from about 0.2 to 1.0 mole equivalents per mole of the pharmaceutically active agent(s).

22. The capsule of claim 19 wherein the deionizing agent is selected from the group consisting of hydrogen ion and hydroxide ion.

23. The capsule of claim 19 further comprising polyethylene glycol.

24. The capsule of claim 23 wherein polyethylene glycol is present in an amount from about 10% to about 80% by weight

25. The capsule of claim 23 wherein polyethylene glycol is one or more polyethylene glycols with a molecular weight between 300 and 1500.

26. The capsule of claim 19 further comprising water.

27. The capsule of claim 26 wherein water is present in an amount from about 1% to about 18% by weight.

28. The capsule of claim 19 further comprising one or more excipients.

29. The capsule of claim 28 wherein the excipients are selected from the group consisting of plasticizers, crystallization inhibitors, wetting agents, bulk filling agents, solubilizers, bioavailability enhancers, solvents, pH-adjusting agents, dyes, preservatives, solvents, surfactants, and combinations thereof.

30. The capsule of claim 29 wherein the solubilizer is selected from the group consisting of glycerin, polyvinylpyrrolidone, propylene glycol and combinations thereof.

31. The capsule of claim 29 wherein the solubilizer is present in amount from about 1% to about 10% by weight.

SOLVENT SYSTEM FOR ENHANCING THE SOLUBILITY OF PHARMACEUTICAL AGENTS

ABSTRACT OF THE DISCLOSURE

Liquid and semi-solid pharmaceutical compositions, which can be administered in liquid form or can be used for preparing capsules, are described herein. The composition comprises the salt of one ore more active agents, polyethylene glycol, 0.2-1.0 mole equivalents of a de-ionizing agent per mole of active agent, and water. The pH of the composition is adjusted within the range of 2.5 – 7.5. The de-ionizing agent causes partial de-ionization (neutralization) of the salt of the active agent resulting in enhanced bioavailability of salts of weakly acidic, basic or amphoteric active agents as well as lesser amounts of polyethylene glycol (PEG) esters.

PTO/SB/01A (09-04)
Approved for use through 07/31/2006. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

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

Title of Invention	SOLVENT SYSTEM FOR ENHANCING THE SOLUBILITY OF PHARMACEUTICAL AGENTS

As the below named inventor(s), I/we declare that:

This declaration is directed to:

☑ The attached application, or

☐ Application No. _____, filed on _____,

☐ as amended on _____(if applicable);

I/we believe that I/we am/are the original and first inventor(s) of the subject matter which is claimed and for which a patent is sought;

I/we have reviewed and understand the contents of the above-identified application, including the claims, as amended by any amendment specifically referred to above;

I/we acknowledge the duty to disclose to the United States Patent and Trademark Office all information known to me/us to be material to patentability as defined in 37 CFR 1.56, including for continuation-in-part applications, material information which became available between the filing date of the prior application and the national or PCT International filing date of the continuation-in-part application.

All statements made herein of my/own knowledge are true, all statements made herein on information and belief are believed to be true, and further that these statements were made with the knowledge that willful false statements and the like are punishable by fine or imprisonment, or both, under 18 U.S.C. 1001, and may jeopardize the validity of the application or any patent issuing thereon.

FULL NAME OF INVENTOR(S)

Inventor one: Nachiappan Chidambaram

Signature: _____ 03/02/06 Citizen of: India

Inventor two: Aqeel Fatmi

Signature: _____ Citizen of: United States

Inventor three: _____

Signature: _____ Citizen of: _____

Inventor four: _____

Signature: _____ Citizen of: _____

☐ Additional inventors or a legal representative are being named on _____ additional form(s) attached hereto.

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

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

PTO/SB/06 (12-04)
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PATENT APPLICATION FEE DETERMINATION RECORD

Substitute for Form PTO-875 Effective December 8, 2004

Application or Docket Number: 11367238

APPLICATION AS FILED – PART I

FOR	(Column 1) NUMBER FILED	(Column 2) NUMBER EXTRA	SMALL ENTITY RATE ($)	SMALL ENTITY FEE ($)	OR	OTHER THAN SMALL ENTITY RATE ($)	OTHER THAN SMALL ENTITY FEE ($)
BASIC FEE (37 CFR 1.16(a), (b), or (c))	N/A	N/A	N/A	150.00		N/A	300.00
SEARCH FEE (37 CFR 1.16(k), (l), or (m))	N/A	N/A	N/A	$250		N/A	$500
EXAMINATION FEE (37 CFR 1.16(o), (p), or (q))	N/A	N/A	N/A	$100		N/A	$200
TOTAL CLAIMS (37 CFR 1.16(i))	31 minus 20 =	* 11	X$ 25 =		OR	X$50 =	550
INDEPENDENT CLAIMS (37 CFR 1.16(h))	4 minus 3 =	* 1	X100 =			X200 =	200
APPLICATION SIZE FEE (37 CFR 1.16(s))	If the specification and drawings exceed 100 sheets of paper, the application size fee due is $250 ($125 for small entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(s).						
MULTIPLE DEPENDENT CLAIM PRESENT (37 CFR 1.16(j))			+180=			+360=	
* If the difference in column 1 is less than zero, enter "0" in column 2.			TOTAL			TOTAL	1750

APPLICATION AS AMENDED – PART II

AMENDMENT A	(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA	SMALL ENTITY RATE ($)	SMALL ENTITY ADDITIONAL FEE ($)	OR	OTHER THAN SMALL ENTITY RATE ($)	OTHER THAN SMALL ENTITY ADDITIONAL FEE ($)
Total (37 CFR 1.16(i))	*	Minus	**	=	X$ 25 =		OR	X$50 =	
Independent (37 CFR 1.16(h))	*	Minus	***	=	X100 =		OR	X200 =	
Application Size Fee (37 CFR 1.16(s))									
FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))					+180=		OR	+360=	
					TOTAL ADD'L FEE		OR	TOTAL ADD'L FEE	

1-14-18-19-

AMENDMENT B	(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA	RATE ($)	ADDITIONAL FEE ($)	OR	RATE ($)	ADDITIONAL FEE ($)
Total (37 CFR 1.16(i))	*	Minus	**	=	X$ 25 =		OR	X$50 =	
Independent (37 CFR 1.16(h))	*	Minus	***	=	X100 =		OR	X200 =	
Application Size Fee (37 CFR 1.16(s))									
FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))					+180=		OR	+360=	
					TOTAL ADD'L FEE		OR	TOTAL ADD'L FEE	

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

This collection of information is required by 37 CFR 1.16. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: **Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

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PATENT APPLICATION SERIAL NO. _____

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

03/07/2006 FFANAEIA 00000051 503129 11367238

01 FC:1011	300.00	DA
02 FC:1111	500.00	DA
03 FC:1311	200.00	DA
04 FC:1201	200.00	DA
05 FC:1202	550.00	DA

PTO-1556
(5/87)

*U.S Government Printing Office: 2002 — 466-267/69033

APPLICATION DATA SHEET

Inventor Information

Inventor One Given Name::	Nachiappan
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State or Prov. of Residence::	North Carolina
Country of Residence::	United States
Citizenship Country::	India

Inventor Two Given Name::	Aqeel A.
Family Name::	Fatmi
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Country::	United States
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State or Prov. of Residence::	North Carolina
Country of Residence::	United States
Citizenship Country::	United States

Correspondence Information:

Correspondence Customer Number::	23579
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Fax::	404-879-2160
Electronic Mail One::	Jeanette@pabstpatent.com
Electronic Mail Two::	Patrea@pabstpatent.com

Application Information:

Title Line One::	SOLVENT SYSTEM FOR ENHANCING THE
Title Line Two::	SOLUBILITY OF PHARMACEUTICAL AGENTS
Title Line Three::	
Total Drawing Sheets::	0
Formal Drawings?::	No
Application Type::	Utility
Docket Number::	BAN 102
Licensed US Govt. Agency::	
Contract or Grant Numbers One::	
Contract or Grant Numbers Two::	
Secrecy Order in Parent Appl.?::	No

Assignee::	Banner Pharmacaps, Inc.
State of Incorporation::	Delaware

Representative Information

Representative Customer Number:: 23579

Continuity Information

This application is a::	Non Prov. of Provisional
>Application One::	60/659,679
Filing Date::	March 8, 2005
Patent Number::	

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
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APPLICATION NUMBER	FILING OR 371 (c) DATE	FIRST NAMED APPLICANT	ATTORNEY DOCKET NUMBER
11/367,238	03/03/2006	Nachiappan Chidambaram	BAN 102

CONFIRMATION NO. 5524

FORMALITIES LETTER

23579
PATREA L. PABST
PABST PATENT GROUP LLP
400 COLONY SQUARE
SUITE 1200
ATLANTA, GA 30361

Date Mailed: 03/28/2006

NOTICE TO FILE MISSING PARTS OF NONPROVISIONAL APPLICATION

FILED UNDER 37 CFR 1.53(b)

Filing Date Granted

Items Required To Avoid Abandonment:

An application number and filing date have been accorded to this application. The item(s) indicated below, however, are missing. Applicant is given **TWO MONTHS** from the date of this Notice within which to file all required items and pay any fees required below to avoid abandonment. Extensions of time may be obtained by filing a petition accompanied by the extension fee under the provisions of 37 CFR 1.136(a).

- The signature of the following inventor(s) is missing from the oath or declaration:
  Aqeel Fatmi

The applicant needs to satisfy supplemental fees problems indicated below.

The required item(s) identified below must be timely submitted to avoid abandonment:

- To avoid abandonment, a surcharge (for late submission of filing fee, search fee, examination fee or oath or declaration) as set forth in 37 CFR 1.16(f) of $130 for a non-small entity, must be submitted with the missing items identified in this letter.

SUMMARY OF FEES DUE:

Total additional fee(s) required for this application is **$130** for a Large Entity

- **$130** Surcharge.

Replies should be mailed to: Mail Stop Missing Parts
Commissioner for Patents
P.O. Box 1450

Alexandria VA 22313-1450

A copy of this notice MUST be returned with the reply.

Office of Initial Patent Examination (571) 272-4000, or 1-800-PTO-9199, or 1-800-972-6382
PART 3 - OFFICE COPY

PTO/SB/81 (04-08)
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POWER OF ATTORNEY and CORRESPONDENCE ADDRESS INDICATION FORM

Application Number	11/367,238
Filing Date	March 3, 2006
First Named Inventor	Nachiappan Chidambaram
Title	Solvent System for Enhancing the Solubility of Pharmaceutical Agents
Art Unit	1618
Examiner Name	
Attorney Docket Number	BAN 102

I hereby revoke all previous powers of attorney given in the above-identified application.

I hereby appoint:

☑ Practitioners associated with the Customer Number: **23579**

OR

☐ Practitioner(s) named below:

Name	Registration Number

as my/our attorney(s) or agent(s) to prosecute the application identified above, and to transact all business in the United States Patent and Trademark Office connected therewith.

Please recognize or change the correspondence address for the above-identified application to:

☐ The address associated with the above-mentioned Customer Number:

OR

☑ The address associated with Customer Number: **23579**

OR

☐ Firm or Individual Name					
Address					
City		State		Zip	
Country					
Telephone		Email			

I am the:

☐ Applicant/Inventor

☑ Assignee of record of the entire interest. See 37 CFR 3.71.
Statement under 37 CFR 3.73(b) is enclosed. (Form PTO/SB/96)

SIGNATURE of Applicant or Assignee of Record

Signature	[signature] on behalf of Banner Pharmacaps, Inc.	Date	April 15, 2006
Name	[illegible]	Telephone	[illegible]
Title and Company	[illegible]

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

☐ *Total of _____ forms are submitted.

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

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

BAN 102 095161/00005

PTO/SB/96 (12-05)
Approved for use through 07/31/2006. OMB 0651-0031
U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

STATEMENT UNDER 37 CFR 3.73(b)

Applicant/Patent Owner: Nachiappan Chidambaram and Aqeel A. Fatmi

Application No./Patent No./Control No.: 11/367,238 Filed/Issue Date: March 3, 2006

Entitled: SOLVENT SYSTEM FOR ENHANCING THE SOLUBILITY OF PHARMACEUTICAL AGENTS

Banner Pharmacaps, Inc., a corporation
(Name of Assignee) (Type of Assignee: corporation, partnership, university, government agency, etc.)

states that it is:

1. ☒ the assignee of the entire right, title, and interest; or

2. ☐ an assignee of less than the entire right, title and interest
(The extent (by percentage) of its ownership interest is _____%)

in the patent application/patent identified above by virtue of either:

A. ☒ An assignment from the inventor(s) of the patent application/patent identified above. The assignment was recorded in the United States Patent and Trademark Office at Reel 017602, Frame 0314, or a true copy of the original assignment is attached.

OR

B. ☐ A chain of title from the inventor(s), of the patent application/patent identified above, to the current assignee as follows:

1. From: _____ To: _____
The document was recorded in the United States Patent and Trademark Office at
Reel _____, Frame _____, or for which a copy thereof is attached.

2. From: _____ To: _____
The document was recorded in the United States Patent and Trademark Office at
Reel _____, Frame _____, or for which a copy thereof is attached.

3. From: _____ To: _____
The document was recorded in the United States Patent and Trademark Office at
Reel _____, Frame _____, or for which a copy thereof is attached.

☐ Additional documents in the chain of title are listed on a supplemental sheet.

As required by 37 CFR 3.73(b)(1)(i), the documentary evidence of the chain of title from the original owner to the assignee was, or concurrently is being, submitted for recordation pursuant to 37 CFR 3.11.

[NOTE: A separate copy (*i.e.*, a true copy of the original assignment document(s)) must be submitted to Assignment Division in accordance with 37 CFR Part 3, to record the assignment in the records of the USPTO. See MPEP 302.08]

The undersigned (whose title is supplied below) is authorized to act on behalf of the assignee.

Charles L Cain — April 15, 2006
Signature — Date

Charles L Cain — 336 812 7077
Printed or Typed Name — Telephone Number

Sr VP/Legal Counsel
Title

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
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APPLICATION NUMBER	FILING OR 371 (c) DATE	FIRST NAMED APPLICANT	ATTORNEY DOCKET NUMBER
11/367,238	03/03/2006	Nachiappan Chidambaram	BAN 102

CONFIRMATION NO. 5524

FORMALITIES LETTER

23579
PATREA L. PABST
PABST PATENT GROUP LLP
400 COLONY SQUARE
SUITE 1200
ATLANTA, GA 30361

Date Mailed: 03/28/2006

NOTICE TO FILE MISSING PARTS OF NONPROVISIONAL APPLICATION

FILED UNDER 37 CFR 1.53(b)

Filing Date Granted

Items Required To Avoid Abandonment:

An application number and filing date have been accorded to this application. The item(s) indicated below, however, are missing. Applicant is given **TWO MONTHS** from the date of this Notice within which to file all required items and pay any fees required below to avoid abandonment. Extensions of time may be obtained by filing a petition accompanied by the extension fee under the provisions of 37 CFR 1.136(a).

- The signature of the following inventor(s) is missing from the oath or declaration:
  Aqeel Fatmi

The applicant needs to satisfy supplemental fees problems indicated below.

The required item(s) identified below must be timely submitted to avoid abandonment:

- To avoid abandonment, a surcharge (for late submission of filing fee, search fee, examination fee or oath or declaration) as set forth in 37 CFR 1.16(f) of $130 for a non-small entity, must be submitted with the missing items identified in this letter.

SUMMARY OF FEES DUE:

Total additional fee(s) required for this application is **$130** for a Large Entity

- **$130** Surcharge.

Replies should be mailed to: Mail Stop Missing Parts
Commissioner for Patents
P.O. Box 1450

Alexandria VA 22313-1450

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PART 2 - COPY TO BE RETURNED WITH RESPONSE

PTO/SB/01A (09-04)
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U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

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

Title of Invention	SOLVENT SYSTEM FOR ENHANCING THE SOLUBILITY OF PHARMACEUTICAL AGENTS

As the below named inventor(s), I/we declare that:

This declaration is directed to:

☐ The attached application, or

☑ Application No. 11/367,238 filed on March 3, 2006

☐ as amended on _____ (if applicable);

I/we believe that I/we am/are the original and first inventor(s) of the subject matter which is claimed and for which a patent is sought;

I/we have reviewed and understand the contents of the above-identified application, including the claims, as amended by any amendment specifically referred to above;

I/we acknowledge the duty to disclose to the United States Patent and Trademark Office all information known to me/us to be material to patentability as defined in 37 CFR 1.56, including for continuation-in-part applications, material information which became available between the filing date of the prior application and the national or PCT International filing date of the continuation-in-part application.

All statements made herein of my/own knowledge are true, all statements made herein on information and belief are believed to be true, and further that these statements were made with the knowledge that willful false statements and the like are punishable by fine or imprisonment, or both, under 18 U.S.C. 1001, and may jeopardize the validity of the application or any patent issuing thereon.

FULL NAME OF INVENTOR(S)

Inventor one: Nachiappan Chidambaram

Signature: _____ Citizen of: India

Inventor two: Aqeel Fatmi

Signature: Aqeel Fatmi Citizen of: United States

Inventor three: _____

Signature: _____ Citizen of: _____

Inventor four: _____

Signature: _____ Citizen of: _____

☐ Additional inventors or a legal representative are being named on _____ additional form(s) attached hereto.

PTO/SB/01A (09-04)
Approved for use through 07/31/2006. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

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FULL NAME OF INVENTOR(S)

Inventor one: Nachiappan Chidambaram

Signature: _____ Citizen of: India

Inventor two: Ageel Fatmi

Signature: _____ Citizen of: United States

Inventor three: _____

Signature: _____ Citizen of: _____

Inventor four: _____

Signature: _____ Citizen of: _____

☐ Additional inventors or a legal representative are being named on _____ additional form(s) attached hereto.

Electronic Patent Application Fee Transmittal

Application Number:	11367238
Filing Date:	03-Mar-2006
Title of Invention:	Solvent system for enhancing the solubility of pharmaceutical agents
First Named Inventor:	Nachiappan Chidambaram
Filer:	Rivka D. Monheit/Ronna Berman
Attorney Docket Number:	BAN 102

Filed as Large Entity

Utility Filing Fees

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Basic Filing:				
Pages:				
Claims:				
Miscellaneous-Filing:				
Late filing fee or oath or declaration	1051	1	130	130
Petition:				
Patent-Appeals-and-Interference:				
Post-Allowance-and-Post-Issuance:				
Extension-of-Time:				

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Miscellaneous:				
		Total in USD ($)		**130**

Electronic Acknowledgement Receipt

EFS ID:	1045584
Application Number:	11367238
Confirmation Number:	5524
Title of Invention:	Solvent system for enhancing the solubility of pharmaceutical agents
First Named Inventor:	Nachiappan Chidambaram
Customer Number:	23579
Filer:	Rivka D. Monheit/Ronna Berman
Filer Authorized By:	Rivka D. Monheit
Attorney Docket Number:	BAN 102
Receipt Date:	12-MAY-2006
Filing Date:	03-MAR-2006
Time Stamp:	11:23:42
Application Type:	Utility
International Application Number:	

Payment information:

Submitted with Payment	yes
Payment was successfully received in RAM	$130.0
RAM confirmation Number	444
Deposit Account	503129
The Director of the USPTO is hereby authorized to charge indicated fees and credit any overpayment as follows: Charge any Additional Fees required under 37 C.F.R. Section 1.16 and 1.17	

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)	Multi Part	Pages
1	Transmittal letter	BAN_102_Response.pdf	26351	no	2
Warnings:					
Information:					
2	Power of Attorney (may include Associate POA)	BAN_102_Power_of_Attorney.pdf	240727	no	1
Warnings:					
Information:					
3	Assignee showing of ownership per 37 CFR 3.73(b).	BAN_102_Statement_Under_373b.pdf	252295	no	1
Warnings:					
Information:					
4	Miscellaneous Incoming Letter	BAN_102_Notice_Missing_Parts.pdf	219167	no	2
Warnings:					
Information:					
5	Oath or Declaration filed	BAN_102_Declaration.pdf	493594	no	2
Warnings:					
Information:					
6	Fee Worksheet (PTO-875)	fee-info.pdf	8166	no	2
Warnings:					
Information:					
		Total Files Size (in bytes):	1240300		

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

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

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants:	Nachiappan Chidambaream Aqeel A. Fatmi		
Serial No.:	11/367,238	Group Art Unit:	1618
Filed:	March 3, 2006	Examiner:	Not yet assigned
For:	SOLVENT FOR ENHANCING THE SOLUBILITY OF PHARMACEUTICAL AGENTS		

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

RESPONSE TO NOTICE TO FILE MISSING PARTS OF NONPROVISIONAL APPLICATION

Sir:

Responsive to the Notice to File Missing Parts of Nonprovisional Application, mailed March 28, 2006, Applicants enclose the following for filing in the above-identified application:

1. Declaration for Patent Application executed by Nachiappan Chidambaram and Aqeel A. Fatmi;

2. Power of Attorney and Correspondence Address Indication Form executed by Banner Pharmacaps, Inc.;

3. Statement Under 37 C.F.R. § 3.73(b) executed by Banner Pharmacaps, Inc.; and

4. Authorization for the Commissioner to charge Deposit Account No. 50-3129 in the amount of $130.00 for the large entity surcharge for late filing the Declaration for Patent Application.

This application is not entitled to claim small entity status pursuant to 37 C.F.R. § 1.27.

Applicants also enclose a copy of the Notice to File Missing Parts of Nonprovisional Application, mailed March 28, 2006.

The Commissioner is hereby authorized to charge any additional fees that may be due, or credit any overpayment in connection with this matter, to Deposit Account No. 50-3129.

Respectfully submitted,

/Rivka D. Monheit/
Rivka D. Monheit
Reg. No. 48,731

Date: May 12, 2006

PABST PATENT GROUP LLP
400 Colony Square, Suite 1200
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Atlanta, Georgia 30361
(404) 879-2152 (Telephone)
(404) 879-2160 (Fax)

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(use as many sheets as necessary)

Complete if Known	
Application Number	11/367,238
Filing Date	March 3, 2006
First Named Inventor	Nachiappan Chidambaram
Group Art Unit	1618
Examiner Name	
Attorney Docket Number	BAN 102

Sheet 1 of 1

U.S. PATENT DOCUMENTS

Examiner Initials*	Cite No.[1]	US Patent Document Number	Kind Code[2] (if known)	Name of Patentee or Applicant of Cited Document	Date of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		5,360,615		Yu, et al.	11-01-1994	
		5,505,961		Shelley, et al.	04-09-1996	
		6,383,515		Sawyer, et al.	05-07-2002	
		6,689,382		Berthel, et al.	02-10-2004	
		2001/0007668		Sawyer, et al.	07-12-2001	
		2002/0187195		Sawyer, et al.	12-12-2002	

FOREIGN PATENT DOCUMENTS

Examiner Initials*	Cite No.[1]	Foreign Patent Document Office.[3]	Number[4]	Kind Code[5] (if known)	Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T[6]

Examiner's Signature		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 application.

[1] Unique citation designation number [2] See attached Kinds of U.S. Patent Documents. [3] Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). [4] For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. [5] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. [6] Applicant to place a check mark here if English language Translation is attached.

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Electronic Acknowledgement Receipt

EFS ID:	1121035
Application Number:	11367238
Confirmation Number:	5524
Title of Invention:	Solvent system for enhancing the solubility of pharmaceutical agents
First Named Inventor:	Nachiappan Chidambaram
Customer Number:	23579
Filer:	Patrea L. Pabst/Carla Stone
Filer Authorized By:	Patrea L. Pabst
Attorney Docket Number:	BAN 102
Receipt Date:	20-JUL-2006
Filing Date:	03-MAR-2006
Time Stamp:	14:47:30
Application Type:	Utility
International Application Number:	

Payment information:

Submitted with Payment	no

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)	Multi Part	Pages
1	Transmittal letter	BAN_102_IDS.pdf	26424	no	2

Warnings:					
Information:					
2	Information Disclosure Statement (IDS) Filed	BAN_102_PTO_Form_1449.pdf	240006	no	1
Warnings:					
Information:					
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			Total Files Size (in bytes):	266430	

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants:	Nachiappan Chidambaram and Aqeel A. Fatmi		
Serial No.:	11/367,238	Art Unit:	1618
Filed:	March 3, 2006	Examiner:	Not Yet Assigned
For:	*SOLVENT SYSTEM FOR ENHANCING THE SOLUBILITY OF PHARMACEUTICAL AGENTS*		

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

INFORMATION DISCLOSURE STATEMENT

Sir:

Pursuant to 37 C.F.R. §1.56 and 37 C.F.R. §1.97, Applicants submit an Information Disclosure Statement, including one (1) page of Form PTO-1449. Pursuant to the waiver in the notice entitled "Information Disclosure Statements May Be Filed Without Copies of U.S. Patents and Published Applications in Patent Applications Filed After June 30, 2003" published on August 5, 2003 in 1273 OG 55, copies of U.S Patents and Published Applications are not enclosed. Copies will be provided upon request, however.

This Information Disclosure Statement is being filed under 37 C.F.R. § 1.97(b) prior to a first Office Action on the merits. It is believed that no fee is required with this submission. However, should a fee be required, the Commissioner is hereby authorized to charge any required fees to Deposit Account No. 50-1329.

U.S. Patents

Number	Issue Date	Patentee	Class/Subclass
5,360,615	11-01-1994	Yu, et al.	424/455
5,505,961	04-09-1996	Shelley, et al.	424/451
6,383,515	05-07-2002	Sawyer, et al.	424/456
6,689,382	02-10-2004	Berthel, et al.	424/456

U.S. Patent Applications

Number	Publication Date	Inventor	Class/Subclass
2001/0007668	07-12-2001	Sawyer, et al.	424/400
2002/0187195	12-12-2002	Sawyer, et al.	424/486

Remarks

This statement should not be interpreted as a representation that an exhaustive search has been conducted or that no better art exists. Moreover, Applicants invite the Examiner to make an independent evaluation of the cited art to determine its relevance to the subject matter of the present application. Applicants are of the opinion that their claims patentably distinguish over the art referred to herein, either alone or in combination.

Respectfully submitted,

/Patrea L. Pabst/
Patrea L. Pabst
Reg. No. 31,284

Dated: July 20, 2006

PABST PATENT GROUP LLP
400 Colony Square, Suite 1200
1201 Peachtree Street
Atlanta, Georgia 30361
(404) 879-2151 (Telephone)
(404) 879-2160 (Fax)

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(use as many sheets as necessary)

Sheet	1	of	1

Complete if Known	
Application Number	11/367,238
Filing Date	March 3, 2006
First Named Inventor	Nichiappan Chidambaram
Group Art Unit	1618
Examiner Name	Not Yet Assigned
Attorney Docket Number	BAN 102

U.S. PATENT DOCUMENTS

Examiner Initials*	Cite No.[1]	US Patent Document Number	Kind Code[2] (if known)	Name of Patentee or Applicant of Cited Document	Date of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		5,484,606		Dhabar, et al.	01-16-1996	
		5,912,011		Makino, et al.	06-15-1999	
		2004/157928		Kim Jae-Hwan, et al.	08-12-2004	

FOREIGN PATENT DOCUMENTS

Examiner Initials*	Cite No.[1]	Foreign Patent Document Office.[3]	Number[4]	Kind Code[5] (if known)	Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T[6]
		PCT	WO 95/31979		R.P Scherer International Corporation	11-30-1995		

Examiner's Signature		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 application.

[1] Unique citation designation number [2] See attached Kinds of U.S. Patent Documents. [3] Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). [4] For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. [5] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. [6] Applicant to place a check mark here if English language Translation is attached.

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International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 6 : A61K 31/19, 47/14

A1

(11) International Publication Number: **WO 95/31979**

(43) International Publication Date: 30 November 1995 (30.11.95)

(21) International Application Number: PCT/US95/06183

(22) International Filing Date: 19 May 1995 (19.05.95)

(30) Priority Data:
08/247,028 19 May 1994 (19.05.94) US

(60) Parent Application or Grant
(63) Related by Continuation
US 08/247,028 (CIP)
Filed on 19 May 1994 (19.05.94)

(71) Applicant *(for all designated States except US)*: R.P. SCHERER INTERNATIONAL CORPORATION [US/US]; 2075 West Big Beaver Road, P.O. Box 7060, Troy, MI 48007-7060 (US).

(72) Inventors; and
(75) Inventors/Applicants *(for US only)*: SHELLEY, Rickey, S. [US/US]; 986 Wood Street, Largo, FL 31640 (US). WEI, Youching [US/US]; 2275 Willowbrook Drive, Clearwater, FL 34624 (US).

(74) Agent: SARUSSI, Steven, J.; Banner & Allegretti, Ltd., Ten South Wacker Drive, Chicago, IL 60606 (US).

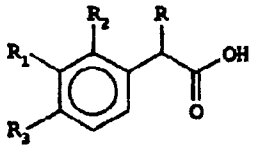
(81) Designated States: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT, UA, UG, US, UZ, VN, European patent (AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG), ARIPO patent (KE, MW, SD, SZ, UG).

Published
With international search report.
Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.

(54) Title: SOLUTIONS OF ARYL OR HETEROARYL SUBSTITUTED ALKANOIC ACIDS IN LIPOPHILIC SOLVENTS AND SOFT GELATIN CAPSULES CONTAINING SUCH SOLUTIONS

(57) Abstract

Methods and compositions are disclosed for preparing liquid mixtures of aryl or heteroaryl alkanoic acids suitable for encapsulation in soft gelatin capsules. The compositions comprise alkanoic acids of formulas (I), (Ia), (Ib) or pharmaceutically acceptable salts thereof, wherein R, R_1, R_2, R_3, and R_5 represent hydrogen or various organic substituents, and an effective solubilizing amount of at least one lipophilic solvent.



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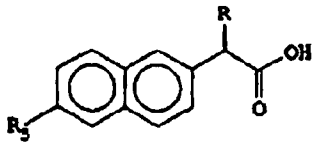

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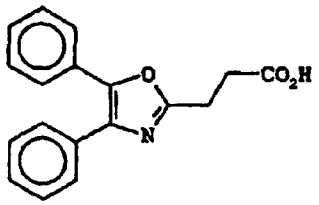

(Ib)

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SOLUTIONS OF ARYL OR HETEROARYL SUBSTITUTED ALKANOIC ACIDS IN LIPOPHILIC SOLVENTS AND SOFT GELATIN CAPSULES CONTAINING SUCH SOLUTIONS

BACKGROUND OF THE INVENTION

Field of the Invention

The present invention relates to solutions containing therapeutically useful substituted alkanoic acids in combination with at least one lipophilic solvent for encapsulation in soft gelatin capsules (softgel capsules).

Description of the Related Art

Hydrophilic softgels are well known for the oral administration of pharmaceutical agents. Typically, softgel capsules consist of an outer shell of gelatin containing a plasticizer and an inner filling of hydrophilic liquid containing a dissolved hydrophobic pharmaceutical agent. The plasticizer is chosen so that the solubility in the fill liquid is as low as possible. If the plasticizer is soluble in the fill liquid, it can migrate out of the shell over time into the fill, leaving the shell brittle and subject to rupture.

With respect to pharmaceutical agents of relatively low solubility and/or relatively high dosage amount, softgel capsules can pose problems for the pharmaceutical formulator. For example, if a given pharmaceutical agent has a relatively low solubility, it may need a relatively large volume of solution in order to deliver a pharmaceutically acceptable unit dose. While theoretically possible to encapsulate such a large volume of solution in a softgel capsule, for example, the practical

limitations on the size of capsules suitable for conventional oral administration to human patients could well preclude pharmaceutical use of the resulting softgel.

Similarly, if a pharmaceutical agent requires a relatively high dose, a large volume of solution may again be a necessity for delivery of the require dosage. Softgel encapsulation of such a large solution volume may be impractical because the size of the needed softgel would likely exceed the maximum limit for conventional oral administration to human patients.

As one approach to handling the problems of encapsulating low solubility or high dose pharmaceutical agents, U.S. Patent No. 5,071,643 (Yu et. al.) discloses the use of polyethylene glycol based solutions for acidic, basic and amphoteric pharmaceutical agents. These polyethylene glycol based solutions contain either an hydroxide species or a hydrogen ion species that causes the appropriate pharmaceutical agent to partially ionize, i.e., the pharmaceutical agent is present in both the free form and the salt form. The partial ionization described in Yu et al. results in enhanced solubility for the acidic, basic or amphoteric pharmaceutical agent. This enhanced solubility, in turn, may permit the preparation of a solution of pharmaceutical agent that is highly concentrated enough to be encapsulated in a capsule acceptably sized for oral administration to human patients. The Yu et al. patent discloses that enhanced solubility solutions can be prepared using polyethylene glycol and contemplated equivalents of polyethylene

glycol, such as polyethylene glycol ethers or various alcohols and copolymers of polyethylene glycol.

Softgel encapsulation is sometimes the preferred delivery system for many pharmaceutical agents that are administered orally to human patients. Generally, to be suitable for softgel encapsulation, a pharmaceutical formulation should be in the form of a clear, stable solution. The present inventors have discovered that the enhanced solubility solutions disclosed by the Yu et al. patent are not as effective with various substituted alkanoic acid pharmaceutical agents.

Therapeutically useful 2- or 3-aryl or 2- or 3-heteroaryl substituted alkanoic acids function as anti-inflammatory and analgesic agents and may be administered orally. They are also essentially insoluble in water. An example of such a useful alkanoic acid suitable for use in the present invention is ketoprofen which is 2-(3-benzoylphenyl) propionic acid.

Ketoprofen is an anti-inflammatory, analgesic agent that is principally indicated for the acute and long-term management of rheumatoid arthritis and osteoarthritis. Additionally it is a nonsteroidal compound and poorly water soluble. Some gastrointestinal irritation is ordinarily associated with oral dosage forms of ketoprofen. The properties of ketoprofen render it a good candidate for formulation with the enhanced solubility solutions disclosed in the Yu et al. patent. In a number of experiments, the present inventors applied the Yu et al. enhanced solubility solutions in formulations of ketoprofen for softgel encapsulation.

In one formulation, polyethylene glycol 400 and potassium hydroxide were used to solubilize the ketoprofen, with the mole ratio of potassium hydroxide to ketoprofen being in the range of 0.4 to 1. It was surprisingly found that the resulting formulation was not sufficiently stable for softgel encapsulation due to the undesirable formation of ketoprofen esters.

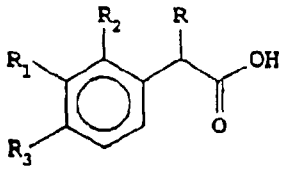
In an attempt to completely ionize the ketoprofen to prevent the formation of undesirable esters, the potassium hydroxide to ketoprofen mole ratio was adjusted to range from 1.1 to 1. With this second formulation, concerns arose that the ketoprofen salt thus formed and/or the high pH caused by the excess potassium hydroxide used could affect the physical stability of the softgel capsule when the formulation was encapsulated. Additionally, if an equilibrium amount of the ketoprofen free acid remained in the solution, it could form ketoprofen esters that could drive the reaction to form more ketoprofen free acid species, which could eventually result in a chemically unstable formulation.

The present inventors have discovered that non-hydroxyl containing solvents may be used to form pharmaceutically acceptable solutions of 2- or 3-aryl or 3-heteroaryl substituted alkanoic acids that are stable and suitable for softgel encapsulation.

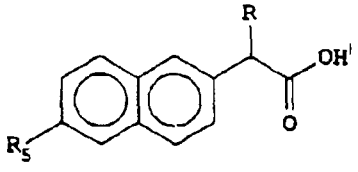
SUMMARY OF THE INVENTION

The present invention provides enhanced solubility pharmaceutically acceptable solutions of therapeutically useful substituted alkanoic acids, preferably 2- or 3-aryl or 2- or 3-heteroaryl alkanoic acids, that can be encapsulated in softgel capsules of a size suitable for subsequent oral administration to human patients, having improved chemical stability compared with polyethylene glycol water miscible formulations of the alkanoic acids.

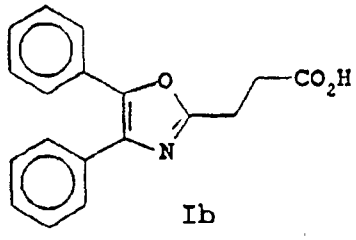
The therapeutically useful active agents, i.e., substituted alkanoic acids, preferred for use in the present invention have general formulas I, Ia or Ib:



I



Ia

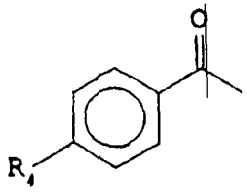


Ib

or pharmaceutically acceptable salts thereof, wherein

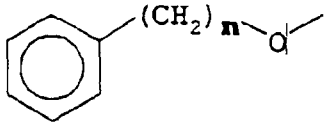
R represents a hydrogen atom or an alkyl group containing 1 to 4 carbon atoms;

R_1 represents hydrogen, halogen, C_1-C_6 alkyl, phenylalkyl where the alkyl is C_1-C_6 alkyl, a benzoyl group of the formula:



where R_4 represents hydrogen, C_1-C_6 alkyl, or an alkylthio group having 1 to 4 carbon atoms; or

R_1 represents a group of the formula:



where n is 0, 1 or 2;

R_2 represents hydrogen, hydroxy or C_1-C_6 alkoxy;

R_3 represents hydrogen, C_1-C_6 alkyl or phenyl; and

R_5 is C_1-C_6 alkoxy.

The enhanced solubility pharmaceutically acceptable solutions of therapeutically useful alkanoic acids can be encapsulated in softgel capsules of a size suitable for subsequent oral administration to human patients, which improves the physical stability of the softgel capsules used to encapsulate the pharmaceutical solutions compared with polyethylene glycol water miscible formulations of the alkanoic acids.

The present invention also provides enhanced solubility pharmaceutically acceptable solutions of alkanoic acids that unexpectedly can be encapsulated in a softgel capsule of a size smaller than what is required to encapsulate the same dose of the acid in polyethylene glycol water miscible formulations.

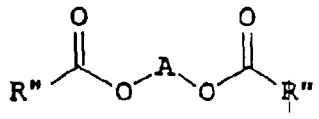
The enhanced solubility pharmaceutically acceptable solutions of 2- or 3-aryl or 3-heteroaryl alkanoic acids provided

by the present invention may reduce or eliminate the gastrointestinal irritation associated with oral dosage forms of these agents.

The lipophilic solvent and the hydroxyl containing softgel capsule plasticizers, such as glycerin, are immiscible, thereby improving both the chemical stability of the acid solution and improving the physical stability of the softgel capsule by greatly reducing the migration of capsule plasticizers into the encapsulated pharmaceutical formulation. Additionally, the use of the lipophilic solvent prevents the formation of esters which can decrease the chemical stability of the alkanoic acid solution.

Suitable lipophilic solvents are polyol esters of fatty acids. The polyol esters of fatty acids may be mono-, di-, tri-, etc, esters of the polyols. Thus, there may be free hydroxyl groups present in the polyol esters of fatty acids useful as lipophilic solvents of the invention.

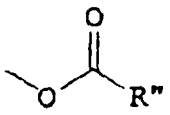
The lipophilic solvent preferred for use in the present invention is an alkylene glycol derivative of formula II:



II

wherein

A represents C_1-C_4 alkylene optionally substituted with alkyl or a group of the formula



; and

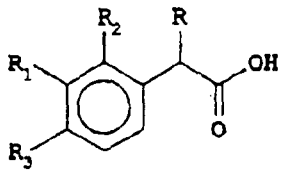
the R" groups are the same of different and represent C_1-C_{12} alkyl.

Further objects and embodiments of the present invention will be described in the following description of the preferred embodiments.

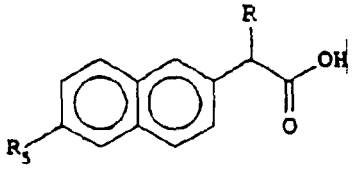
DESCRIPTION OF THE PREFERRED EMBODIMENTS

The present invention is useful for providing pharmaceutically acceptable solutions of substituted alkanoic acids dissolved in at least one lipophilic solvent, which are chemically stable and suitable for softgel encapsulation.

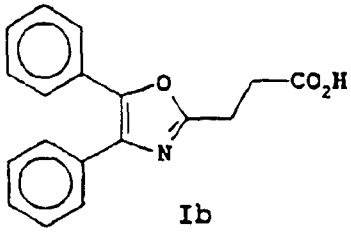
The therapeutically useful active agents, i.e., substituted alkanoic acids, preferred for use in the present invention have general formulas I, Ia or Ib:



I



Ia



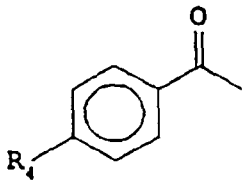
Ib

or pharmaceutically acceptable salts thereof,

wherein

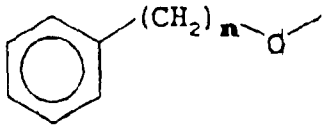
R represents a hydrogen atom or an alkyl group containing 1 to 4 carbon atoms;

R_1 represents hydrogen, halogen, C_1-C_6 alkyl, phenylalkyl where the alkyl is C_1-C_6 alkyl, a benzoyl group of the formula:



where R_4 represents hydrogen, C_1-C_6 alkyl, or an alkylthio group having 1 to 4 carbon atoms; or

R_1 represents a group of the formula:



where n is 0, 1 or 2;

R_2 represents hydrogen, hydroxy or C_1-C_6 alkoxy;

R_3 represents hydrogen, C_1-C_6 alkyl or phenyl; and

R_5 is C_1-C_6 alkoxy.

Suitable pharmaceutically acceptable, non-toxic salts include salts such as, for example, alkali metal, alkaline earth metal, ammonium and amine salts. Compounds of general formulas I, Ia, and Ib in which R represents an alkyl group can exist in optically active forms, including isomers and racemates thereof. Preferred alkanoic acids suitable for use in the present invention include ketoprofen (formula I where R is methyl, R_1 is benzoyl, and R_2 and R_3 are hydrogen, i.e., 2-(3-benzoylphenyl)propionic acid); ibuprofen (formula I where R is methyl, R_1 and R_2 are hydrogen, and R_3 is isobutyl, i.e., 2-(4-isobutylphenyl)propionic acid); naproxen (formula Ia where R is methyl and R_5 is methoxy, i.e., 2-(6-methoxy naphthyl)propionic acid); and oxaprozin, (formula Ib, i.e., 4,5-diphenyl-2-oxazolepropionic acid).

The enhanced solubility pharmaceutically acceptable solutions of therapeutically useful substituted alkanoic acids can be encapsulated in softgel capsules of a size suitable for

subsequent oral administration to human patients, which improves the physical stability of the softgel capsules used to encapsulate the pharmaceutical solutions compared with polyethylene glycol water miscible formulations of the alkanoic acids.

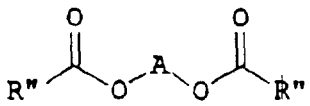
The present invention also provides enhanced solubility pharmaceutically acceptable solutions of ketoprofen that can be encapsulated in a softgel capsule of a size smaller than what is required to encapsulate the same dose of the acids in polyethylene glycol water miscible formulations.

The present invention provides pharmaceutically acceptable solutions containing from about 0.1 to 1000 mg, preferably about 5 to 200 mg, and most preferably about 10 to 100 mg, of an alkanoic acid dissolved in at least one lipophilic solvent, resulting in a clear solution suitable for softgel encapsulation. The lipophilic solvent and the hydroxyl containing softgel capsule plasticizers, such as glycerin, are immiscible, thereby improving both the chemical stability of the alkanoic acid solution and improving the physical stability of the softgel capsule by greatly reducing the migration of capsule plasticizers into the encapsulated pharmaceutical formulation. Additionally, the use of the lipophilic solvent prevents the formation of esters which can decrease the chemical stability of the alkanoic acid solution.

Suitable lipophilic solvents are polyol esters of fatty acids. The polyol esters of fatty acids may be mono-, di-, tri-, etc, esters of the polyols. Thus, there may be free hydroxyl

groups present in the polyol esters of fatty acids useful as lipophilic solvents of the invention.

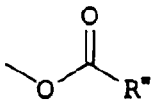
The lipophilic solvent preferred for use in the present invention is an alkylene glycol derivative of formula II:



II

wherein

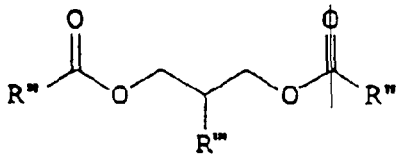
A represents C_1-C_4 alkylene optionally substituted with alkyl or



; and

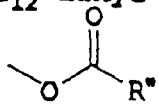
the R" groups are the same or different and represent C_1-C_{12} alkyl,

Suitable lipophilic solvents include those of formula III:



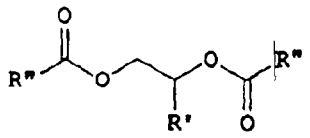
III

where the R" groups are the same or different and represent C_1-C_{12} alkyl and R''' is hydrogen or



.

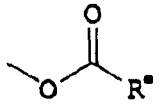
Suitable lipophilic solvents also include those of formula IV:



IV

where the R" groups are the same or different and represent C_1-C_{12} alkyl and R' is C_1-C_6 alkyl.

Other suitable lipophilic solvents are those of formula III where the R" groups are the same and represent C_1-C_4 alkyl and R''' is



Still other suitable lipophilic solvents are those of formula IV where the R" groups are the same or different and represent C_1-C_4 alkyl and R' is methyl.

Most preferred lipophilic solvents of formula III are those where R" is methyl. Most preferred lipophilic solvents of formula IV are those where the R" groups are the same or different and represent $CH_3(CH_2)_6$ or $CH_3(CH_2)_8$.

Particularly preferred solvents are selected from the group consisting of propylene glycol dicaprylate/dicaprate, 1,2,3-propanetriol triacetate and mixtures thereof. Most preferably the solvents suitable for use in the present invention include

propylene glycol dicaprylate/dicaprate, 1,2,3-propanetriol triacetate and mixtures thereof. Propylene glycol dicaprylate/dicaprate is available under the trade name Captex 200 from Karlshamn Lipid Specialties and 1,2,3-propanetriol triacetate is available under the trade name Triacetin from Eastman Chemicals.

The inventive solutions may also contain optional, additional ingredients to improve the dispersivity and dissolution of the substituted alkanoic acid. Suitable additional components include surfactants such as, for example, polyglyceryl esters of fatty acids, polyglycolyzed glycerides, propylene glycol esters, mono- and di-glycerides, sorbitan fatty acid esters, polyoxyethylene sorbitan fatty acid esters, polyoxyethylene sorbitol esters, polyoxyethylene acids, polyoxyethylene alcohols, and mixtures thereof. A preferred class of surfactants for use in combination with the lipophilic solvents is the polyoxyethylene sorbitan fatty acid esters. Suitable sorbitan esters are sold under the trade name Tween. A particularly useful Tween is polyoxyethylene (20) sorbitan mono-oleate (Tween 80).

The active substituted alkanoic acid pharmaceutical agent may be present in the solution in amounts ranging up to about 30% by weight of the solution. Preferred concentrations of the active agent are from about 5-20%, more preferably about 10-15%, by weight of the final solution. Combinations of lipophilic solvents may be used to obtain a desired final concentration.

For example, ketoprofen may be present in the solution in amounts ranging up to about 5% by weight of the solution when dissolved only in propylene glycol dicaprylate/dicaprate. Ketoprofen may be present in the solution in amounts ranging up to about 14% by weight of the solution when dissolved only in 1,2,3-propanetriol triacetate. When dissolved in a mixture of propylene glycol dicaprylate/dicaprate, 1,2,3-propanetriol triacetate and Tween, the ketoprofen pharmaceutical agent may be present in solution in amounts ranging up to about 22% by weight of solution.

In addition to the ketoprofen pharmaceutical agent and the lipophilic solvents, other adjuncts may optionally be present. Polyoxyethylene (20) sorbitan mono-oleate (Tween 80) may be included in the solution up to about 50% by weight of the solution.

Once the appropriate pharmaceutically acceptable solution of the substituted alkanoic acid is formulated, it can be encapsulated into conventional softgel capsules using any suitable encapsulation method, such as for example, the rotary die process.

All documents, e.g., patents and journal articles, cited above or below are hereby incorporated by reference in their entirety.

One skilled in the art will recognize that modifications may be made in the present invention without deviating from the spirit or scope of the invention. The invention is illustrated further by the following examples which are not to be construed

as limiting the invention or scope of the specific procedures described herein.

Example 1

Pharmaceutically acceptable solutions containing ketoprofen are prepared in the following manner. First, mix the following until homogeneous:

(1) about 92 mg of propylene glycol dicaprylate/dicaprate;

(2) about 92mg of 1,2,3-propanetriol acetate; and

(3) about 10 mg of polyoxyethylene (20) sorbitan mono-oleate.

Second, add about 25 mg of ketoprofen to the homogeneous mixture of propylene glycol dicaprylate, 1,2,3-propanetriol acetate and polyoxyethylene (20) sorbitan mono-oleate, and mix again. While mixing in the ketoprofen, heat the mixture and maintain the temperature between 110-125°F until the ketoprofen is dissolved. Once the ketoprofen is fully dissolved, the solution is then cooled and deaerated. After being cooled and deaerated, the ketoprofen solution can be encapsulated in suitable softgel capsules, such as 4 oval softgel. The filled softgel capsules are thereafter dry finished to the appropriate hardness.

Example 2

Pharmaceutically acceptable solutions containing ketoprofen are prepared in the following manner. First, mix the following until homogeneous:

(1) about 112 mg of propylene glycol dicaprylate/dicaprate;

(2) about 72 mg of 1,2,3-propanetriol acetate; and

(3) about 14 mg of polyoxyethylene (20) sorbitan mono-oleate.

Second, add about 25 mg of ketoprofen to the homogeneous mixture of propylene glycol dicaprylate, 1,2,3-propanetriol acetate and polyoxyethylene (20) sorbitan mono-oleate, and mix again. While mixing in the ketoprofen, heat the mixture and maintain the temperature between 110-125°F until the ketoprofen is dissolved. Once the ketoprofen is fully dissolved, the solution is then cooled and deaerated. After being cooled and deaerated, the ketoprofen solution can be encapsulated in suitable softgel capsules, such as 4 oval softgel. The filled softgel capsules are thereafter dry finished to the appropriate hardness.

Example 3

Pharmaceutically acceptable solutions containing up to about 22% ketoprofen by weight of solution are prepared in the following manner, which provides a self-emulsifying system. First, mix the following until homogeneous:

(1) propylene glycol dicaprylate/dicaprate in an amount ranging from about 40% to about 98% by weight;

(2) 1,2,3-propanetriol acetate in an amount ranging from about 1% to about 55% by weight; and

(3) polyoxyethylene (20) sorbitan mono-oleate in an amount ranging from about 1% to about 50% by weight.

Second, add ketoprofen to the homogeneous mixture of propylene glycol dicaprylate, 1,2,3-propanetriol triacetate and polyoxyethylene (20) sorbitan mono-oleate, and mix again. While mixing in the ketoprofen, heat the mixture and maintain the temperature between 110-125°F until the ketoprofen is dissolved. Once the ketoprofen is fully dissolved, the solution is then cooled and deaerated. After being cooled and deaerated, the ketoprofen solution can be encapsulated in suitable softgel capsules. The filled softgel capsules are thereafter dry finished to the appropriate hardness.

Example 4

Pharmaceutically acceptable solutions containing up to about 14% ketoprofen by weight of solution are prepared in the following manner. First, mix the following until homogeneous:

(1) propylene glycol dicaprylate/dicaprate in an amount ranging from about 1% to about 50% by weight; and

(2) 1,2,3-propanetriol acetate in an amount ranging from about 50% to about 99% by weight.

Second, add ketoprofen to the homogeneous mixture of propylene glycol dicaprylate and 1,2,3-propanetriol acetate and mix again. While mixing in the ketoprofen, heat the mixture and maintain the temperature between 110-125°F until the ketoprofen is dissolved. Once the ketoprofen is fully dissolved, the solution is then cooled and deaerated. After being cooled and deaerated, the ketoprofen solution can be encapsulated in suitable softgel

capsules. The filled softgel capsules are thereafter dry finished to the appropriate hardness.

Example 5

Pharmaceutically acceptable solutions containing up to about 5% ketoprofen by weight of solution are prepared by mixing the ketoprofen with propylene glycol dicaprylate/dicaprate while heating the mixture. The temperature of the mixture should be maintained between 110-125°F until the ketoprofen is dissolved. Once the ketoprofen is fully dissolved, the solution is then cooled and deaerated. After being cooled and deaerated, the ketoprofen solution can be encapsulated in suitable softgel capsules. The filled softgel capsules are thereafter dry finished to the appropriate hardness.

Example 6

Pharmaceutically acceptable solutions containing up to about 14% ketoprofen by weight of solution are prepared by mixing the ketoprofen with 1,2,3-propanetriol acetate while heating the mixture. The temperature of the mixture should be maintained between 110-125°F until the ketoprofen is dissolved. Once the ketoprofen is fully dissolved, the solution is then cooled and deaerated. After being cooled and deaerated, the ketoprofen solution can be encapsulated in suitable softgel capsules. The filled softgel capsules are thereafter dry finished to the appropriate hardness.

Example 7

The following formulations are prepared according to the invention using the procedure set forth above in Example 1.

Ingredient	A (mg)	B (mg)	C (mg)
Propylene glycol dicaprylate/dicaprate	92	184	276
1,2,3-Propanetriol triacetate	92	184	276
Polyoxyethylene (20) sorbitan mono-oleate	10	20	30
Ketoprofen	25	50	75
Final softgel size	4 oval	7.5 oval	12 oval

Example 8

The following comparative formulations are prepared essentially as in the procedure set forth above in Example 1 but do not include the lipophilic solvent according to the invention.

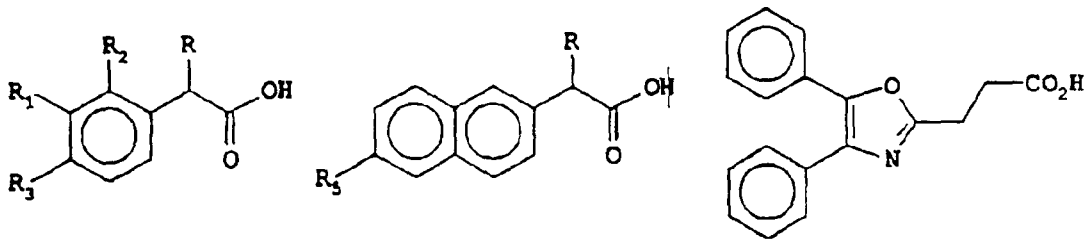
Ingredient	D (mg)	E (mg)	F (mg)
Water	5.46	10.92	16.38
Potassium hydroxide	6.06	12.12	18.18
Polyoxyethylene glycol 400	438.48	876.96	1315.44
Propylene glycol	25	50	75
Ketoprofen	25	50	75
Final softgel size	12 oval	20 oval	30 oval

Certain specific embodiments of the present invention have been discussed and disclosed in detail. Many other embodiments

that have not been disclosed or described are nevertheless the equivalent of and fall within the scope of the present invention and/or the following claims.

WE CLAIM:

1. A pharmaceutical composition comprising alkanoic acids selected from the group consisting of alkanoic acids of the formulas:

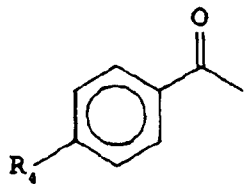


or pharmaceutically acceptable salts thereof,

wherein

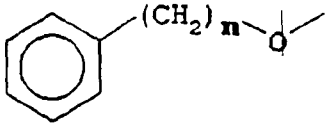
R represents a hydrogen atom or an alkyl group containing 1 to 4 carbon atoms;

R_1 represents hydrogen, halogen, C_1-C_6 alkyl, phenylalkyl where the alkyl is C_1-C_6 alkyl, a benzoyl group of the formula:



where R_4 represents hydrogen, C_1-C_6 alkyl, or an alkylthio group having 1 to 4 carbon atoms; or

R_1 represents a group of the formula:



where n is 0, 1 or 2;

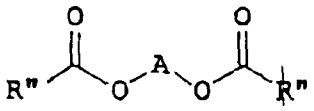
R_2 represents hydrogen, hydroxy or C_1-C_6 alkoxy;

R_3 represents hydrogen, C_1-C_6 alkyl or phenyl; and

R_5 is C_1-C_6 alkoxy.

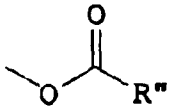
the 2-phenyl or naphthyl alkanoic acid being solubilized in a lipophilic solvent.

2. A pharmaceutical composition according to Claim 1 wherein the lipophilic solvent has the formula:



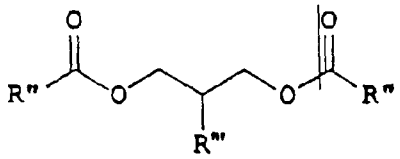
wherein

A represents C_1-C_4 alkylene optionally substituted with alkyl or

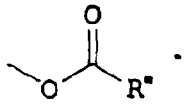
 ; and

the R" groups are the same of different and represent C_1-C_{12} alkyl.

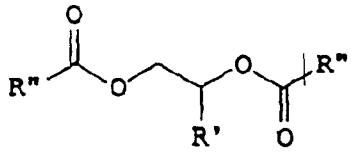
3. A pharmaceutical composition according to Claim 1 wherein the lipophilic solvent has the formula:



where the R" groups are the same or different and represent C_1-C_{12} alkyl and R''' is hydrogen or

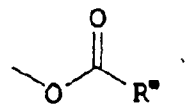


4. A pharmaceutical composition according to Claim 1 wherein the lipophilic solvent has the formula:



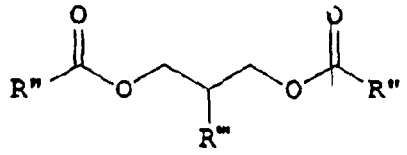
where the R" groups are the same or different and represent C_1-C_{12} alkyl and R' is C_1-C_6 alkyl.

5. A pharmaceutical composition according to Claim 3, where the R" groups are the same and represent C_1-C_4 alkyl and R''' is

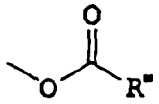


6. A pharmaceutical composition accoriding to Claim 4, where the R" groups are the same or different and represent C_1-C_4 alkyl and R' is methyl.

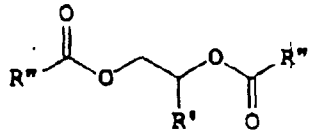
7. A pharmaceutical composition accoriding to Claim 1, wherein the lipophilic solvent comprises a mixture of a alkylene glycol derivative of the formula:



where the R" groups are the same or different and represent C_1-C_{12} alkyl and R''' is hydrogen or

 and

a alkylene glycol derivative of the formula:



where the R" groups are the same or different and represent C_1-C_{12} alkyl and R' is C_1-C_6 alkyl.

8. A pharmaceutical composition of Claim 1 wherein at least one lipophilic solvent has no free hydroxyl groups.

9. A pharmaceutical composition comprising ketoprofen, naproxen, oxaprozin or ibuprofen solubilized up to 14% by weight in 1,2,3-propanetriol triacetate.

10. A pharmaceutical composition comprising ketoprofen, ibuprofen, oxaprozin or naproxen solubilized up to 5% by weight in propylene glycol dicaprylate/dicaprate.

11. The pharmaceutical composition of Claim 9, wherein the ketoprofen, naproxen, oxaprozin or ibuprofen is solubilized in a mixture of 1 to 50% by weight of propylene glycol dicaprylate/dicaprate and 50 to 99% by weight of 1,2,3-propanetriol triacetate.

12. A pharmaceutical composition comprising ketoprofen, oxaprozin, naproxen, oxaprozin or ibuprofen solubilized up to 22% by weight in a mixture of 40 to 98% by weight of propylene glycol dicaprylate/dicaprate, 1 to 55% by weight of 1,2,3-propanetriol triacetate, and 1 to 50% by weight of a surfactant.

13. A solution comprising from about 0.1 to about 30% by weight of ibuprofen, naproxen, oxaprozin or ketoprofen in a lipophilic solvent.

14. A solution according to Claim 13, comprising from about 5 to about 20% by weight of ibuprofen, naproxen, oxaprozin or ketoprofen in a lipophilic solvent.

15. A solution according to Claim 13, comprising from about 10 to about 15% by weight of ibuprofen, naproxen, oxaprozin or ketoprofen in a lipophilic solvent.

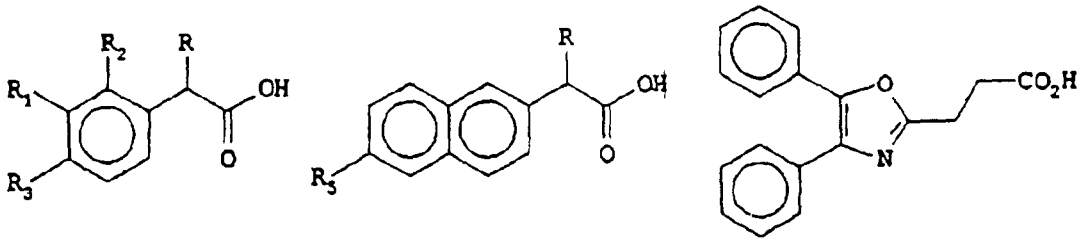
16. A soft gelatin capsule comprising a solution of ketoprofen, naproxen, or ibuprofen in a lipophilic solvent.

17. A soft gelatin capsule according to Claim 16, wherein the amount of ketoprofen, naproxen, oxaprozin or ibuprofen in the solution is from about 10 to 15% by weight of the solution.

18. A solution according to Claim 13, wherein the lipophilic solvent is suitable for encapsulation by a gelatin shell.

19. A pharmaceutical composition comprising an amount of ketoprofen, ibuprofen, oxaprozin or naproxen effective to produce analgesia in a patient, the ketoprofen, ibuprofen, oxaprozin or naproxen being present as a solution in a pharmaceutically acceptable lipophilic solvent.

20. A method for preparing a liquid mixture of a 2- or 3-aryl or 3-heteroaryl alkanoic acid suitable for encapsulation in a soft gelatin capsule comprising mixing a 2- or 3-aryl or 3-heteroaryl alkanoic acid of the formula:

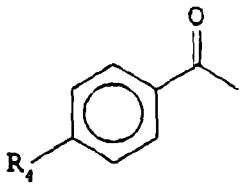


or pharmaceutically acceptable salts thereof,

wherein

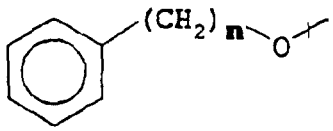
R represents a hydrogen atom or an alkyl group containing 1 to 4 carbon atoms;

R_1 represents hydrogen, halogen, C_1-C_6 alkyl, phenylalkyl where the alkyl is C_1-C_6 alkyl, a benzoyl group of the formula:



where R_4 represents hydrogen, C_1-C_6 alkyl, or an alkylthio group having 1 to 4 carbon atoms; or

R_1 represents a group of the formula:



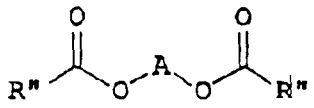
where n is 0, 1 or 2;

R_2 represents hydrogen, hydroxy or C_1-C_6 alkoxy;

R_3 represents hydrogen, C_1-C_6 alkyl or phenyl; and

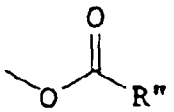
R_5 is C_1-C_6 alkoxy,

with an effective solubilizing amount of at least one lipophilic solvent of the formula:



wherein

A represents C_1-C_4 alkylene optionally substituted with alkyl or


; and

the R" groups are the same of different and represent C_1-C_{12} alkyl.

INTERNATIONAL SEARCH REPORT

Interna ıl Application No
PCT/US 95/06183

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 A61K31/19 A61K47/14

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X Y	US,A,5 059 626 (PARK MOO W ET AL) 22 October 1991 see column 1, line 59 - line 60; example 1; table II	1-7,9, 10,13-20 8,11,12
X Y	WO,A,92 08445 (AFFINITY BIOTECH INC) 29 May 1992 see claims 1-3	1-6,9, 10,13-20 7,8,11, 12
X Y	US,A,4 727 109 (SCHMIDT PETER C ET AL) 23 February 1988 see claims 1-8; examples 4,7,8	1-7,9, 13-20 8,10-12
Y	WO,A,92 10996 (MERRELL DOW PHARMA) 9 July 1992 see page 7, paragraph 1; claims 1-3	7,10

-/--

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
28 September 1995	27. 10. 95

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+ 31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+ 31-70) 340-3016	Foerster, W

Form PCT/ISA/210 (second sheet) (July 1992)

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US,A,5 071 643 (YU MAN S ET AL) 10 December 1991 cited in the application see example IX; table 1 ---	1-20
A	WO,A,94 07488 (PFIZER ;AHMED IMRAN (US)) 14 April 1994 see the whole document -----	1-20

INTERNATIONAL SEARCH REPORT

Information on patent family members

Interna' ·l Application No
PCT/US 95/06183

Patent document cited in search report	Publication date	Patent family member(s)		Publication date
US-A-5059626	22-10-91	US-A-	4918103	17-04-90
		US-A-	5011852	30-04-91
WO-A-9208445	29-05-92	US-A-	5110606	05-05-92
		AU-B-	648483	21-04-94
		AU-A-	9054191	11-06-92
		CA-A-	2095819	14-05-92
		EP-A-	0561874	29-09-93
		JP-T-	5509332	22-12-93
US-A-4727109	23-02-88	DE-A-	3500103	10-07-86
WO-A-9210996	09-07-92	AT-T-	117200	15-02-95
		AU-B-	647563	24-03-94
		AU-A-	9067891	22-07-92
		DE-D-	69106892	02-03-95
		DE-T-	69106892	18-05-95
		EP-A-	0563112	06-10-93
		ES-T-	2069987	16-05-95
		HU-B-	210565	29-05-95
		HU-A-	64218	28-12-93
		JP-T-	6503340	14-04-94
		NZ-A-	240961	25-03-94
US-A-5071643	10-12-91	AU-B-	606367	07-02-91
		AU-A-	8157387	06-05-88
		CA-A-	1316823	27-04-93
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		KR-B-	9408030	01-09-94
		KR-B-	9408031	01-09-94
		WO-A-	8802625	21-04-88
		US-A-	5360615	01-11-94
WO-A-9407488	14-04-94	AU-B-	4839293	26-04-94
		CN-A-	1089138	13-07-94
		EP-A-	0662831	19-07-95
		FI-A-	934387	08-04-94

INTERNATIONAL SEARCH REPORT

Information on patent family members

Interna al Application No
PCT/US 95/06183

Patent document cited in search report	Publication date	Patent family member(s)		Publication date
WO-A-9407488		HU-A-	68533	27-04-95
		NO-A-	951350	06-06-95
		PL-A-	308307	24-07-95

Form PCT/ISA/210 (patent family annex) (July 1992)

Electronic Acknowledgement Receipt

EFS ID:	1142927
Application Number:	11367238
Confirmation Number:	5524
Title of Invention:	Solvent system for enhancing the solubility of pharmaceutical agents
First Named Inventor:	Nachiappan Chidambaram
Customer Number:	23579
Filer:	Patrea L. Pabst/Carla Stone
Filer Authorized By:	Patrea L. Pabst
Attorney Docket Number:	BAN 102
Receipt Date:	07-AUG-2006
Filing Date:	03-MAR-2006
Time Stamp:	13:18:15
Application Type:	Utility
International Application Number:	

Payment information:

Submitted with Payment	no

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)	Multi Part	Pages
1	Transmittal letter	BAN_102_Supplemental_IDS.pdf	30845	no	4

Warnings:					
Information:					
2	Information Disclosure Statement (IDS) Filed	BAN_102_PTO_Form_1449.pdf	211453	no	1
Warnings:					
Information:					
This is not an USPTO supplied IDS fillable form					
3	Foreign Reference	WO95031979A1.pdf	945144	no	35
Warnings:					
Information:					
4	NPL Documents	International_Search_Report.pdf	1125583	no	6
Warnings:					
Information:					
		Total Files Size (in bytes):	2313025		

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

New Applications Under 35 U.S.C. 111

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

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

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

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants:	Nichiappan Chidambaram, Aqeel A. Fatmi		
Serial No.:	11/367,238	Art Unit:	1618
Filed:	March 3, 2006	Examiner:	Not Yet Assigned
For:	*SOLVENT SYSTEM FOR ENHANCING THE SOLUBILITY OF PHARMACEUTICAL AGENTS*		

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

SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT

Sir:

Pursuant to the duty of disclosure under 37 C.F.R. §1.56 and 37 C.F.R. §1.97, Applicants submit a Supplemental Information Disclosure Statement, including (1) page of Form PTO-1449, and a copy of one (1) document cited therein, and a copy of the International Search Report, mailed June 7, 2006, in the corresponding PCT application PCT/US06/007788. Pursuant to the waiver in the notice entitled "Information Disclosure Statements May Be Filed Without Copies of U.S. Patents and Published Applications in Patent Applications Filed After June 30, 2003" published on August 5, 2003 in 1273 OG 55, copies of U.S Patents and Published Applications are not enclosed. Copies will be provided upon request, however.

This Supplemental Information Disclosure Statement is being filed under 37 C.F.R. § 1.97(b) prior to a first Office Action on the merits. It is believed that no fee is required with this

submission. However, should a fee be required, the Commissioner is hereby authorized to charge any fees to Deposit Account No. 50-1329.

Certification Under 37 C.F.R. §1.97 (e)(1)

Each item of information contained in this Supplemental Information Disclosure Statement was first cited in a communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of this Supplemental Information Disclosure Statement.

Certification Under 37 C.F.R. §1.704 (d)

Each item of information contained in this Supplemental Information Disclosure Statement was first cited in a communication from a foreign patent office in a counterpart foreign application and this communication was not received by any individual designated in §1.56(c) more than thirty days prior to the filing of this Supplemental Information Disclosure Statement.

U.S. Patents

Number	Issue Date	Patentee	Class/Subclass
5,484,606	01-16-1996	Dhabar, et al.	424/455
5,912,011	06-15-1999	Makino, et al.	424/455

U.S. Patent Applications

Number	Filing Date	Patentee	Class/Subclass
2004/157928	08-12-2004	Kim Jae-Hwan, et al.	514/570

Foreign Documents

Number	Publication Date	Patentee	Country
WO 95/31979	11-30-1995	R.P Scherer International Corporation	PCT

Remarks

This statement should not be interpreted as a representation that an exhaustive search has been conducted or that no better art exists. Moreover, Applicants invite the Examiner to make an independent evaluation of the cited art to determine its relevance to the subject matter of the present application. Applicants are of the opinion that their claims patentably distinguish over the art referred to herein, either alone or in combination.

Respectfully submitted,

/Patrea L. Pabst/
Patrea L. Pabst
Reg. No. 31,284

Dated: August 7, 2006

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APPLICATION NUMBER	FILING or 371(c) DATE	GRP ART UNIT	FIL FEE REC'D	ATTY.DOCKET.NO	DRAWINGS	TOT CLAIMS	IND CLAIMS
11/367,238	03/03/2006	1618	1880	BAN 102		31	4

CONFIRMATION NO. 5524

UPDATED FILING RECEIPT

23579
PATREA L. PABST
PABST PATENT GROUP LLP
400 COLONY SQUARE
SUITE 1200
ATLANTA, GA30361

Date Mailed: 11/30/2006

Receipt is acknowledged of this regular Patent Application. It will be considered in its order and you will be notified as to the results of the examination. Be sure to provide the U.S. APPLICATION NUMBER, FILING DATE, NAME OF APPLICANT, and TITLE OF INVENTION when inquiring about this application. Fees transmitted by check or draft are subject to collection. Please verify the accuracy of the data presented on this receipt. **If an error is noted on this Filing Receipt, please mail to the Commissioner for Patents P.O. Box 1450 Alexandria Va 22313-1450. Please provide a copy of this Filing Receipt with the changes noted thereon. If you received a "Notice to File Missing Parts" for this application, please submit any corrections to this Filing Receipt with your reply to the Notice. When the USPTO processes the reply to the Notice, the USPTO will generate another Filing Receipt incorporating the requested corrections (if appropriate).**

Applicant(s)

Nachiappan Chidambaram, High Point, NC;
Aqeel Fatmi, Greensboro, NC;

Assignment For Published Patent Application

Banner Pharmacaps, Inc.

Power of Attorney: The patent practitioners associated with Customer Number 23579

Domestic Priority data as claimed by applicant

This appln claims benefit of 60/659,679 03/08/2005

Foreign Applications

If Required, Foreign Filing License Granted: 03/28/2006

The country code and number of your priority application, to be used for filing abroad under the Paris Convention, is **US11/367,238**

Projected Publication Date: 03/08/2007

Non-Publication Request: No

Early Publication Request: No

Title

Solvent system for enhancing the solubility of pharmaceutical agents

Preliminary Class

424

PROTECTING YOUR INVENTION OUTSIDE THE UNITED STATES

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

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

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

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

For information on preventing theft of your intellectual property (patents, trademarks and copyrights), you may wish to consult the U.S. Government website, http://www.stopfakes.gov. Part of a Department of Commerce initiative, this website includes self-help "toolkits" giving innovators guidance on how to protect intellectual property in specific countries such as China, Korea and Mexico. For questions regarding patent enforcement issues, applicants may call the U.S. Government hotline at 1-866-999-HALT (1-866-999-4158).

LICENSE FOR FOREIGN FILING UNDER

Title 35, United States Code, Section 184

Title 37, Code of Federal Regulations, 5.11 & 5.15

GRANTED

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

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

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

NOT GRANTED

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

UNITED STATES PATENT AND TRADEMARK OFFICE

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
11/367,238	03/03/2006	Nachiappan Chidambaram	BAN 102	5524

23579 7590 08/20/2009

Pabst Patent Group LLP
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ATLANTA, GA 30309

EXAMINER	
VU, JAKE MINH	
ART UNIT	**PAPER NUMBER**
1618	
MAIL DATE	**DELIVERY MODE**
08/20/2009	PAPER

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

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

Office Action Summary	Application No.	Applicant(s)	
	11/367,238	CHIDAMBARAM ET AL.	
	Examiner	Art Unit	
	Jake M. Vu	1618	

-- 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 *03 March 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) *1-31* 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) *1-31* 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 1-13 and 19-31, drawn to a composition, classified in class 424, subclass 486.

II. Claims 14-17, drawn to a method of making a pharmaceutical composition, classified in class 424, subclass 451.

III. Claim 18, drawn to a method of using a pharmaceutical composition, classified in class 424, subclass 464.

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

Inventions I and II are related as process of making and product made. The inventions are distinct if either or both of the following can be shown: (1) that the process as claimed can be used to make another and materially different product or (2) that the product as claimed can be made by another and materially different process (MPEP § 806.05(f)). In the instant case, the composition in claim 1 could be made by compression.

Inventions I and II 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 product could be used for diagnosing or for treating headaches.

Restriction for examination purposes as indicated is proper because all these inventions listed in this action are independent or distinct for the reasons given above and there would be a serious search and examination burden if restriction were not required because one or more of the following reasons apply:

(a) the inventions have acquired a separate status in the art in view of their different classification;

(b) the inventions have acquired a separate status in the art due to their recognized divergent subject matter;

(c) the inventions require a different field of search (for example, searching different classes/subclasses or electronic resources, or employing different search queries);

(d) the prior art applicable to one invention would not likely be applicable to another invention;

(e) the inventions are likely to raise different non-prior art issues under 35 U.S.C. 101 and/or 35 U.S.C. 112, first paragraph.

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

The election of an invention 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. Traversal must be presented at the time of election in order to be considered timely. Failure to timely traverse the requirement will result in the loss of right to petition under 37 CFR 1.144. If claims are added after the election, applicant must indicate which of these claims are readable on the elected invention.

If claims are added after the election, applicant must indicate which of these claims are readable upon the elected invention.

Should applicant traverse on the ground that the inventions are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the inventions 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.

This application contains claims directed to the following patentably distinct species of: polyethylene glycol, water, plasticizers, crystallization inhibitors, wetting agents, bulk filling agents, solubilizers, bioavailability enhancers, solvents, pH-adjusting agents, dyes, preservatives, solvents, surfactants.

The species are independent or distinct because claims to the different species recite the mutually exclusive characteristics of such species. In addition, these species are not obvious variants of each other based on the current record.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, claim 1 is generic.

There is an examination and search burden for these patentably distinct species due to their mutually exclusive characteristics. The species require a different field of search (e.g., searching different classes/subclasses or electronic resources, or employing different search queries); and/or the prior art applicable to one species would not likely be applicable to another species; and/or the species are likely to raise different non-prior art issues under 35 U.S.C. 101 and/or 35 U.S.C. 112, first paragraph.

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

The election of the species may be made with or without traverse. To preserve 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 election of species requirement, the

election shall be treated as an election without traverse. Traversal must be presented at the time of election in order to be considered timely. Failure to timely traverse the requirement will result in the loss of right to petition under 37 CFR 1.144. If claims are added after the election, applicant must indicate which of these claims are readable on the elected species.

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the 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 species 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 species.

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.

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).

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.

Telephonic Inquiries

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jake M. Vu whose telephone number is (571)272-8148. The examiner can normally be reached on Mon-Tue and Thu-Fri 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Hartley can be reached on (571) 272-0616. 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.

/Jake M. Vu/
Primary Examiner, Art Unit 1618

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Nachiappan Chidambaram and Aqeel A. Fatmi		
Serial No.:	11/367,238	Group Art Unit:	1618
Filed:	March 3, 2006	Examiner:	Vu, Jake Minh
For:	*SOLVENT SYSTEM FOR ENHANCING THE SOLUBILITY OF PHARMACEUTICAL AGENTS*		

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

RESPONSE TO RESTRICTION REQUIREMENT

Sir:

Responsive to the Office Action mailed on August 20, 2009, please consider the following remarks. It is believed that no fee is required with this submission. However, should a fee be required, the Commissioner is hereby authorized to charge any fees to Deposit Account No. 50-3129.

Amendment

In the Claims

1. (original) A pharmaceutical composition comprising

(a) a salt of one or more pharmaceutically active agents; and

(b) a deionizing agent.

2. (original) The composition of claim 1 wherein the pharmaceutically active agent is selected from the group consisting of therapeutically active agents, diagnostic agents, and prophylactic agents.

3. (original) The composition of claim 1 wherein the deionizing agent is present in an amount from about 0.2 to 1.0 mole equivalents per mole of the pharmaceutically active agent(s).

4. (original) The composition of claim 1 wherein the deionizing agent is selected from the group consisting of hydrogen ion and hydroxide ion.

5. (original) The composition of claim 1 further comprising polyethylene glycol.

6. (original) The composition of claim 5 wherein polyethylene glycol is present in an amount from about 10% to about 80% by weight

7. (original) The composition of claim 5 wherein polyethylene glycol is one or more polyethylene glycols with a molecular weight between 300 and 1500.

8. (original) The composition of claim 1 further comprising water.

9. (original) The composition of claim 8 wherein water is present in an amount from about 1% to about 18% by weight.

10. (original) The composition of claim 1 further comprising one or more excipients.

11. (currently amended) The composition of claim 7 wherein the one or more excipients are selected from the group consisting of plasticizers, crystallization inhibitors, wetting agents, bulk filling agents, solubilizers, bioavailability enhancers, solvents, pH-adjusting agents, dyes, preservatives, solvents, surfactants, and combinations thereof.

12. (original) The composition of claim 11 wherein the solubilizer is selected from the group consisting of glycerin, polyvinylpyrrolidone, propylene glycol and combinations thereof.

13. (original) The composition of claim 12 wherein the solubilizer is present in amount from about 1% to about 10% by weight.

14. (withdrawn) A method of making a pharmaceutical composition comprising a salt of one or more pharmaceutically active agents; and a deionizing agent comprising

(a) mixing the salt of one or more pharmaceutically active agents, and the deionizing agent at an appropriate temperature; and

(b) encapsulating the mixture in a softgel capsule.

15. (withdrawn) The method of claim 14 further comprising polyethylene glycol.

16. (withdrawn) The method of claim 14 further comprising water.

17. (withdrawn) The method of claim 14 wherein the appropriate temperature is from about 50°C to about 70°C.

18. (withdrawn-currently amended) A method of using a pharmaceutical composition comprising

(a) a salt of one or more pharmaceutically active agents; and

(b) a deionizing agent

comprising administering the composition to a patient in need thereof ~~the salt of one or more pharmaceutically active agents~~.

19. (original) A softgel capsule comprising a fill material wherein the fill material comprises

(a) a salt of one or more pharmaceutically active agents; and

(b) a deionizing agent.

20. (original) The capsule of claim 19 wherein the pharmaceutically active agent is selected from the group consisting of therapeutically active agents, diagnostic agents, and prophylactic agents.

21. (original) The capsule of claim 19 wherein the deionizing agent is present in an amount from about 0.2 to 1.0 mole equivalents per mole of the pharmaceutically active agent(s).

22. (original) The capsule of claim 19 wherein the deionizing agent is selected from the group consisting of hydrogen ion and hydroxide ion.

23. (original) The capsule of claim 19 further comprising polyethylene glycol.

24. (original) The capsule of claim 23 wherein polyethylene glycol is present in an amount from about 10% to about 80% by weight

25. (original) The capsule of claim 23 wherein polyethylene glycol is one or more polyethylene glycols with a molecular weight between 300 and 1500.

26. (original) The capsule of claim 19 further comprising water.

27. (original) The capsule of claim 26 wherein water is present in an amount from about 1% to about 18% by weight.

28. (original) The capsule of claim 19 further comprising one or more excipients.

29. (currently amended) The capsule of claim 28 wherein the one or more excipients are selected from the group consisting of plasticizers, crystallization inhibitors, wetting agents, bulk filling agents, solubilizers, bioavailability enhancers, solvents, pH-adjusting agents, dyes, preservatives, solvents, surfactants, and combinations thereof.

30. (original) The capsule of claim 29 wherein the solubilizer is selected from the group consisting of glycerin, polyvinylpyrrolidone, propylene glycol and combinations thereof.

31. (original) The capsule of claim 29 wherein the solubilizer is present in amount from about 1% to about 10% by weight.

Remarks

Response to Restriction Requirement

1. In the Office Action mailed August 20, 2009, the claims were divided into three groups, Group I, claims 1-13 and 19-31, drawn to a composition; Group II, claims 14-17, drawn to a method of making a pharmaceutical composition; and Group III, claim 18, drawn to a method of using a pharmaceutical composition.

In response, Applicants elect Group I, claims 1-13 and 19-31, without traverse. Claim 14-18 are withdrawn.

Applicants elect the composition claims with the understanding that should the composition claims be found allowable, any withdrawn process claims that depend from or otherwise include all of the limitations of the claims to the composition will be rejoined in accordance with the provisions of MPEP § 821.4. Applicants also reserve the right to pursue the withdrawn claims in one or more divisional applications.

2. The Office Action also required election of a species from among polyethylene glycol ("PEG") (claims 5 and 23), water (claims 8 and 27), and the excipients in claims 11 and 29. In response, Applicants elect for examination polyethylene glycol with traverse.

Applicants initially note that the requirement for election of species appears to be improperly drawn. The solvents PEG and water and the excipients listed in claims 11 and 29 species are not embodiments reciting mutually exclusive characteristics as required to make a proper election of species requirement. In this regard applicants refer to MPEP § 806.04(f) which states in relevant part:

> The general test as to when claims are restricted, respectively, to different species is the fact that one claim recites limitations which *under the disclosure* are found

> in a first species but not in a second, while a second claim recites limitations *disclosed* only for the second species and not the first. (emphasis added)

Thus, this test requires that the subject matter of claims have mutually exclusive subject matter, as disclosed in the specification, for restriction to different species. The fact that a limitation recited in one claim is not recited in another claim that recites a different limitation (the situation here) is not enough to make the subject matter of the respective claims distinct species. The species identified by the Examiner are excipients used in manufacturing fill materials for gelatin capsules.

In regard to designation of generic claims, Applicants refer to MPEP § 806.04(e) which states that "[c]laims may be restricted to a single disclosed embodiment (i.e. a single species, and thus be designated *a specific or species claim*), or a claim may include two or more of the disclosed embodiment...(and thus be designated *a generic or genus claim*)" (emphasis in original). In this regard, Applicants note that claims 5-7 and 23-25 are limited to the species PEG. Thus, claims 5-7 and 23-25 are specific claims.. Accordingly, Applicants note that, with respect to the species PEG, claims 1-4 and 19-22 are generic to PEG.

Favorable consideration of claims 1-13 and 19-31 is respectfully solicited.

Respectfully submitted,

/Michael J. Terapane, J.D., Ph.D./
Michael J. Terapane, J.D., Ph.D.
Reg. No. 57,633

Date: September 21, 2009

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Electronic Acknowledgement Receipt

EFS ID:	6112492
Application Number:	11367238
International Application Number:	
Confirmation Number:	5524
Title of Invention:	Solvent system for enhancing the solubility of pharmaceutical agents
First Named Inventor/Applicant Name:	Nachiappan Chidambaram
Customer Number:	23579
Filer:	Michael John Terapane/Candace Andrews
Filer Authorized By:	Michael John Terapane
Attorney Docket Number:	BAN 102
Receipt Date:	21-SEP-2009
Filing Date:	03-MAR-2006
Time Stamp:	16:40:26
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	no

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1		BAN_102_Response_to_Restriction_Requirement.pdf	307171 6e57da5e2882f43ab3d9a3d1b61ce9394eb54b4d	yes	8

	Multipart Description/PDF files in .zip description		
	Document Description	**Start**	**End**
	Response to Election / Restriction Filed	1	1
	Claims	2	5
	Applicant Arguments/Remarks Made in an Amendment	6	8
Warnings:			
Information:			
	Total Files Size (in bytes):	307171	

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

New Applications Under 35 U.S.C. 111

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

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

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

New International Application Filed with the USPTO as a Receiving Office

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

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

PATENT APPLICATION FEE DETERMINATION RECORD

Substitute for Form PTO-875

Application or Docket Number	Filing Date	☐ To be Mailed
11/367,238	03/03/2006	

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))							
			TOTAL			TOTAL	

* If the difference in column 1 is less than zero, enter "0" in column 2.

APPLICATION AS AMENDED – PART II

AMENDMENT	09/21/2009	(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))	* 31	Minus	** 31	= 0	X $ =		OR	X $52=	0
	Independent (37 CFR 1.16(h))	* 4	Minus	***4	= 0	X $ =		OR	X $220=	0
	☐ Application Size Fee (37 CFR 1.16(s))									
	☐ FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))							OR		
						TOTAL ADD'L FEE		OR	TOTAL ADD'L FEE	0

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

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

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

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

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

Legal Instrument Examiner:
/SANDRA F. GARNETT/

This collection of information is required by 37 CFR 1.16. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
11/367,238	03/03/2006	Nachiappan Chidambaram	BAN 102	5524

23579 7590 12/01/2009

Pabst Patent Group LLP
1545 PEACHTREE STREET NE
SUITE 320
ATLANTA, GA 30309

EXAMINER	
VU, JAKE MINH	
ART UNIT	PAPER NUMBER
1618	
MAIL DATE	DELIVERY MODE
12/01/2009	PAPER

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

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

Office Action Summary	Application No.	Applicant(s)	
	11/367,238	CHIDAMBARAM ET AL.	
	Examiner	Art Unit	
	Jake M. Vu	1618	

-- 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 *21 September 2009*.

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

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

Disposition of Claims

4)☒ Claim(s) *1-31* is/are pending in the application.

4a) Of the above claim(s) *14-18* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13 and 19-31* 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 *8/7/06, 7/20/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Receipt is acknowledged of Applicant's Restriction Requirement Response and Amendment filed on 09/21/2009; and Information Disclosure Statements filed on 08/07/2006 and 07/20/2006.

- Claims 11, 18, 29 have been amended.
- Claims 1-31 are pending in the instant application.
- Claims 14-18 are withdrawn from consideration.

Election/Restrictions

Applicant's election with traverse of Group I (claims 1-13 and 19-31) and specie election of "polyethylene glycol" in the reply filed on 09/21/2009 is acknowledged. The traversal is on the ground(s) that the species are not mutual exclusive. This is not found persuasive; however, upon searching the subject matter, both species were found. Thus, only the election of specie is withdrawn.

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.

Claim 11 is 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 11 recites the limitation "wherein the one or more excipients" in claim 7. There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-13 and 19-31 are rejected under 35 U.S.C. 102(b) as being anticipated by YU et al (5,360,615).

Applicant's claims are directed to a composition comprising of: a salt of a therapeutically active agent; a deionizing agent, such as hydrogen ion; 10-80% of polyethylene glycol with molecular weight between 300 and 1500; 1-18% of water; excipients, such as preservatives; 1-10% of solubilizers, such as polyvinyl pyrrolidone. Additional limitation includes: softgel capsule.

YU teaches a composition comprised of: a salt of a therapeutically active agent, such as diclofenac sodium (see col. 12, Example 8); a deionizing agent, such as hydrochloric acid (see col. 12, Example 8), which reads on hydrogen ion; 71.5% of polyethylene glycol with molecular weight of 600 (see col. 12, Example 8); 7.16% of water (see col. 12, Example 8); excipients, such as preservatives (see col. 9, line 34); 4-8% of solubilizers, such as polyvinyl pyrrolidone (see col. 8, line 51-68). Additional limitation includes: softgel capsule (see col. 1, line 20).

Telephonic Inquiries

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jake M. Vu whose telephone number is (571)272-8148. The examiner can normally be reached on Mon-Tue and Thu-Fri 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Hartley can be reached on (571) 272-0616. 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.

/Jake M. Vu/
Primary Examiner, Art Unit 1618

Notice of References Cited	Application/Control No. 11/367,238	Applicant(s)/Patent Under Reexamination CHIDAMBARAM ET AL.	
	Examiner Jake M. Vu	Art Unit 1618	Page 1 of 1

U.S. PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Name	Classification
*	A	US-5,360,615	11-1994	Yu et al.	424/455
	B	US-			
	C	US-			
	D	US-			
	E	US-			
	F	US-			
	G	US-			
	H	US-			
	I	US-			
	J	US-			
	K	US-			
	L	US-			
	M	US-			

FOREIGN PATENT DOCUMENTS

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

NON-PATENT DOCUMENTS

*		Include as applicable: Author, Title Date, Publisher, Edition or Volume, Pertinent Pages)
	U	
	V	
	W	
	X	

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

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants:	Nachiappan Chidambaram and Aqeel A. Fatmi		
Serial No.:	11/367,238	Art Unit:	1618
Filed:	March 3, 2006	Examiner:	Not Yet Assigned

For: *SOLVENT SYSTEM FOR ENHANCING THE SOLUBILITY OF PHARMACEUTICAL AGENTS*

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

INFORMATION DISCLOSURE STATEMENT

Sir:

Pursuant to 37 C.F.R. §1.56 and 37 C.F.R. §1.97, Applicants submit an Information Disclosure Statement, including one (1) page of Form PTO-1449. Pursuant to the waiver in the notice entitled "Information Disclosure Statements May Be Filed Without Copies of U.S. Patents and Published Applications in Patent Applications Filed After June 30, 2003" published on August 5, 2003 in 1273 OG 55, copies of U.S Patents and Published Applications are not enclosed. Copies will be provided upon request, however.

This Information Disclosure Statement is being filed under 37 C.F.R. § 1.97(b) prior to a first Office Action on the merits. It is believed that no fee is required with this submission. However, should a fee be required, the Commissioner is hereby authorized to charge any required fees to Deposit Account No. 50-1329.

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /J.V./

U.S. Patents

Number	Issue Date	Patentee	Class/Subclass
5,360,615	11-01-1994	Yu, et al.	424/455
5,505,961	04-09-1996	Shelley, et al.	424/451
6,383,515	05-07-2002	Sawyer, et al.	424/456
6,689,382	02-10-2004	Berthel, et al.	424/456

U.S. Patent Applications

Number	Publication Date	Inventor	Class/Subclass
2001/0007668	07-12-2001	Sawyer, et al.	424/400
2002/0187195	12-12-2002	Sawyer, et al.	424/486

Remarks

This statement should not be interpreted as a representation that an exhaustive search has been conducted or that no better art exists. Moreover, Applicants invite the Examiner to make an independent evaluation of the cited art to determine its relevance to the subject matter of the present application. Applicants are of the opinion that their claims patentably distinguish over the art referred to herein, either alone or in combination.

Respectfully submitted,

/Patrea L. Pabst/
Patrea L. Pabst
Reg. No. 31,284

Dated: July 20, 2006

PABST PATENT GROUP LLP
400 Colony Square, Suite 1200
1201 Peachtree Street
Atlanta, Georgia 30361
(404) 879-2151 (Telephone)
(404) 879-2160 (Fax)

/Jake Vu/ 11/25/2009

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /J.V./

Search Notes	Application/Control No.	Applicant(s)/Patent Under Reexamination
	11367238	CHIDAMBARAM ET AL.
	Examiner	Art Unit
	Jake M Vu	1618

SEARCHED			
Class	Subclass	Date	Examiner

SEARCH NOTES		
Search Notes	Date	Examiner
Inventors' name search (PALM)	11/24/09	JMV
EPO website	11/24/09	JMV

INTERFERENCE SEARCH			
Class	Subclass	Date	Examiner

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Substitute for form 1449A/PTO

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(use as many sheets as necessary)

Complete if Known	
Application Number	11/387,238
Filing Date	March 3, 2006
First Named Inventor	Nichiappan Chidambaram
Group Art Unit	1618
Examiner Name	Not Yet Assigned
Attorney Docket Number	BAN 102

Sheet 1 of 1

U.S. PATENT DOCUMENTS

Examiner Initials*	Cite No.[1]	US Patent Document Number	Kind Code[2] (if known)	Name of Patentee or Applicant of Cited Document	Date of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		5,484,606		Dhabar, et al.	01-16-1996	
		5,912,011		Makino, et al.	06-15-1999	
		2004/157928		Kim Jae-Hwan, et al.	08-12-2004	

FOREIGN PATENT DOCUMENTS

Examiner Initials*	Cite No.[1]	Foreign Patent Document Office.[3]	Number[4]	Kind Code[5] (if known)	Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T[6]
		PCT	WO 95/31979		R.P Scherer International Corporation	11-30-1995		

Examiner's Signature	/Jake Vu/	Date Considered	11/25/2009

*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.

[1] Unique citation designation number [2] See attached Kinds of U.S. Patent Documents. [3] Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). [4] For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. [5] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. [6] Applicant to place a check mark here if English language Translation is attached.

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants:	Nachiappan Chidambaram and Aqeel Fatmi		
Serial No.:	11/367,238	Art Unit:	1618
Filed:	March 3, 2006	Examiner:	Jake Minh Vu
For:	*SOLVENT SYSTEM FOR ENHANCING THE SOLUBILITY OF PHARMACEUTICAL AGENTS*		

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

AMENDMENT AND RESPONSE

Sir:

Responsive to the Office Action mailed on December 1, 2009, please amend the application as follows and consider the following remarks. A Petition for a Two Month extension of time, up to and including May 1, 2010, is enclosed. The Commissioner is hereby authorized to charge the fee of $1,074.00, for a large entity, to Deposit Account No. 50-3129.

It is believed that no additional fee is required with this submission. However, should an additional fee be required, the Commissioner is hereby authorized to charge the fee to Deposit Account No. 50-3129.

Amendment

In the Claims

1. (currently amended) A pharmaceutical composition comprising

(a) a salt of one or more either acidic or basic pharmaceutically active agents; and

(b) a deionizing agent;

wherein the pharmaceutically active agent is present in a therapeutically effective amount; and

wherein the deionizing agent at least partially neutralizes the pharmaceutically active agent.

2. (original) The composition of claim 1 wherein the pharmaceutically active agent is selected from the group consisting of therapeutically active agents, diagnostic agents, and prophylactic agents.

3. (original) The composition of claim 1 wherein the deionizing agent is present in an amount from about 0.2 to 1.0 mole equivalents per mole of the pharmaceutically active agent(s).

4. (original) The composition of claim 1 wherein the deionizing agent is selected from the group consisting of hydrogen ion and hydroxide ion.

5. (original) The composition of claim 1 further comprising polyethylene glycol.

6. (currently amended) The composition of claim 5 wherein polyethylene glycol is present in an amount from about 10% to about 80% by weight.

7. (original) The composition of claim 5 wherein polyethylene glycol is one or more polyethylene glycols with a molecular weight between 300 and 1500.

8. (original) The composition of claim 1 further comprising water.

9. (original) The composition of claim 8 wherein water is present in an amount from about 1% to about 18% by weight.

10. (original) The composition of claim 1 further comprising one or more excipients.

11. (currently amended) The composition of claim 10 [[7]] wherein the one or more excipients are selected from the group consisting of plasticizers, crystallization inhibitors, wetting agents, bulk filling agents, solubilizers, bioavailability enhancers, solvents, pH-adjusting agents, dyes, preservatives, ~~solvents,~~ surfactants, and combinations thereof.

12. (original) The composition of claim 11 wherein the solubilizer is selected from the group consisting of glycerin, polyvinylpyrrolidone, propylene glycol and combinations thereof.

13. (original) The composition of claim 12 wherein the solubilizer is present in amount from about 1% to about 10% by weight.

14. (withdrawn-currently amended) A method of making a pharmaceutical composition comprising

a salt of one or more either acidic or basic pharmaceutically active agents; and a deionizing agent comprising

(a) mixing the salt of one or more pharmaceutically active agents, and the deionizing agent at an appropriate temperature; and

(b) encapsulating the mixture in a softgel capsule;

wherein the pharmaceutically active agent is present in a therapeutically effective amount; and

wherein the deionizing agent at least partially neutralizes the pharmaceutically active agent.

15. (withdrawn) The method of claim 14 further comprising polyethylene glycol.

16. (withdrawn) The method of claim 14 further comprising water.

17. (withdrawn) The method of claim 14 wherein the appropriate temperature is from about 50°C to about 70°C.

18. (withdrawn-currently amended) A method of using a pharmaceutical composition comprising

(a) a salt of one or more either acidic or basic pharmaceutically active agents; and

(b) a deionizing agent;

wherein the pharmaceutically active agent is present in a therapeutically effective amount; and

wherein the deionizing agent at least partially neutralizes the pharmaceutically active agent

comprising administering the composition to a patient in need thereof.

19. (currently amended) A softgel capsule comprising a fill material wherein the fill material comprises

(a) a salt of one or more either acidic or basic pharmaceutically active agents; and

(b) a deionizing agent;

wherein the pharmaceutically active agent is present in a therapeutically effective amount; and

wherein the deionizing agent at least partially neutralizes the pharmaceutically active agent.

20. (original) The capsule of claim 19 wherein the pharmaceutically active agent is selected from the group consisting of therapeutically active agents, diagnostic agents, and prophylactic agents.

21. (original) The capsule of claim 19 wherein the deionizing agent is present in an amount from about 0.2 to 1.0 mole equivalents per mole of the pharmaceutically active agent(s).

22. (original) The capsule of claim 19 wherein the deionizing agent is selected from the group consisting of hydrogen ion and hydroxide ion.

23. (original) The capsule of claim 19 further comprising polyethylene glycol.

24. (original) The capsule of claim 23 wherein polyethylene glycol is present in an amount from about 10% to about 80% by weight

25. (original) The capsule of claim 23 wherein polyethylene glycol is one or more polyethylene glycols with a molecular weight between 300 and 1500.

26. (original) The capsule of claim 19 further comprising water.

27. (original) The capsule of claim 26 wherein water is present in an amount from about 1% to about 18% by weight.

28. (original) The capsule of claim 19 further comprising one or more excipients.

29. (currently amended) The capsule of claim 28 wherein the one or more excipients are selected from the group consisting of plasticizers, crystallization inhibitors, wetting agents, bulk filling agents, solubilizers, bioavailability enhancers, solvents, pH-adjusting agents, dyes, preservatives, ~~solvents~~, surfactants, and combinations thereof.

30. (original) The capsule of claim 29 wherein the solubilizer is selected from the group consisting of glycerin, polyvinylpyrrolidone, propylene glycol and combinations thereof.

31. (original) The capsule of claim 29 wherein the solubilizer is present in amount from about 1% to about 10% by weight.

32. (new) The composition of claim 1 wherein the pharmaceutically active agent is naproxen sodium and the deionizing agent is a hydrogen ion species.

33. (new) The composition of claim 19 wherein the pharmaceutically active agent is naproxen sodium and the deionizing agent is a hydrogen ion species.

34. (new) The composition of claim 32 wherein the hydrogen ion species is selected from the group consisting of hydrochloric acid, hydrobromic acid, hydroiodic acid, sulfuric acid, fumaric cid, maleic acid, tartaric acid, methane-, ethane-, and benzene sulfonates, citric acid, malic acid, acetic acid, proprionic acid, pyruvic acid, butanoic acid, and lactic acid.

35. (new) The composition of claim 33 wherein the hydrogen ion species is selected from the group consisting of hydrochloric acid, hydrobromic acid, hydroiodic acid, sulfuric acid, fumaric cid, maleic acid, tartaric acid, methane-, ethane-, and benzene sulfonates, citric acid, malic acid, acetic acid, proprionic acid, pyruvic acid, butanoic acid, and lactic acid.

36. (new) The composition of claim 34 wherein the hydrogen ion species is lactic acid.

37. (new) The composition of claim 35 wherein the hydrogen ion species is lactic acid.

38. (new) A softgel capsule comprising a fill material comprising about 65% polyethylene glycol 600 by weight, about 24% (wt/wt) naproxen sodium by weight, about 4.8% of 88-92% lactic acid by weight, about 1.9% propylene glycol by weight, and about 1.9% polyvinyl pyrrolidine K-30 by weight.

Remarks

Applicants thank the Examiner for withdrawal of the election of species requirement in the Office Action mailed December 1, 2009.

The Claimed Invention

The claims are drawn to a pharmaceutical composition containing the salt of a pharmaceutically active agent and a deionizing agent, and methods of making and using thereof. The pharmaceutically active agent can have either an acidic or basic functionality, and is in the form of a salt. The deionizing agent partially de-ionizes (protonates or deprotonates) the pharmaceutically active agent salt such that an increased quantity of the de-ionized form of the pharmaceutically active agent is present. Partial deionization can result in enhanced bioavailability. For acidic agents, partial deionization minimizes the formation of polyethylene glycol (PEG) esters which occur from the condensation of terminal hydroxyl groups of PEG polymers and carboxylic acids contained within acidic pharmaceutically active agents.

Claim Amendments

Claims 1, 14, 18, and 19 have been amended to specify that the pharmaceutically active agent is either an acidic or basic compound and that the pharmaceutically active agent is present in a therapeutically effective amount. Support for these amendments is found at least on page 4, line 23 to page 6, line 10. Claims 1, 14, 18, and 19 have also been amended to specify that the deionizing agent at least partially neutralizes the pharmaceutically active agent. Support for these amendments is found at least on page 3, lines 19-23.

Claim 6 has been amended to correct a typographical error. A period was added.

Claims 11 and 29 have been amended to delete the second recitation of "solvent."

New claims 32 and 33 have been added to specify that the pharmaceutically active agent is naproxen sodium and the deionizing agent is a hydrogen ion species. Support for these amendments is found at least on pages 11-15, in Examples 1-12.

New claims 34 and 35 have been added to specify the hydrogen ion species is selected from hydrochloric acid, hydrobromic acid, hydroiodic acid, sulfuric acid, fumaric cid, maleic acid, tartaric acid, methane-, ethane-, and benzene sulfonates, citric acid, malic acid, acetic acid, proprionic acid, pyruvic acid, butanoic acid, and lactic acid. Support for these amendments is found at least on page 6, lines 22-25.

New claims 36 and 37 have been added to specify that the hydrogen ion species is lactic acid. Support for this amendment is found at least on page 6, lines 22-25.

New claim 38 has been added that specifies weight percentages of the fill material of a softgel capsule comprising polyethylene glycol, naproxen sodium, lactic acid, propylene glycol, and polyvinyl pyrrolidine K-30. Support for these amendments is found at least on page 9, lines 8-14 and Examples 1-12.

Rejection Under 35 U.S.C. § 112, second paragraph

Claim 11 was rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for lack of antecedent basis. Applicants respectfully traverse this rejection to the extent that it is applied to the claims as amended.

Claim 11 has been amended to depend from claim 10. Support for this amendment is found at least on page 7, lines 8-12.

Rejection Under 35 U.S.C. § 102

Claims 1-13 and 19-31 were rejected under 35 U.S.C. § 102(b) as being anticipated by U.S. Patent No. 5,360,615 to Yu, et al. ("Yu"). Applicants respectfully traverse this rejection to the extent that it is applied to the claims as amended.

The Legal Standard

For a rejection of claims to be properly founded under 35 U.S.C. § 102, it must be established that a prior art reference discloses each and every element of the claims. *Hybritech Inc. v. Monoclonal Antibodies Inc.*, 231 USPQ 81 (Fed. Cir. 1986); *Scripps Clinic & Research Found. v. Genentech Inc.*, 18 USPQ2d 1001 (Fed. Cir. 1991). The Federal Circuit held in *Scripps*:

> Invalidity for anticipation requires that all of the elements and limitations of the claim are found within a single prior art reference. There must be *no difference* between the claimed invention and the reference disclosure, as viewed by a person of ordinary skill in the field of the invention. (18 USPQ2d at 1010, emphasis added).

Further, a reference that fails to disclose even one limitation will not be found to anticipate, even if the missing limitation could be discoverable through further experimentation.

Analysis

Yu

Yu discloses a solvent system for enhancing the solubility of acidic, basic, or amphoteric pharmaceutical agents (abstract). The solvent system contains polyethylene glycol, a pharmaceutical agent, and an ionizing agent. Yu discloses generating salts of pharmaceutically active agents derived from treatment of non-salt forms of acidic or basic pharmaceutically active agents with an ionizing agent (col. 4, lines 25-51). Yu describes the combination of basic reagents (alkaline hydroxides) and pharmaceutically active agents containing acidic moieties (such as the carboxylic acid of naproxen, Example IV). In addition, Yu describes the combination of acidic reagents and non-ionized pharmaceutically active agents containing basic moieties (Example VII).

In contrast, the amended claims specify the combination of the salt of an acidic or basic pharmaceutically active agent and a deionizing agent, which neutralizes (protonates or deprotonates), at least in part, the salt of the pharmaceutically active agent. For example, if the salt is a salt of an acidic pharmaceutically active agent, such as naproxen sodium, the deionizing agent is a hydrogen ion species, such as hydrochloric acid.

In the Office Action dated December 1, 2009, the Examiner cited Example VIII of Yu. Example VIII describes treatment of the salt of the amphoteric compound, diclofenac sodium,

with the deionizing agent hydrochloric acid. The amended claims specify compositions comprising salts of either acidic or basic pharmaceutically active agents, and therefore exclude amphoteric compounds such as diclofenac sodium. Moreover, it is known in the art that strong acids, such as hydrochloric acid, catalyze the cyclization of diclofenac sodium to an indolinone derivative (see Figure 1 of Palomo, et al., *J. Pharm Biomed. Anal.*, 21: 83-94 (1999), attached, and M.A. Christianan et al., Analytical Profiles of Drug Substances, New York, 1999 pp. 123-141). Palomo states that the cyclized indolinone is pharmaceutically inactive. Therefore, Example VIII of Yu does not disclose a composition comprising a pharmaceutically active agent present in a therapeutically effective amount, as required by the amended claims.

For at least the reasons above, Yu does not disclose each and every limitation of amended claims 1 and 19. Accordingly, claims 1-3, 5-13, 19-21, and 23-35 are novel over Yu.

The amended claims are also non-obvious over Yu. As described above, Yu does not teach or suggest the combination of the salt of an acidic or basic pharmaceutically active agent and a deionizing agent. In fact, Yu teaches away from the presently amended claims.

A reference may be said to teach away when a person of ordinary skill, upon reading the reference, *would be discouraged from following the path set out in the reference, or would be led in a direction divergent from the path that was taken by the applicant* (emphasis added). The degree of teaching away will of course depend on the particular facts; in general, *a reference will teach away if it suggests that the line of development flowing from the reference's disclosure is unlikely to be productive of the result sought by the applicant* (emphasis added). See *United*

States v. Adams, 383 U.S. 39, 52, 148 U.S.P.Q. (BNA) 479, 484, 15 L. Ed. 2d 572, 86 S. Ct. 708 (1966) ("known disadvantages in old devices which would naturally discourage the search for new inventions may be taken into account in determining obviousness"); *W.L. Gore & Assoc., Inc. v. Garlock, Inc.*, 721 F.2d 1540, 1550-51, 220 U.S.P.Q. (BNA) 303, 311 (Fed. Cir. 1983) (the totality of a reference's teachings must be considered), cert. denied, 469 U.S. 851 (1984); *In re Caldwell*, 50 C.C.P.A. 1464, 319 F.2d 254, 256, 138 U.S.P.Q. (BNA) 243, 245 (CCPA 1963) (*reference teaches away if it leaves the impression that the product would not have the property sought by the applicant* (emphasis added)).

Yu teaches formation of a salt by addition of an ionizing agent to an acidic, basic, or amphoteric compound. The present claims teach neutralization of an acidic or basic salt. Therefore, one of ordinary skill in the art, reading Yu, would be led on a path divergent from the one taken by the Applicants. Moreover, Palomo (described above) states that the cyclized diclofenac sodium derivative has decreased solubility, decreased bioavailability, and is pharmaceutically inactive. Therefore, one of ordinary skill in the art, reading Example VIII of Yu and Palomo, would be motivated to start with a neutral composition and add an ionizing agent because this method forms a therapeutically effective salt composition. One of ordinary skill in the art would not be motivated to start with a salt and add a deionizing agent because Palomo teaches that, in the case of diclofenac sodium, this method does not yield a therapeutically effective composition. Accordingly, claims 1-3, 5-13, 19-21, and 23-35 are not obvious over Yu.

Allowance of claims 1-13 and 19-38 is respectfully solicited.

Respectfully submitted,

/Michael J. Terapane, Ph.D., J.D./
Michael J. Terapane, Ph.D., J.D.
Reg. No. 57,633

Date: May 3, 2010

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(404) 879-2155
(404) 879-2160 (Facsimile)

Electronic Patent Application Fee Transmittal

Application Number:	11367238
Filing Date:	03-Mar-2006
Title of Invention:	Solvent system for enhancing the solubility of pharmaceutical agents
First Named Inventor/Applicant Name:	Nachiappan Chidambaram
Filer:	Michael John Terapane/Candace Andrews
Attorney Docket Number:	BAN 102

Filed as Large Entity

Utility under 35 USC 111(a) Filing Fees

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Basic Filing:				
Pages:				
Claims:				
Claims in excess of 20	1202	7	52	364
Independent claims in excess of 3	1201	1	220	220
Miscellaneous-Filing:				
Petition:				
Patent-Appeals-and-Interference:				
Post-Allowance-and-Post-Issuance:				

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Extension-of-Time:				
Extension - 2 months with $0 paid	1252	1	490	490
Miscellaneous:				
			Total in USD ($)	**1074**

Electronic Acknowledgement Receipt

EFS ID:	7541549
Application Number:	11367238
International Application Number:	
Confirmation Number:	5524
Title of Invention:	Solvent system for enhancing the solubility of pharmaceutical agents
First Named Inventor/Applicant Name:	Nachiappan Chidambaram
Customer Number:	23579
Filer:	Michael John Terapane/Candace Andrews
Filer Authorized By:	Michael John Terapane
Attorney Docket Number:	BAN 102
Receipt Date:	03-MAY-2010
Filing Date:	03-MAR-2006
Time Stamp:	19:19:25
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	Deposit Account
Payment was successfully received in RAM	$1074
RAM confirmation Number	11824
Deposit Account	503129
Authorized User	

File Listing:

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

1	Extension of Time	BAN_102_Petition_for_a_Two_Month_EOT.pdf	83611 f92c7771725488c3c1dba75d8a382b8fc2b2ef6a	no	1
Warnings:					
Information:					
2		BAN_102_Amendment_and_Response.pdf	625821 607c53f439968309ee285e7602111cef52cf50e2	yes	14

	Multipart Description/PDF files in .zip description		
	Document Description	**Start**	**End**
	Amendment/Req. Reconsideration-After Non-Final Reject	1	1
	Claims	2	7
	Applicant Arguments/Remarks Made in an Amendment	8	14

Warnings:					
Information:					
3	Fee Worksheet (PTO-875)	fee-info.pdf	33369 686082e8dc9d75d5defe574c0a4ddd4414e3e54b	no	2
Warnings:					
Information:					
		Total Files Size (in bytes):	742801		

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

New Applications Under 35 U.S.C. 111

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

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

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

New International Application Filed with the USPTO as a Receiving Office

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

PTO/SB/22 (07-09)
Approved for use through 07/31/2012. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARMENT OF COMMERCE

PETITION FOR EXTENSION OF TIME UNDER 37 CFR 1.136(a) **FY 2009** ***(Fees pursuant to the Consolidated Appropriations Act, 2005 (H.R. 4818).)***	Docket Number (Optional) BAN 102
Application Number 11/367,238	Filed March 3, 2006
For SOLVENT SYSTEM FOR ENHANCING THE SOLUBILITY OF PHARMACEUTICAL AGENTS	
Art Unit 1618	Examiner Jake Minh Vu

This is a request under the provisions of 37 CFR 1.136(a) to extend the period for filing a reply in the above identified application.

The requested extension and fee are as follows (check time period desired and enter the appropriate fee below):

		Fee	Small Entity Fee	
☐	One month (37 CFR 1.17(a)(1))	$130	$65	$
☑	Two months (37 CFR 1.17(a)(2))	$490	$245	$ 490.00
☐	Three months (37 CFR 1.17(a)(3))	$1110	$555	$
☐	Four months (37 CFR 1.17(a)(4))	$1730	$865	$
☐	Five months (37 CFR 1.17(a)(5))	$2350	$1175	$

☐ Applicant claims small entity status. See 37 CFR 1.27.

☐ A check in the amount of the fee is enclosed.

☐ Payment by credit card. Form PTO-2038 is attached.

☐ The Director has already been authorized to charge fees in this application to a Deposit Account.

☑ The Director is hereby authorized to charge any fees which may be required, or credit any overpayment, to Deposit Account Number 50-3129.

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.

I am the

☐ applicant/inventor.

☐ assignee of record of the entire interest. See 37 CFR 3.71.
Statement under 37 CFR 3.73(b) is enclosed (Form PTO/SB/96).

☑ attorney or agent of record. Registration Number 57,633

☐ attorney or agent under 37 CFR 1.34.
Registration number if acting under 37 CFR 1.34 _____

/Michael J. Terapane, Ph.D., J.D.	May 3, 2010
Signature	Date
Michael J. Terapane, Ph.D., J.D.	404-879-2155
Typed or printed name	Telephone Number

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

☐ Total of _____ forms are submitted.

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
11/367,238	03/03/2006	

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	05/03/2010	(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))	* 38	Minus	** 31	= 7	X $ =		OR	X $52=	364
	Independent (37 CFR 1.16(h))	* 5	Minus	***4	= 1	X $ =		OR	X $220=	220
	☐ 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	**584**

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

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

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

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

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

Legal Instrument Examiner:
/ELMIRA HALL/

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
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Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
11/367,238	03/03/2006	Nachiappan Chidambaram	BAN 102	5524

23579 7590 07/14/2010

Pabst Patent Group LLP
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ATLANTA, GA 30309

EXAMINER	
VU, JAKE MINH	
ART UNIT	**PAPER NUMBER**
1618	
MAIL DATE	**DELIVERY MODE**
07/14/2010	PAPER

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

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

Office Action Summary	Application No.	Applicant(s)	
	11/367,238	CHIDAMBARAM ET AL.	
	Examiner	Art Unit	
	JAKE M. VU	1618	

-- 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 *03 May 2010*.

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

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

Disposition of Claims

4)☒ Claim(s) *1-38* is/are pending in the application.

4a) Of the above claim(s) *14-18* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13, 19-38* 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

Receipt is acknowledged of Applicant's Amendment filed on 05/03/2010.

- Claims 1, 6, 11, 14, 18-19 have been amended.
- Claims 32-38 have been added.
- Claims 1-38 are pending in the instant application.
- Claims 14-18 have been previously withdrawn from consideration.

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.

Claim 38 is 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. This is a new matter rejection.

Claim 38 recites the newly amended limitation of "about 65% polyethylene glycol 600 by weight, about 24% (wt/wt) naproxen sodium by weight, about 4.8% of 88-92% lactic acid by weight, about 1.9% propylene glycol by weight, and about 1.9% polyvinyl pyrrolidine K-30 by weight"; however, the specification as-filed does not provide a written description or set forth the metes and bounds of this phrase. The instant claims now recite limitations which were not clearly disclosed in the specification as-filed and

now change the scope of the instant disclosure as-filed. Such limitations recited in the present claims, introduce new concepts and thus violate the written description requirement of the first paragraph of 35 U.S.C. §112.

Applicant is required to cancel the new matter in the response to this Office action. Alternatively, Applicant is invited to identify sufficient written support in the original specification for the "limitations" indicated above.

Claim Rejections - 35 USC § 112, 2nd paragraph

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.

Claim 38 is 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.

Its unclear what is the amount of the limitation of "about 4.8% of 88-92% lactic acid by weight" would encompass. Please amend or clarify.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-13 and 19-31 are rejected under 35 U.S.C. 102(b) as being anticipated by YU et al (5,360,615) **are maintained** for reasons of record in the previous office action filed on 12/01/2009 and as discussed below.

Note, the claims do not recite that an acidic active agent should be used with hydrogen ions or that the basic active agent should be used with hydroxide ions.

Note, the term deionizing agent is a broad term that would include water, which has a balance of hydrogen ions and hydroxide ions at neutral pH.

Upon further consideration of Applicant's Amendment, a new ground(s) of rejection is made as discussed below.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-2, 4, 8-13, 19-20, 22, 26-35 are rejected under 35 U.S.C. 102(b) as being anticipated by MITRA et al (US 5,648,358).

MITRA teaches a composition comprised of: salt of an acidic active agent, such as naproxen sodium (see col. 6, Example IV and line 26; claim 3); deionizing agents, such as citric acid (see col. 6, line 12). Additional disclosures include: about 15% of water (see col. 6, line 16); solubilizers, such as 5-25% of propylene glycol (see col. 4,

line 35-42; and col. 6, line 10); and soft gel capsules (see col. 3, line 58; and col. 4, line 7-8).

Note, the amount of naproxen added would inherently be a "therapeutically effective amount", since the active agent is added to treat flu-like symptoms (see col. 6, line 34-36).

Note, deionizing agent inherently would partially neutralize the pharmaceutically active agent, since this is an inherent chemical property of the deionizing agent and the prior art's deionizing agent is the same as claimed by Applicant.

Claims 1-13, 19-35 are rejected under 35 U.S.C. 102(b) as being anticipated by SAWYER et al (US 6,383,515).

SAWYER teaches a composition comprised of: 21.67% naproxen sodium (see abstract; and col. 14, line 32); deionizing agent, such as 5.88% of sodium propionate in water (see col. 14, line 23 and 35), which would inherently have propionic acid (see col. 4, line 40-44) when the sodium propionate salt goes into solution. Additional disclosures include: 10-70% of polyethylene glycol 400-600 (see col. 3, line 48 - col. 4, line 19); 0-25% of water (see col. 3, line 33; col. 5, line 4-5; col. 14, line 23; and examples); 2% of propylene glycol (see col. 3, line 48-54; col. 8, line 24) or polyvinyl pyrrolidone (see col. 3, line 49) ; soft gel capsule (see abstract); other organic acids can be used in place of propionic acid, such as citric acid or organic acids with at least 3 carbon atoms (see col. 4, line 31-44).

Note, the term deionizing agent is a broad term that would include water, which has a balance of hydrogen ions and hydroxide ions at neutral pH.

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.

Claims 1-13, 19-38 are rejected under 35 U.S.C. 103(a) as being unpatentable over SAWYER et al (US 6,383,515) in view of McENTEE et al (US 5,885,608).

As discussed above, SAWYER teaches a composition comprised of: 21.67% naproxen sodium (see abstract; and col. 14, line 32); deionizing agent, such as 5.88% of sodium propionate in water (see col. 14, line 23 and 35), which would inherently have propionic acid (see col. 4, line 40-44) when the sodium propionate salt goes into solution. Additional disclosures include: 10-70% of polyethylene glycol 400-600 (see col. 3, line 48 - col. 4, line 19); 0-25% of water (see col. 3, line 33; col. 5, line 4-5; col. 14, line 23; and examples); 2% of propylene glycol (see col. 3, line 48-54; col. 8, line 24) or polyvinyl pyrrolidone (see col. 3, line 49) ; soft gel capsule (see abstract); other organic acids can be used in place of propionic acid, such as citric acid or organic acids with at least 3 carbon atoms (see col. 4, line 31-44). Note, the term deionizing agent is a broad term that would include water, which has a balance of hydrogen ions and hydroxide ions at neutral pH.

SAWYER does not teach using an organic acid, such as lactic acid.

McENTEE teaches that organic acids, such as citric acid and lactic acid are known in the prior art (see col. 10, line 17-19).

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to incorporate lactic acid or sodium lactate into SAWYER's composition. The person of ordinary skill in the art would have been motivated to make those modifications, because lactic acid is an organic functional equivalent of citric acid, and reasonably would have expected success because SAWYER teaches using organic acids with at least 3 carbons, wherein lactic acid has at least 3 carbons.

The references do not specifically teach adding the ingredients in the amounts claimed by Applicant. The amount of a specific ingredient in a composition is clearly a result effective parameter that a person of ordinary skill in the art would routinely optimize. Optimization of parameters is a routine practice that would be obvious for a person of ordinary skill in the art to employ and reasonably would expect success. It would have been customary for an artisan of ordinary skill to determine the optimal amount of each ingredient to add in order to best achieve the desired results, such as solubility of the active agent. Thus, absent some demonstration of unexpected results from the claimed parameters, this optimization of ingredient amount would have been obvious at the time of Applicant's invention.

Note, Applicant's specification has not provided with any increased solubility data.

Response to Arguments

Applicant argues that the amended claims specify the combination of the salt of an acidic or basic pharmaceutically active agent and a deionizing agent, which neutralizes (protonates or deprotonates), at least in part, the salt of the pharmaceutically active agent. For example, if the salt is a salt of an acidic pharmaceutically active agent, such as naproxen sodium, the deionizing agent is a hydrogen ion species, such as hydrochloric acid.

The Examiner finds this argument unpersuasive, because YU teaches using the drug, diclofenac (see col. 12, Example VIII), which is one of the drug disclosed in Applicant's specification; therefore diclofenac would meet the definition of basic or acid drug, wherein the sodium would make the diclofenac a salt. YU further teaches using hydrochloric acid (see col. 12, Example VIII). Additionally, these rejected claims do not recite naproxen as the drug.

Applicant argues that the Examiner cited Example VIII of Yu. Example VIII describes treatment of the salt of the amphoteric compound, diclofenac sodium, with the deionizing agent hydrochloric acid. The amended claims specify compositions comprising salts of either acidic or basic pharmaceutically active agents, and therefore exclude amphoteric compounds such diclofenac sodium.

The Examiner finds this argument unpersuasive, because amphoteric compounds have both acid and basic groups; thus, amphoteric compounds would meet

the requirement of either basic or acid drug. Additionally, diclofenac is one of the drugs disclosed in Applicant's specification.

Applicant argues that it is known in the art that strong acids, such as hydrochloric acid, catalyze the cyclization of diclofenac sodium to an indolinone derivative (see Figure 1 of Paloma, et al., J. Pharrn Biomed. Anal., 2 1 : 83-94 (1 9991, attached, and M.A. Christianan et al,, Analytical Profiles of lDrua Substances, New York, 1999 pp. 123-141). Palomo states that the cyclized indolinone is pharmceutically inactive. Therefore, Example VIII of Yu does not disclose a composition comprising a pharmaceutically active agent present in a therapeutically effective mount, as required by the amended claims.

The Examiner finds this argument unpersuasive, because Palomo is not a reference in the rejection.

Applicant argues that Yu teaches formation of a salt by addition of an ionizing agent to an acidic, basic, or amphoteric compound. The present claims teach neutralization of an acidic or basic salt. Therefore, one of ordinary skill in the art, reading Yu, would be led on a path divergent from the one taken by the Applicants. Moreover, Palomo (described above) states that the cyclized diclofenac sodium derivative has decreased solubility, decreased bioavailability, and is pharmaceutically inactive, Therefore, one of ordinary skill in the art, reading Example VIII of Yu and Palomo, would be motivated to start with a neutral composition and add an ionizing agent because this method forms a therapeutically effective salt composition. One of ordinary skill in the art would not be motivated to start with a salt and add a deionizing

agent because Palomo teaches that, in the case of diclofenac sodium, this method does not yield a therapeutically effective composition. Accordingly, the claims are not obvious over Yu.

The Examiner finds this argument unpersuasive, because this is a 102 rejection, not a 103 obvious rejection, and Palomo is not used in the 102 rejection. Thus, there is no motivation necessary.

Conclusion

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

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

Telephonic Inquiries

Any inquiry concerning this communication or earlier communications from the examiner should be directed to JAKE M. VU whose telephone number is (571)272-8148. The examiner can normally be reached on Mon-Tue and Thu-Fri 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Hartley can be reached on (571) 272-0616. 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.

/Jake M. Vu/
Primary Examiner, Art Unit 1618

Notice of References Cited	Application/Control No. 11/367,238	Applicant(s)/Patent Under Reexamination CHIDAMBARAM ET AL.	
	Examiner JAKE M. VU	Art Unit 1618	Page 1 of 1

U.S. PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Name	Classification
*	A	US-5,648,358	07-1997	Mitra, Sekhar	514/263.32
*	B	US-6,383,515	05-2002	Sawyer et al.	424/456
*	C	US-5,885,608	03-1999	McEntee, William J.	424/423
	D	US-			
	E	US-			
	F	US-			
	G	US-			
	H	US-			
	I	US-			
	J	US-			
	K	US-			
	L	US-			
	M	US-			

FOREIGN PATENT DOCUMENTS

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

NON-PATENT DOCUMENTS

*		Include as applicable: Author, Title Date, Publisher, Edition or Volume, Pertinent Pages)
	U	
	V	
	W	
	X	

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

UNITED STATES PATENT AND TRADEMARK OFFICE

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
11/367,238	03/03/2006	Nachiappan Chidambaram	BAN 102	5524

23579 7590 10/13/2010

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EXAMINER	
VU, JAKE MINH	
ART UNIT	**PAPER NUMBER**
1618	

MAIL DATE	DELIVERY MODE
10/13/2010	PAPER

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

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

Interview Summary	Application No.	Applicant(s)	
	11/367,238	CHIDAMBARAM ET AL.	
	Examiner	Art Unit	
	JAKE M. VU	1618	

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

(1) *JAKE M. VU*. (3)_____.

(2) *Michael Terapane (App's Rep)*. (4)_____.

Date of Interview: *05 October 2010*.

Type: a)☒ Telephonic b)☐ Video Conference
c)☐ Personal [copy given to: 1)☐ applicant 2)☐ applicant's representative]

Exhibit shown or demonstration conducted: d)☐ Yes e)☒ No.
If Yes, brief description: _____.

Claim(s) discussed: *claims of record*.

Identification of prior art discussed: *YU, MITRA, and SAWYER*.

Agreement with respect to the claims f)☐ was reached. g)☐ was not reached. h)☒ N/A.

Substance of Interview including description of the general nature of what was agreed to if an agreement was reached, or any other comments: *Discussed prior art and interpretation of the claims*.

(A fuller description, if necessary, and a copy of the amendments which the examiner agreed would render the claims allowable, if available, must be attached. Also, where no copy of the amendments that would render the claims allowable is available, a summary thereof must be attached.)

THE FORMAL WRITTEN REPLY TO THE LAST OFFICE ACTION MUST INCLUDE THE SUBSTANCE OF THE INTERVIEW. (See MPEP Section 713.04). If a reply to the last Office action has already been filed, APPLICANT IS GIVEN A NON-EXTENDABLE PERIOD OF THE LONGER OF ONE MONTH OR THIRTY DAYS FROM THIS INTERVIEW DATE, OR THE MAILING DATE OF THIS INTERVIEW SUMMARY FORM, WHICHEVER IS LATER, TO FILE A STATEMENT OF THE SUBSTANCE OF THE INTERVIEW. See Summary of Record of Interview requirements on reverse side or on attached sheet.

/Jake M. Vu/ Primary Examiner, Art Unit 1618	

Summary of Record of Interview Requirements

Manual of Patent Examining Procedure (MPEP), Section 713.04, Substance of Interview Must be Made of Record
A complete written statement as to the substance of any face-to-face, video conference, or telephone interview with regard to an application must be made of record in the application whether or not an agreement with the examiner was reached at the interview.

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

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

37 CFR §1.2 Business to be transacted in writing.
All business with the Patent or Trademark Office should be transacted in writing. The personal attendance of applicants or their attorneys or agents at the Patent and Trademark Office is unnecessary. The action of the Patent and Trademark Office will be based exclusively on the written record in the Office. No attention will be paid to any alleged oral promise, stipulation, or understanding in relation to which there is disagreement or doubt.

———

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

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

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

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

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

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

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

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

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

Examiner to Check for Accuracy

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

AMENDMENT UNDER 37 C.F.R. 1.116
EXPEDITED PROSECUTION
ART UNIT 1618

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Nachiappan Chidambaram and Aqeel Fatmi

Serial No.: 11/367,238 Art Unit: 1618

Filed: March 3, 2006 Examiner: Jake Minh Vu

For: *SOLVENT SYSTEM FOR ENHANCING THE SOLUBILITY OF PHARMACEUTICAL AGENTS*

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

AMENDMENT AND RESPONSE

Sir:

Responsive to the Office Action mailed on July 14, 2010, please amend the application as follows. A Petition for a One Month extension of time is submitted with this Amendment and Response extending the time to respond to November 14, 2010. The Commissioner is authorized to charge $130.00, the fee for the Petition for a One Month extension of time for a large entity, to Deposit Account No. 50-3129.

It is believed that no additional fee is required with this submission. However, should an additional fee be required, the Commissioner is hereby authorized to charge the fee to Deposit Account No. 50-3129.

Amendment

In the Claims

1. (currently amended) A pharmaceutical composition comprising

(a) a salt of one or more either acidic or basic pharmaceutically active agents; and

(b) a deionizing agent, which at least partially neutralizes the pharmaceutically active agent; and

(c) polyethylene glycol;

wherein when the active agent is a salt of a weak acid and a strong base, the deionizing agent is a hydrogen ion species and when the active agent is a salt of a weak base and a strong acid, the deionizing agent is a hydroxide ion species

~~wherein the pharmaceutically active agent is present in a therapeutically effective amount; and~~

~~wherein the deionizing agent at least partially neutralizes the pharmaceutically active agent~~.

2. (original) The composition of claim 1 wherein the pharmaceutically active agent is selected from the group consisting of therapeutically active agents, diagnostic agents, and prophylactic agents.

3. (original) The composition of claim 1 wherein the deionizing agent is present in an amount from about 0.2 to 1.0 mole equivalents per mole of the pharmaceutically active agent(s).

4. (original) The composition of claim 1 wherein the deionizing agent is selected from the group consisting of hydrogen ion and hydroxide ion.

5. (canceled)

6. (currently amended) The composition of claim 1 [[5]] wherein polyethylene glycol is present in an amount from about 10% to about 80% by weight.

7. (currently amended) The composition of claim 1 [[5]] wherein polyethylene glycol is one or more polyethylene glycols with a molecular weight between 300 and 1500.

8. (original) The composition of claim 1 further comprising water.

9. (original) The composition of claim 8 wherein water is present in an amount from about 1% to about 18% by weight.

10. (original) The composition of claim 1 further comprising one or more excipients.

11. (previously presented) The composition of claim 10, wherein the one or more excipients are selected from the group consisting of plasticizers, crystallization inhibitors, wetting agents, bulk filling agents, solubilizers, bioavailability enhancers, solvents, pH-adjusting agents, dyes, preservatives, surfactants, and combinations thereof.

12. (original) The composition of claim 11 wherein the solubilizer is selected from the group consisting of glycerin, polyvinylpyrrolidone, propylene glycol and combinations thereof.

13. (original) The composition of claim 12 wherein the solubilizer is present in amount from about 1% to about 10% by weight.

14. (withdrawn-currently amended) A method of making [[a]] the ~~pharmaceutical composition~~ capsule of claim 19 comprising ~~a salt of one or more either acidic or basic pharmaceutically active agents; and a deionizing agent comprising~~

(a) mixing the salt of one or more pharmaceutically active agents, ~~and~~ the deionizing agent, and polyethylene glycol at an appropriate temperature; and

(b) encapsulating the mixture in a softgel capsule;

~~wherein the pharmaceutically active agent is present in a therapeutically effective amount; and~~

~~wherein the deionizing agent at least partially neutralizes the pharmaceutically active agent~~.

15. (canceled)

16. (withdrawn) The method of claim 14 further comprising water.

17. (withdrawn) The method of claim 14 wherein the appropriate temperature is from about 50°C to about 70°C.

18. (withdrawn-currently amended) A method of using [[a]] the pharmaceutical composition of claim 1 or the capsule of claim 19 or 38 comprising

~~(a) a salt of one or more either acidic or basic pharmaceutically active agents; and~~

~~(b) a deionizing agent;~~

~~wherein the pharmaceutically active agent is present in a therapeutically effective amount; and~~

~~wherein the deionizing agent at least partially neutralizes the pharmaceutically active agent~~

~~comprising~~ administering ~~the composition~~ to a patient in need thereof an effective amount of the composition of claim 1 or the capsule of claim 19 or 38.

19. (currently amended) A softgel capsule comprising a fill material wherein the fill material comprises

(a) a salt of one or more either acidic or basic pharmaceutically active agents; and

(b) a deionizing agent, which at least partially neutralizes the pharmaceutically active agent; and

~~wherein the pharmaceutically active agent is present in a therapeutically effective amount; and~~

~~wherein the deionizing agent at least partially neutralizes the pharmaceutically active agent~~

(c) polyethylene glycol;

wherein, when the active agent is a salt of a weak acid and a strong base, the deionizing agent is a hydrogen ion species and when the active agent is a salt of a weak base and a strong acid, the deionizing agent is a hydroxide ion species.

20. (original) The capsule of claim 19 wherein the pharmaceutically active agent is selected from the group consisting of therapeutically active agents, diagnostic agents, and prophylactic agents.

21. (original) The capsule of claim 19 wherein the deionizing agent is present in an amount from about 0.2 to 1.0 mole equivalents per mole of the pharmaceutically active agent(s).

22. (original) The capsule of claim 19 wherein the deionizing agent is selected from the group consisting of hydrogen ion and hydroxide ion.

23. (canceled)

24. (currently amended) The capsule of claim 19 [[23]] wherein polyethylene glycol is present in an amount from about 10% to about 80% by weight

25. (currently amended) The capsule of claim 19 [[23]] wherein polyethylene glycol is one or more polyethylene glycols with a molecular weight between 300 and 1500.

26. (original) The capsule of claim 19 further comprising water.

27. (original) The capsule of claim 26 wherein water is present in an amount from about 1% to about 18% by weight.

28. (original) The capsule of claim 19 further comprising one or more excipients.

29. (previously presented) The capsule of claim 28 wherein the one or more excipients are selected from the group consisting of plasticizers, crystallization inhibitors, wetting agents, bulk filling agents, solubilizers, bioavailability enhancers, solvents, pH-adjusting agents, dyes, preservatives, surfactants, and combinations thereof.

30. (original) The capsule of claim 29 wherein the solubilizer is selected from the group consisting of glycerin, polyvinylpyrrolidone, propylene glycol and combinations thereof.

31. (original) The capsule of claim 29 wherein the solubilizer is present in amount from about 1% to about 10% by weight.

32. (previously presented) The composition of claim 1 wherein the pharmaceutically active agent is naproxen sodium and the deionizing agent is a hydrogen ion species.

33. (previously presented) The composition of claim 19 wherein the pharmaceutically active agent is naproxen sodium and the deionizing agent is a hydrogen ion species.

34. (previously presented) The composition of claim 32 wherein the hydrogen ion species is selected from the group consisting of hydrochloric acid, hydrobromic acid, hydroiodic acid, sulfuric acid, fumaric cid, maleic acid, tartaric acid, methane-, ethane-, and benzene sulfonates, citric acid, malic acid, acetic acid, proprionic acid, pyruvic acid, butanoic acid, and lactic acid.

35. (previously presented) The composition of claim 33 wherein the hydrogen ion species is selected from the group consisting of hydrochloric acid, hydrobromic acid, hydroiodic acid, sulfuric acid, fumaric cid, maleic acid, tartaric acid, methane-, ethane-, and benzene sulfonates, citric acid, malic acid, acetic acid, proprionic acid, pyruvic acid, butanoic acid, and lactic acid.

36. (previously presented) The composition of claim 34 wherein the hydrogen ion species is lactic acid.

37. (previously presented) The composition of claim 35 wherein the hydrogen ion species is lactic acid.

38. (currently amended) A softgel capsule comprising a fill material comprising

~~about 65%~~ from about 10% to about 80% by weight polyethylene glycol ~~600 by weight~~ having a molecular weight between 300 and 1500, ~~about 24% (wt/wt)~~ about 10% to about 50% by weight naproxen sodium, and ~~by weight, about 4.8% of 88-92%~~ 0.2 to 1.0 moles of a deionizing agent ~~lactic acid by weight~~ per mole of naproxen sodium~~, about 1.9% propylene glycol by weight, and about 1.9% polyvinyl pyrrolidine K-30 by weight~~.

39. (new) The softgel capsule of claim 38 wherein the deionizing agent is selected from the group consisting of hydrochloric acid, hydrobromic acid, hydroiodic acid, sulfuric acid, fumaric cid, maleic acid, tartaric acid, methane-, ethane-, and benzene sulfonates, citric acid, malic acid, acetic acid, proprionic acid, pyruvic acid, butanoic acid, and lactic acid.

Remarks

Interview with the Examiner

The undersigned would like to thank Examiner Vu for his time in discussing the present application in the telephone interview on October 5, 2010. The pending claims and the references cited by Examiner Vu were discussed. Examiner Vu indicated that amending the claims to define the relationship between the deionizing species and the salt of the drug would likely overcome the rejections over U.S. Patent No. 5,360,615 to Yu *et al.* ("Yu") and U.S. Patent No. 6,383,515 to Sawyer *et al.* ("Sawyer"). In order to facilitate prosecution, independent claims 1, 14, 18, and 19 have been amended as suggested by Examiner Vu. Support for the amendment is found at least at page 6, lines 12-17.

Independent claims 1, 14, 18, and 19 have also been amended to specify that the composition contains polyethylene glycol. Support for this amendment is found in dependent claims 5, 15, and 23. Claims 5, 15, and 23 have been canceled. Claims 6, 7, 24, and 25 have been amended to correct the dependencies.

Applicant believe that it is proper for the present amendment to be entered since it places the application in condition for allowance and does not require further search or consideration by the Examiner. Applicant reserve the right to file one or more continuation applications to pursue claims of a different or broader scope.

Rejection Under 35 U.S.C. § 112, first paragraph

Claim was were rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventor had possession of the claimed invention. Applicants respectfully traverse this rejection to the extent that it is applied to the claims as amended.

Without making any admissions and solely for the purpose of facilitating prosecution, claim 38 has been amended to define the amounts provided at page 7, lines 5-14.

Rejection Under 35 U.S.C. § 112, second paragraph

Claim 38 was rejected under 35 U.S.C. § 112, second paragraph, as being indefinite. Applicants respectfully traverse this rejection to the extent that it is applied to the claims as amended.

Without making any admissions and solely for the purpose of facilitating prosecution, claim 38 has been amended to define the amounts provided at page 7, lines 5-14.

Rejection Under 35 U.S.C. § 102

Claims 1-13 and 19-31 were rejected under 35 U.S.C. § 102(b) as being anticipated by U.S. Patent No. 5,360,615 to Yu *et al.* ("Yu"). Claims 1, 2, 4, 8-13, 19, 20, 22, and 26-35 were rejected under 35 U.S.C. § 102(b) as being anticipated by U.S. Patent No. 5,648,358 to Mitra *et al.*, ("Mitra"). Claims 1-13 and 19-35 were rejected under 35 U.S.C. § 102(b) as being anticipated by U.S. Patent No. 6,383,515 to Sawyer *et al.*, ("Sawyer"). Applicants respectfully traverse this rejection.

Yu

As discussed above, Examiner Vu indicated during the telephone interview on October 5, 2010 that amending the independent claims to specify the chemical nature of the deionizing agent would likely overcome the rejection over Yu. Therefore, in order to facilitate prosecution, the independent claims have been amended as suggested by the Examiner. Support for the amendment is found at least at page 6, lines 12-17.

Yu does not disclose or suggest a pharmaceutical composition comprising (a) a salt of one or more either acidic or basic pharmaceutically active agents; and (b) a deionizing agent, which at least partially neutralizes the pharmaceutically active agent, wherein when the active agent is a salt of a weak acid and a strong base, the deionizing agent is a hydrogen ion species and when the active agent is a salt of a weak base and a strong acid, the deionizing agent is a hydroxide ion species. Accordingly, claims 1-13, 19-21, 38, and 39 are novel over Yu.

Mitra

Independent claims 1 and 19 have been amended to incorporate the limitation of claims 5 and 23 respectively. Independent claims 14 and 18 have been amended to incorporate the limitation of claim 15. Dependent claims 5, 15, and 23 were not rejected by the Examiner over Mitra. Accordingly, claims 1, 2, 4, 8-13, 19, 20, 26-35, 38, and 39 as amended, are novel over Mitra.

Sawyer

Sawyer describes a pharmaceutically acceptable solution containing a medicament and a solvent (abstract). The solvent contains a polymer and an acid salt of a compound having at least three or more carbon atoms (abstract). Sawyer discloses that the salt of the organic acid ionizes the medicament. Ionization is the opposite of deionization, which is required by the pending claims.

The Examiner specifically cited Example 17 in Sawyer. Example 17 is a formulation containing naproxen sodium, polyethylene glycol, potassium hydroxide, and sodium propionate. Potassium hydroxide and sodium propionate are bases, i.e., ionizing agents, which function to maintain naproxen as the sodium salt. Potassium hydroxide and sodium propionate are not deionizing agents. Sawyer does not disclose a salt of an either acidic or basic drug and a deionizing agent as required by the claims. Accordingly, claims 1-13, 19-35, 38, and 39 are novel over Sawyer.

Rejection Under 35 U.S.C. § 103

Claims 1-13 and 19-38 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Sawyer, in view of U.S. Patent No. 5,885,608 to McEntee *et al.* ("McEntee"). Applicants respectfully traverse this rejection to the extent that it is applied to the claims as amended.

Sawyer is discussed above. Sawyer does not disclose a salt of an either acidic or basic drug and a deionizing agent as required by the claims. McEntee does not cure the deficiencies of Sawyer. Moreover, one of ordinary skill in the art would not be motivated to modify Sawyer to

arrive at the claimed compositions since Sawyer discloses ionizing the active agent, not deionizing the active agent as required by the claims. Sawyer teaches away from the claimed compositions. Finally, modifying Sawyer in the manner suggested by the Examiner would make Sawyer inoperable for its intended purpose, which is improper under 35 U.S.C. § 103. Accordingly, claims 1-13 and 19-39 are not obvious over Sawyer in view of McEntee.

Allowance of claims 1-4, 6-13, 19-22, and 24-39, as amended, is respectfully solicited.

Respectfully submitted,

/Michael J. Terapane, Ph.D., J.D./
Michael J. Terapane, Ph.D., J.D.
Reg. No. 57,633

Date: October 22, 2010

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Electronic Patent Application Fee Transmittal	
Application Number:	11367238
Filing Date:	03-Mar-2006
Title of Invention:	Solvent system for enhancing the solubility of pharmaceutical agents
First Named Inventor/Applicant Name:	Nachiappan Chidambaram
Filer:	Michael John Terapane/Camdace Andrews
Attorney Docket Number:	BAN 102

Filed as Large Entity

Utility under 35 USC 111(a) Filing Fees

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Basic Filing:				
Pages:				
Claims:				
Miscellaneous-Filing:				
Petition:				
Patent-Appeals-and-Interference:				
Post-Allowance-and-Post-Issuance:				
Extension-of-Time:				
Extension - 1 month with $0 paid	1251	1	130	130

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Miscellaneous:				
		Total in USD ($)		**130**

Electronic Acknowledgement Receipt

EFS ID:	8684407
Application Number:	11367238
International Application Number:	
Confirmation Number:	5524
Title of Invention:	Solvent system for enhancing the solubility of pharmaceutical agents
First Named Inventor/Applicant Name:	Nachiappan Chidambaram
Customer Number:	23579
Filer:	Michael John Terapane/Candace Andrews
Filer Authorized By:	Michael John Terapane
Attorney Docket Number:	BAN 102
Receipt Date:	22-OCT-2010
Filing Date:	03-MAR-2006
Time Stamp:	15:34:22
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	Deposit Account
Payment was successfully received in RAM	$130
RAM confirmation Number	1915
Deposit Account	503129
Authorized User	

File Listing:

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

1	Extension of Time	BAN_102_Petition_for_a_One_Month_EOT.pdf	85478 2655d095574468400eef04631bff02c11d2ef28e	no	1
Warnings:					
Information:					
2		BAN_102_Amendment_and_Response.pdf	559316 2c5da1ae376067a5ebc6442122e76e4a6bdd7372	yes	14

	Multipart Description/PDF files in .zip description		
	Document Description	**Start**	**End**
	Amendment After Final	1	2
	Claims	3	9
	Applicant Arguments/Remarks Made in an Amendment	10	14

Warnings:					
Information:					
3	Fee Worksheet (PTO-875)	fee-info.pdf	30002 b7be0dc5aeb6f55a94038a6701217a3573ac5469	no	2
Warnings:					
Information:					
		Total Files Size (in bytes):	674796		

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

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

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

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

PTO/SB/22 (07-09)
Approved for use through 07/31/2012. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARMENT OF COMMERCE

PETITION FOR EXTENSION OF TIME UNDER 37 CFR 1.136(a) **FY 2009** *(Fees pursuant to the Consolidated Appropriations Act, 2005 (H.R. 4818).)*	Docket Number (Optional) BAN 102
Application Number 11/367,238	Filed March 3, 2006
For SOLVENT SYSTEM FOR ENHANCING THE SOLUBILITY OF PHARMACEUTICAL AGENTS	
Art Unit 1618	Examiner Jake Minh Vu

This is a request under the provisions of 37 CFR 1.136(a) to extend the period for filing a reply in the above identified application.

The requested extension and fee are as follows (check time period desired and enter the appropriate fee below):

	Fee	Small Entity Fee	
☑ One month (37 CFR 1.17(a)(1))	$130	$65	$ 130.00
☐ Two months (37 CFR 1.17(a)(2))	$490	$245	$
☐ Three months (37 CFR 1.17(a)(3))	$1110	$555	$
☐ Four months (37 CFR 1.17(a)(4))	$1730	$865	$
☐ Five months (37 CFR 1.17(a)(5))	$2350	$1175	$

☐ Applicant claims small entity status. See 37 CFR 1.27.

☐ A check in the amount of the fee is enclosed.

☐ Payment by credit card. Form PTO-2038 is attached.

☐ The Director has already been authorized to charge fees in this application to a Deposit Account.

☑ The Director is hereby authorized to charge any fees which may be required, or credit any overpayment, to Deposit Account Number 50-3129.

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.

I am the

☐ applicant/inventor.

☐ assignee of record of the entire interest. See 37 CFR 3.71.
Statement under 37 CFR 3.73(b) is enclosed (Form PTO/SB/96).

☑ attorney or agent of record. Registration Number 57,633

☐ attorney or agent under 37 CFR 1.34.
Registration number if acting under 37 CFR 1.34 _____

/Michael J. Terapane, Ph.D., J.D./	October 22, 2010
Signature	Date
Michael J. Terapane, Ph.D., J.D.	404-879-2155
Typed or printed name	Telephone Number

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

☐ Total of _____ forms are submitted.

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
11/367,238	03/03/2006	

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))							
			TOTAL			TOTAL	

* If the difference in column 1 is less than zero, enter "0" in column 2.

APPLICATION AS AMENDED – PART II

AMENDMENT	10/22/2010	(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))	* 36	Minus	** 38	= 0	X $ =		OR	X $52=	0
	Independent (37 CFR 1.16(h))	* 3	Minus	***5	= 0	X $ =		OR	X $220=	0
	☐ Application Size Fee (37 CFR 1.16(s))									
	☐ FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))							OR		
						TOTAL ADD'L FEE		OR	TOTAL ADD'L FEE	0

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

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

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

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

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

Legal Instrument Examiner:
/FLORENCE R. PATTERSON/

This collection of information is required by 37 CFR 1.16. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

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

UNITED STATES PATENT AND TRADEMARK OFFICE

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

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
11/367,238	03/03/2006	Nachiappan Chidambaram	BAN 102	5524

23579 7590 11/02/2010

Pabst Patent Group LLP
1545 PEACHTREE STREET NE
SUITE 320
ATLANTA, GA 30309

EXAMINER	
VU, JAKE MINH	
ART UNIT	**PAPER NUMBER**
1618	
MAIL DATE	**DELIVERY MODE**
11/02/2010	PAPER

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

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

Advisory Action Before the Filing of an Appeal Brief	**Application No.** 11/367,238	**Applicant(s)** CHIDAMBARAM ET AL.	
	Examiner JAKE M. VU	**Art Unit** 1618	

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

THE REPLY FILED 22 October 2010 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 *3* 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: _____.
   Claim(s) withdrawn from consideration: _____.

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: _____.

/Jake M. Vu/
Primary Examiner, Art Unit 1618

Continuation of 3. NOTE: The newly amended limitation of "polyehtylene glycol, wherein when the agent is a salt of a weak acid and a stong base, the deionizing agent is a hydrogen ion specis…" in independent claims 1 and 19 will require further consideration and/or search.

AMENDMENT UNDER 37 C.F.R. 1.116
EXPEDITED PROSECUTION
ART UNIT 1618

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Nachiappan Chidambaram and Aqeel Fatmi

Serial No.: 11/367,238 Art Unit: 1618

Filed: March 3, 2006 Examiner: Jake Minh Vu

For: *SOLVENT SYSTEM FOR ENHANCING THE SOLUBILITY OF PHARMACEUTICAL AGENTS*

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

DO NOT ENTER: /J.V./

AMENDMENT AND RESPONSE

Sir:

Responsive to the Office Action mailed on July 14, 2010, please amend the application as follows. A Petition for a One Month extension of time is submitted with this Amendment and Response extending the time to respond to November 14, 2010. The Commissioner is authorized to charge $130.00, the fee for the Petition for a One Month extension of time for a large entity, to Deposit Account No. 50-3129.

It is believed that no additional fee is required with this submission. However, should an additional fee be required, the Commissioner is hereby authorized to charge the fee to Deposit Account No. 50-3129.

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

Request for Continued Examination (RCE) Transmittal

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

Application Number	11/367,238
Filing Date	March 3, 2006
First Named Inventor	Nachiappan Chidambaram
Art Unit	1618
Examiner Name	Jake Minh Vu
Attorney Docket Number	BAN 102

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

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

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

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

      ii. [ ] Other _____

   b. [ ] Enclosed

      i. [ ] Amendment/Reply

      ii. [ ] Affidavit(s)/ Declaration(s)

      iii. [ ] Information Disclosure Statement (IDS)

      iv. [ ] Other _____

2. Miscellaneous

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

   b. [ ] Other _____

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

   a. [✓] The Director is hereby authorized to charge the following fees, any underpayment of fees, or credit any overpayments, to Deposit Account No. 50-3129 .

      i. [✓] RCE fee required under 37 CFR 1.17(e)

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

      iii. [ ] Other _____

   b. [ ] Check in the amount of $ _____ enclosed

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

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

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT REQUIRED

Signature	/Michael J. Terapane, Ph.D., J.D./	Date	November 15, 2010
Name (Print/Type)	Michael J. Terapane, Ph.D., J.D.	Registration No.	57,633

CERTIFICATE OF MAILING OR TRANSMISSION

I hereby certify that this correspondence is being electronically submitted.

Signature	/Candace C. Andrews/		
Name (Print/Type)	Candace C. Andrews	Date	November 15, 2010

Electronic Patent Application Fee Transmittal

Application Number:	11367238
Filing Date:	03-Mar-2006
Title of Invention:	Solvent system for enhancing the solubility of pharmaceutical agents
First Named Inventor/Applicant Name:	Nachiappan Chidambaram
Filer:	Michael John Terapane/Candace Andrews
Attorney Docket Number:	BAN 102

Filed as Large Entity

Utility under 35 USC 111(a) Filing Fees

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Basic Filing:				
Pages:				
Claims:				
Miscellaneous-Filing:				
Petition:				
Patent-Appeals-and-Interference:				
Post-Allowance-and-Post-Issuance:				
Extension-of-Time:				
Extension - 2 months with $130 paid	1252	1	360	360

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Miscellaneous:				
		Total in USD ($)		**360**

Electronic Acknowledgement Receipt

EFS ID:	8836848
Application Number:	11367238
International Application Number:	
Confirmation Number:	5524
Title of Invention:	Solvent system for enhancing the solubility of pharmaceutical agents
First Named Inventor/Applicant Name:	Nachiappan Chidambaram
Customer Number:	23579
Filer:	Michael John Terapane/Candace Andrews
Filer Authorized By:	Michael John Terapane
Attorney Docket Number:	BAN 102
Receipt Date:	15-NOV-2010
Filing Date:	03-MAR-2006
Time Stamp:	15:34:31
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	Deposit Account
Payment was successfully received in RAM	$360
RAM confirmation Number	2147
Deposit Account	503129
Authorized User	

File Listing:

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

1	Extension of Time	BAN_102_Petition_for_a_Two_Month_Extension_of_Time.pdf	89195 064fe5b5d9b4b7994b1b68b9d4d5a1d5b84db361	no	1
Warnings:					
Information:					
2	Request for Continued Examination (RCE)	BAN_102_Request_for_Continued_Examination.pdf	102660 834c75051dc93e263d6e69ea29dab38face5092e	no	1
Warnings:					
This is not a USPTO supplied RCE SB30 form.					
Information:					
3	Fee Worksheet (PTO-875)	fee-info.pdf	30122 7cba47b30130f2ecba61f5d291cc1ce44917bdc0	no	2
Warnings:					
Information:					
		Total Files Size (in bytes):	221977		

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

New Applications Under 35 U.S.C. 111

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

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

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

New International Application Filed with the USPTO as a Receiving Office

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

PTO/SB/22 (07-09)
Approved for use through 07/31/2012. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARMENT OF COMMERCE

PETITION FOR EXTENSION OF TIME UNDER 37 CFR 1.136(a) **FY 2009** ***(Fees pursuant to the Consolidated Appropriations Act, 2005 (H.R. 4818).)***	Docket Number (Optional) BAN 102
Application Number 11/367,238	Filed March 3, 2006
For SOLVENT SYSTEM FOR ENHANCING THE SOLUBILITY OF PHARMACEUTICAL AGENTS	
Art Unit 1618	Examiner Jake Minh Vu

This is a request under the provisions of 37 CFR 1.136(a) to extend the period for filing a reply in the above identified application.

The requested extension and fee are as follows (check time period desired and enter the appropriate fee below):

	Fee	Small Entity Fee	
☐ One month (37 CFR 1.17(a)(1))	$130	$65	$
☑ Two months (37 CFR 1.17(a)(2))	$490	$245	$ 360*
☐ Three months (37 CFR 1.17(a)(3))	$1110	$555	$
☐ Four months (37 CFR 1.17(a)(4))	$1730	$865	$
☐ Five months (37 CFR 1.17(a)(5))	$2350	$1175	$

☐ Applicant claims small entity status. See 37 CFR 1.27.

☐ A check in the amount of the fee is enclosed.

☐ Payment by credit card. Form PTO-2038 is attached.

*Applicant previously paid for a one-month extension of time in the amount of $130.00 on October 22, 2010.

☐ The Director has already been authorized to charge fees in this application to a Deposit Account.

☑ The Director is hereby authorized to charge any fees which may be required, or credit any overpayment, to Deposit Account Number 50-3129.

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.

I am the

☐ applicant/inventor.

☐ assignee of record of the entire interest. See 37 CFR 3.71.
Statement under 37 CFR 3.73(b) is enclosed (Form PTO/SB/96).

☑ attorney or agent of record. Registration Number 57,633

☐ attorney or agent under 37 CFR 1.34.
Registration number if acting under 37 CFR 1.34 _____

/Michael J. Terapane, Ph.D., J.D./	November 15, 2010
Signature	Date
Michael J. Terapane, Ph.D., J.D.	404-879-2155
Typed or printed name	Telephone Number

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

☐ Total of _____ forms are submitted.

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
11/367,238	03/03/2006	

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 11/15/2010	(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))	* 36	Minus	** 38	= 0	X $ =		OR	X $52=	0
Independent (37 CFR 1.16(h))	* 3	Minus	***5	= 0	X $ =		OR	X $220=	0
☐ Application Size Fee (37 CFR 1.16(s))									
☐ FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))							OR		
					TOTAL ADD'L FEE		OR	TOTAL ADD'L FEE	0

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

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

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

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

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

Legal Instrument Examiner:
/WILLIAM N. PHILLIPS/

Document code: WFEE

United States Patent and Trademark Office
Sales Receipt for Accounting Date: 11/22/2010

WPHILLIP SALE #00000023 Mailroom Dt: 11/15/2010 503129 11367238
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United States Patent and Trademark Office
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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
11/367,238	03/03/2006	Nachiappan Chidambaram	BAN 102	5524

23579 7590 12/02/2010

Pabst Patent Group LLP
1545 PEACHTREE STREET NE
SUITE 320
ATLANTA, GA 30309

EXAMINER	
VU, JAKE MINH	
ART UNIT	PAPER NUMBER
1618	
MAIL DATE	DELIVERY MODE
12/02/2010	PAPER

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

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

Interview Summary	Application No.	Applicant(s)	
	11/367,238	CHIDAMBARAM ET AL.	
	Examiner	Art Unit	
	JAKE M. VU	1618	

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

(1) *JAKE M. VU*. (3)_____.

(2) *Michael Terapane (App's rep)*. (4)_____.

Date of Interview: *30 November 2010*.

Type: a)☒ Telephonic b)☐ Video Conference
c)☐ Personal [copy given to: 1)☐ applicant 2)☐ applicant's representative]

Exhibit shown or demonstration conducted: d)☐ Yes e)☐ No.
If Yes, brief description: _____.

Claim(s) discussed: _____.

Identification of prior art discussed: _____.

Agreement with respect to the claims f)☐ was reached. g)☐ was not reached. h)☒ N/A.

Substance of Interview including description of the general nature of what was agreed to if an agreement was reached, or any other comments: *Discussed the amendments of the claims and the RCE status*.

(A fuller description, if necessary, and a copy of the amendments which the examiner agreed would render the claims allowable, if available, must be attached. Also, where no copy of the amendments that would render the claims allowable is available, a summary thereof must be attached.)

THE FORMAL WRITTEN REPLY TO THE LAST OFFICE ACTION MUST INCLUDE THE SUBSTANCE OF THE INTERVIEW. (See MPEP Section 713.04). If a reply to the last Office action has already been filed, APPLICANT IS GIVEN A NON-EXTENDABLE PERIOD OF THE LONGER OF ONE MONTH OR THIRTY DAYS FROM THIS INTERVIEW DATE, OR THE MAILING DATE OF THIS INTERVIEW SUMMARY FORM, WHICHEVER IS LATER, TO FILE A STATEMENT OF THE SUBSTANCE OF THE INTERVIEW. See Summary of Record of Interview requirements on reverse side or on attached sheet.

/Jake M. Vu/ Primary Examiner, Art Unit 1618	

Summary of Record of Interview Requirements

Manual of Patent Examining Procedure (MPEP), Section 713.04, Substance of Interview Must be Made of Record
A complete written statement as to the substance of any face-to-face, video conference, or telephone interview with regard to an application must be made of record in the application whether or not an agreement with the examiner was reached at the interview.

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

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

37 CFR §1.2 Business to be transacted in writing.
All business with the Patent or Trademark Office should be transacted in writing. The personal attendance of applicants or their attorneys or agents at the Patent and Trademark Office is unnecessary. The action of the Patent and Trademark Office will be based exclusively on the written record in the Office. No attention will be paid to any alleged oral promise, stipulation, or understanding in relation to which there is disagreement or doubt.

———

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

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

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

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

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

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

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

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

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

Examiner to Check for Accuracy

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

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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23579 7590 03/11/2011

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EXAMINER	
VU, JAKE MINH	
ART UNIT	**PAPER NUMBER**
1618	
MAIL DATE	**DELIVERY MODE**
03/11/2011	PAPER

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

Office Action Summary	Application No.	Applicant(s)	
	11/367,238	CHIDAMBARAM ET AL.	
	Examiner	Art Unit	
	JAKE VU	1618	

-- 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 *15 November 2010*.

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

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

Disposition of Claims

4)☒ Claim(s) *1-4,6-14,16-22 and 24-39* is/are pending in the application.

4a) Of the above claim(s) *14 and 16-18* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,6-13,19-22 and 24-39* 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

Receipt is acknowledged of Applicant's Request for Continued Examination filed on 11/15/2010; and Amendment filed on 10/22/2010.

- Claims 1, 6-7, 14, 18-19, 24-25, 38 have been amended.
- Claim 39 has been added.
- Claims 5, 15, 23 have been cancelled.
- Claims 1-4, 6-14, 16-22, 24-39 are pending in the instant application.
- Claims 14, 16-18 have been previously withdrawn from consideration.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 11/15/2010 has been entered.

Claim Rejections - 35 USC § 112, 1st paragraph

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.

Claim 38 rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, pertaining to the new matter rejection of the terms "about 65% polyethylene glycol 600 by weight, about 24% (wt/wt) naproxen sodium by weight, about 4.8% of 88-92% lactic acid by weight, about 1.9% propylene glycol by weight, and about 1.9% polyvinyl pyrrolidone K-30 by weight", **is withdrawn** in view of Applicant's Amendment.

Claim Rejections - 35 USC § 112, 2nd paragraph

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.

Claim 38 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, pertaining to the uncertainty of the limitation of "about 4.8% of 88-92% lactic acid by weight", **is withdrawn** in view of Applicant's Amendment.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4, 6-13 and 19-22, 24-31 are rejected under 35 U.S.C. 102(b) as being anticipated by YU et al (5,360,615) **are maintained** for reasons of record in the previous office action filed on 12/01/2009, 07/14/2010 and as discussed below.

Applicant argues that Yu does not disclose or suggest a pharmaceutical composition comprising (a) a salt of one or more either acidic or basic pharmaceutically active agents; and (b) a deionizing agent, which at least partially neutralizes the pharmaceutically active agent, wherein when the active agent is a salt of a weak acid and a strong base, the deionizing agent is a hydrogen ion species and when the active agent is a salt of a weak base and a strong acid, the deionizing agent is a hydroxide ion species.

The Examiner finds this argument unpersuasive, because the newly added limitation of "wherein when the active agent is a salt *of a weak acid and a strong base*, the deionizing agent is a hydrogen ion species and when the active agent is a salt *of a weak base and a strong acid*, the deionizing agent is a hydroxide ion species" does not add any limits to claim. For instance, the newly added limitation only states that the active agent is a salt made by the reaction of either "a weak acid and a strong base" or by "a weak base and a strong acid". These are the only two reactions that make a salt; thus, this limitation does not limit the active agent to be acidic or basic. In summation, the newly added limitation only recites that the salt of the active agent is neutralized by hydrogen or hydroxide ion species.

Note, as discussed in the previous office action, deionizing agent is a broad term which would include water, wherein water would have a hydrogen ions and hydroxide

ions an H2O; and every salt form would have ions and salts with the reaction going back and forth. The Examiner is providing basic chemistry background in the prior art, such as "Self-ionization of water" in Wikipedia teaches:

"Water molecules dissociate into equal amounts of H_3O^+ and OH^-, so their concentrations are equal to ca. 1.0×10^{-7} mol dm^{-3}. A solution in which the H_3O^+ and OH^- concentrations equal each other is considered a neutral solution. Pure water is neutral, but most water samples contain impurities. If an impurity is an acid or base this will affect the concentrations of hydronium ion and hydroxide ion. Water samples which are exposed to air will absorb the acid carbon dioxide and the concentration of H_3O^+ will increase. The concentration of OH^- will decrease in such a way that the product $[H_3O^+][OH^-]$ remains constant."

Claims 1-4, 6-13 and 19-22, 24-35 are rejected under 35 U.S.C. 102(b) as being anticipated by SAWYER et al (US 6,383,515) **are maintained** for reasons of record in the previous office action filed on 07/14/2010 and as discussed below.

Applicant argues that potassium hydroxide and sodium propionate are not deionizing agents.

The Examiner finds this argument unpersuasive, because as discussed in the previous office action, the sodium propionate is a solution in water, since it is dissolved completely (see col. 14, line 21), wherein the solution would inherently contain sodium propionate, sodium ions, propionate anions, and propionic acid, which is a deionizing

agent as claimed by Applicant. Note, it's well known in chemistry that the ionization and deionization of a salt is continuous going back and forth.

Applicant argues that Sawyer does not disclose a salt of an either acidic or basic drug and a deionizing agent as required by the claims.

The Examiner finds this argument unpersuasive, because the naproxen sodium is the salt of an acidic drug and the sodium propionate in water would inherently have propionic acid, which is a deionizing agent as claimed by Applicant.

Claims 1-2, 4, 8-13, 19-20, 22, 26-35 are rejected under 35 U.S.C. 102(b) as being anticipated by MITRA et al (US 5,648,358) **are withdrawn** in view of Applicant's Amendment.

However, upon further consideration of Applicant's Amendment, a new ground(s) of rejection is made as discussed below.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4, 6, 8-13, 19-22, 24, 26-35, 38-39 rejected under 35 U.S.C. 102(b) as being anticipated by CUPPS et al (US 5,541,210).

CUPPS teaches a composition comprising of: a salt of an active agent, such as 220mg of naproxen sodium (see col. 28, line 66); a deionizing agent, such as 50mg of citric acid (see col. 29, line 12), which is about 0.2-1.0 mole equivalent of naproxen sodium; 3000mg of polyethylene glycol (see col. 29, line 8), which is about 10% by weight; 3800mg of water (see col. 29, line 14), which is about 13% weight; excipients, such as 3000mg of propylene glycol (see col. 29, line 9), which is a solubilizer and is about 10% by weight. Additional disclosures include: preferred composition include softgel capsules (see col. 19, line 4).

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.

Claims 1-4, 6-13, 19-22, 24-39 are rejected under 35 U.S.C. 103(a) as being unpatentable over SAWYER et al (US 6,383,515) in view of McENTEE et al (US 5,885,608) **are maintained** for reasons of record in the previous office action filed on 07/14/2010 and as discussed below.

Applicant argues that potassium hydroxide and sodium propionate are not deionizing agents.

The Examiner finds this argument unpersuasive, because as discussed in the previous office action, the sodium propionate is a solution in water, since it is dissolved

completely (see col. 14, line 21), wherein the solution would inherently contain sodium propionate, sodium ions, propionate anions, and propionic acid, which is a deionizing agent as claimed by Applicant. Note, it's well known in chemistry that the ionization and deionization of a salt is continuous going back and forth.

Applicant argues that Sawyer does not disclose a salt of an either acidic or basic drug and a deionizing agent as required by the claims.

The Examiner finds this argument unpersuasive, because the naproxen sodium is the salt of an acidic drug and the sodium propionate in water would inherently have propionic acid, which is a deionizing agent as claimed by Applicant.

Applicant argues that one of ordinary skill in the art would not be motivated to modify Sawyer to arrive at the claimed compositions since Sawyer discloses ionizing the active agent, not deionizing the active agent as required by the claims. Sawyer teaches away from the claimed compositions.

The Examiner finds this argument unpersuasive, because SAWYER teaches ionizing the free form of the medicament, which would make the salt form of the active agent, which is the same salt form as claimed by Applicant.

Telephonic Inquiries

Any inquiry concerning this communication or earlier communications from the examiner should be directed to JAKE VU whose telephone number is (571)272-8148. The examiner can normally be reached on Mon-Tue and Thu-Fri 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Hartley can be reached on (571) 272-0616. 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.

/Jake M. Vu/
Primary Examiner, Art Unit 1618

Notice of References Cited	Application/Control No. 11/367,238	Applicant(s)/Patent Under Reexamination CHIDAMBARAM ET AL.	
	Examiner JAKE VU	Art Unit 1618	Page 1 of 1

U.S. PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Name	Classification
*	A	US-5,541,210	07-1996	Cupps et al.	514/394
	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	Wikipedia (Self-ionization of water at http://en.wikipedia.org/wiki/Self-ionization_of_water (March 2010)
	V	
	W	
	X	

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

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
11/367,238	03/03/2006	Nachiappan Chidambaram	BAN 102	5524

23579 7590 06/13/2011

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

Interview Summary	Application No.	Applicant(s)
	11/367,238	CHIDAMBARAM ET AL.
	Examiner	Art Unit
	JAKE VU	1618

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

(1) *JAKE VU*.	(3)_____.
(2) *Michael Terrapine (App's Rep)*.	(4)_____.

Date of Interview: *06 June 2011*.

Type: a)☐ Telephonic b)☐ Video Conference
c)☒ Personal [copy given to: 1)☐ applicant 2)☐ applicant's representative]

Exhibit shown or demonstration conducted: d)☐ Yes e)☐ No.
If Yes, brief description: _____.

Claim(s) discussed: *claims of record*.

Identification of prior art discussed: _____.

Agreement with respect to the claims f)☐ was reached. g)☐ was not reached. h)☒ N/A.

Substance of Interview including description of the general nature of what was agreed to if an agreement was reached, or any other comments: *Discussed the broad interpreation of the functional term "deionized" and "partially"; and possible amendments. Discussed that Applicantion's Title and specification disclosed enhancing solubility of pharmacutical agents, but provide no solubility data. The Examienr would like to see some data* .

(A fuller description, if necessary, and a copy of the amendments which the examiner agreed would render the claims allowable, if available, must be attached. Also, where no copy of the amendments that would render the claims allowable is available, a summary thereof must be attached.)

THE FORMAL WRITTEN REPLY TO THE LAST OFFICE ACTION MUST INCLUDE THE SUBSTANCE OF THE INTERVIEW. (See MPEP Section 713.04). If a reply to the last Office action has already been filed, APPLICANT IS GIVEN A NON-EXTENDABLE PERIOD OF THE LONGER OF ONE MONTH OR THIRTY DAYS FROM THIS INTERVIEW DATE, OR THE MAILING DATE OF THIS INTERVIEW SUMMARY FORM, WHICHEVER IS LATER, TO FILE A STATEMENT OF THE SUBSTANCE OF THE INTERVIEW. See Summary of Record of Interview requirements on reverse side or on attached sheet.

/Jake M. Vu/ Primary Examiner, Art Unit 1618		

Summary of Record of Interview Requirements

Manual of Patent Examining Procedure (MPEP), Section 713.04, Substance of Interview Must be Made of Record
A complete written statement as to the substance of any face-to-face, video conference, or telephone interview with regard to an application must be made of record in the application whether or not an agreement with the examiner was reached at the interview.

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

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

37 CFR §1.2 Business to be transacted in writing.
All business with the Patent or Trademark Office should be transacted in writing. The personal attendance of applicants or their attorneys or agents at the Patent and Trademark Office is unnecessary. The action of the Patent and Trademark Office will be based exclusively on the written record in the Office. No attention will be paid to any alleged oral promise, stipulation, or understanding in relation to which there is disagreement or doubt.

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

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

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

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

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

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

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

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

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

Examiner to Check for Accuracy

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

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Nachiappan Chidambaram and Aqeel Fatmi

Serial No.: 11/367,238 Art Unit: 1618

Filed: March 3, 2006 Examiner: Jake Minh Vu

For: *SOLVENT SYSTEM FOR ENHANCING THE SOLUBILITY OF PHARMACEUTICAL AGENTS*

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

AMENDMENT AND RESPONSE

Sir:

Responsive to the Office Action mailed on March 11, 2011, please amend the application as follows. A Petition for a Two Month extension of time is submitted with this Amendment and Response extending the time to respond to August 11, 2011. The Commissioner is authorized to charge $490.00, the fee for the Petition for a Two Month extension of time for a large entity to Deposit Account No. 50-3129.

It is believed that no additional fee is required with this submission. However, should an additional a fee be required, the Commissioner is hereby authorized to charge the fee to Deposit Account No. 50-3129.

Amendment

In the Specification

Please replace the current title of the application with "Solvent System for Salts of Pharmaceutical Agents".

In the Claims

1. (currently amended) A pharmaceutical composition comprising

(a) a salt of one or more either acidic or basic pharmaceutically active agents; and

(b) a deionizing agent in an amount from about 0.2 to about 1.0 mole equivalents per mole of the pharmaceutically active agent(s), which at least partially neutralizes the pharmaceutically active agent; ~~and~~

(c) polyethylene glycol; and optionally

(d) water;

wherein when the ~~active agent~~ salt is a salt of a weak acid and a strong base, the deionizing agent is a hydrogen ion species and when the ~~active agent~~ salt is a salt of a weak base and a strong acid, the deionizing agent is a hydroxide ion species.

2. (original) The composition of claim 1 wherein the pharmaceutically active agent is selected from the group consisting of therapeutically active agents, diagnostic agents, and prophylactic agents.

3. (canceled) The composition of claim 1 wherein the deionizing agent is present in an amount from about 0.2 to 1.0 mole equivalents per mole of the pharmaceutically active agent(s).

4. (canceled) The composition of claim 1 wherein the deionizing agent is selected from the group consisting of hydrogen ion and hydroxide ion.

5. (canceled)

6. (previously presented) The composition of claim 1 wherein polyethylene glycol is present in an amount from about 10% to about 80% by weight.

7. (previously presented) The composition of claim 1 wherein polyethylene glycol is one or more polyethylene glycols with a molecular weight between 300 and 1500.

8. (original) The composition of claim 1 further comprising water.

9. (original) The composition of claim 8 wherein water is present in an amount from about 1% to about 18% by weight.

10. (original) The composition of claim 1 further comprising one or more excipients.

11. (previously presented) The composition of claim 10, wherein the one or more excipients are selected from the group consisting of plasticizers, crystallization inhibitors, wetting agents, bulk filling agents, solubilizers, bioavailability enhancers, solvents, pH-adjusting agents, dyes, preservatives, surfactants, and combinations thereof.

12. (original) The composition of claim 11 wherein the solubilizer is selected from the group consisting of glycerin, polyvinylpyrrolidone, propylene glycol and combinations thereof.

13. (original) The composition of claim 12 wherein the solubilizer is present in amount from about 1% to about 10% by weight.

14. (withdrawn-currently amended) A method of making the capsule of claim 19 comprising

(a) mixing ~~the~~ a salt of one or more acidic or basic pharmaceutically active agents, ~~the~~ a deionizing agent in an amount from about 0.2 to about 1.0 mole equivalents per mole of the pharmaceutically active agent(s), which at least partially neutralizes the pharmaceutically active agent, and polyethylene glycol at an appropriate temperature; and

(b) encapsulating the mixture in a softgel capsule.

15. (canceled)

16. (withdrawn) The method of claim 14 further comprising water.

17. (withdrawn) The method of claim 14 wherein the appropriate temperature is from about 50°C to about 70°C.

18. (withdrawn-previously presented) A method of using the pharmaceutical composition of claim 1 or the capsule of claim 19 or 38 comprising

administering to a patient in need thereof an effective amount of the composition of claim 1 or the capsule of claim 19 or 38.

19. (currently amended) A softgel capsule comprising a fill material wherein the fill material comprises

(a) a salt of one or more either acidic or basic pharmaceutically active agents; and

(b) a deionizing agent in an amount from about 0.2 to about 1.0 mole equivalents per mole of the pharmaceutically active agent(s), which at least partially neutralizes the pharmaceutically active agent; ~~and~~

(c) polyethylene glycol; and optionally

(d) water;

wherein, when the ~~active agent~~ salt is a salt of a weak acid and a strong base, the deionizing agent is a hydrogen ion species and when the ~~active agent~~ salt is a salt of a weak base and a strong acid, the deionizing agent is a hydroxide ion species.

20. (original) The capsule of claim 19 wherein the pharmaceutically active agent is selected from the group consisting of therapeutically active agents, diagnostic agents, and prophylactic agents.

21. (canceled) The capsule of claim 19 wherein the deionizing agent is present in an amount from about 0.2 to 1.0 mole equivalents per mole of the pharmaceutically active agent(s).

22. (canceled) The capsule of claim 19 wherein the deionizing agent is selected from the group consisting of hydrogen ion and hydroxide ion.

23. (canceled)

24. (previously presented) The capsule of claim 19 wherein polyethylene glycol is present in an amount from about 10% to about 80% by weight

25. (previously presented) The capsule of claim 19 wherein polyethylene glycol is one or more polyethylene glycols with a molecular weight between 300 and 1500.

26. (original) The capsule of claim 19 further comprising water.

27. (original) The capsule of claim 26 wherein water is present in an amount from about 1% to about 18% by weight.

28. (original) The capsule of claim 19 further comprising one or more excipients.

29. (previously presented) The capsule of claim 28 wherein the one or more excipients are selected from the group consisting of plasticizers, crystallization inhibitors, wetting agents, bulk filling agents, solubilizers, bioavailability enhancers, solvents, pH-adjusting agents, dyes, preservatives, surfactants, and combinations thereof.

30. (original) The capsule of claim 29 wherein the solubilizer is selected from the group consisting of glycerin, polyvinylpyrrolidone, propylene glycol and combinations thereof.

31. (original) The capsule of claim 29 wherein the solubilizer is present in amount from about 1% to about 10% by weight.

32. (previously presented) The composition of claim 1 wherein the pharmaceutically active agent is naproxen sodium and the deionizing agent is a hydrogen ion species.

33. (previously presented) The composition of claim 19 wherein the pharmaceutically active agent is naproxen sodium and the deionizing agent is a hydrogen ion species.

34. (previously presented) The composition of claim 32 wherein the hydrogen ion species is selected from the group consisting of hydrochloric acid, hydrobromic acid, hydroiodic acid, sulfuric acid, fumaric cid, maleic acid, tartaric acid, methane-, ethane-, and benzene sulfonates, citric acid, malic acid, acetic acid, proprionic acid, pyruvic acid, butanoic acid, and lactic acid.

35. (previously presented) The composition of claim 33 wherein the hydrogen ion species is selected from the group consisting of hydrochloric acid, hydrobromic acid, hydroiodic acid, sulfuric acid, fumaric cid, maleic acid, tartaric acid, methane-, ethane-, and benzene sulfonates, citric acid, malic acid, acetic acid, proprionic acid, pyruvic acid, butanoic acid, and lactic acid.

36. (previously presented) The composition of claim 34 wherein the hydrogen ion species is lactic acid.

37. (previously presented) The composition of claim 35 wherein the hydrogen ion species is lactic acid.

38. (currently amended) A softgel capsule comprising a fill material comprising from about 10% to about 80% by weight polyethylene glycol having a molecular weight between 300 and 1500, about 10% to about 50% by weight naproxen sodium, and about 0.2 to about 1.0 moles of a deionizing agent per mole of naproxen sodium, which at least partially neutralizes the naproxen sodium.

39. (previously presented) The softgel capsule of claim 38 wherein the deionizing agent is selected from the group consisting of hydrochloric acid, hydrobromic acid, hydroiodic acid, sulfuric acid, fumaric cid, maleic acid, tartaric acid, methane-, ethane-, and benzene sulfonates, citric acid, malic acid, acetic acid, proprionic acid, pyruvic acid, butanoic acid, and lactic acid.

40. (new) A pharmaceutical composition prepared by a method comprising

(a) mixing a salt of one or more acidic or basic pharmaceutically active agents;

(b) a deionizing agent in an amount from about 0.2 to about 1.0 mole equivalents per mole of the salt of the pharmaceutically active agent(s), which at least partially neutralizes the salt of pharmaceutically active agent;

(c) polyethylene glycol: and optionally

(d) water

wherein when the salt (a) is a salt of a week acid and a strong base, the deionizing agent is a hydrogen ion species, and when the salt (a) is the salt of a weak base and a strong acid, the deionizing agent is a hydroxide ion species.

41. (new) A softgel capsule prepared by a method comprising

(a) producing a fill material by mixing

(i) a salt of one or more acidic or basic pharmaceutically active agents;

(ii) a deionizing agent in an amount from about 0.2 to about 1.0 mole equivalents per mole of the pharmaceutically active agent(s) to cause partial deionization of the salt of the pharmaceutically active agent(s);

(iii) polyethylene glycol: and optionally

(iv) water; and

(b) encapsulating the mixture in a softgel capsule;

wherein when the salt (a) is a salt of a weak acid and a strong base, the deionizing agent is a hydrogen ion species, and when the salt (a) is the salt of a weak base and a strong acid, the deionizing agent is a hydroxide ion species.

Remarks

The undersigned would like to thank Examiner Vu for his time during the in person interview on June 6, 2011. During the interview, the undersigned and Examiner Vu discussed the cited art and amendments for further distinguishing the prior art.

Independent claims 1, 14, 18, 19, and 38 are amended to incorporate the limitation of claim 3 and to recite that the composition optionally contains water. Support for this amendment is found in claim 8 as originally filed and the examples.

Claims 3, 4, 21, and 22 are canceled.

New claims 40 and 41 are added. Support for these claims is found in the examples and at page 9, line 5 to page 10, line 21.

In the event this Amendment and Response does not overcome the Examiner's rejections, the undersigned requests a telephonic interview with Examiner Vu and his supervisor prior to issuing an Office Action.

Rejection Under 35 U.S.C. § 102

Claims 1-4, 6-13, 19-22, and 24-31 were rejected under 35 U.S.C. § 102(b) as being anticipated by U.S. Patent No. 5,360,615 to Yu ("Yu"). Claims 1-4, 6-13, 19-22, and 24-35 were rejected under 35 U.S.C. § 102(b) as being anticipated by U.S. Patent No. 6,383,515 to Sawyer et al. ("Sawyer"). Claims 1-4, 6, 8-13, 19-22, 24, 26-35, 38, and 39 were rejected under 35 U.S.C.

§ 102(b) as being anticipated by U.S. Patent No. 5,541,210 to Cupps et al ("Cupps"). Applicants respectfully traverse these rejections.

Legal Standard

For a rejection of claims to be properly founded under 35 U.S.C. § 102, it must be established that a prior art reference discloses each and every element of the claims and enables one of skill in the field of the invention to make and use the claimed invention. *Xerox Corp. v. 3Com Corp.*, 458 F.3d 1310, 1322 (Fed. Cir. 2006) ("[I]nvalidity by anticipation requires that the four corners of a single, prior art document describe every element of the claimed invention.") *quoting Advanced Display Sys., Inc. v. Kent State Univ.*, 212 F.3d 1272, 1282 (Fed. Cir. 2000); *Merck & Co. v. Teva Pharmaceuticals USA, Inc.*, 347 F.3d 1367, 1372, 68 USPQ2d 185 (Fed. Cir. 2003) ("An 'anticipating' reference must describe all of the elements and limitations of the claim in a single reference, and enable one of skill in the field of the invention to make and use the claimed invention."); *RCA Corp. v. Applied Digital Data Sys., Inc.*, 730 F.2d 1440, 1444, 221 USPQ 385, 388 (Fed. Cir. 1984) ("Anticipation is established only when a single prior art reference discloses, expressly or under principles of inherency, each and every element of a claimed invention."). A reference that fails to disclose or enable even one limitation will therefore not be found to anticipate, even if the missing limitation could be discoverable through further experimentation.

Analysis

Independent claims 1, 14, 18, 19, 38, 40, and 41 are amended to recite that the deionizing agent is present in an amount from 0.2 to 1.0 mole equivalents of the pharmaceutically active agent(s) and that the composition optionally contains water. The amendments to the claims make clear that the deionizing agent and water, if present, are separate components of the composition. Therefore, independent claims 1, 14, 18, 19, 38, 40, and 41, and the claims dependent thereon, are novel over the cited references for at least the reasons discussed below.

The Applicants appreciate Examiner Vu's acknowledgement that claims 32-39 are novel over Yu, claims 36-39 are novel over Sawyer, and 36 and 37 are novel over Cupps.

Yu

Yu does not disclose or suggest a pharmaceutical composition comprising (a) a salt of one or more either acidic or basic pharmaceutically active agents; and (b) a deionizing agent in an amount from 0.2 to 1.0 mole equivalents of the pharmaceutically active agent(s), which at least partially neutralizes the pharmaceutically active agent, wherein when the active agent is a salt of a weak acid and a strong base, the deionizing agent is a hydrogen ion and when the active agent is a salt of a weak base and a strong acid, the deionizing agent is a hydroxide ion generating species.

In the Office Action, the Examiner alleges that the argument above is unpersuasive because the limitation regarding the relationship between the salt and the deionizing agent does

not limit the claim. Applicants respectfully disagree. The limitation in question defines the nature of the deionizing agent required to partially deionize or neutralize the active agent.

The Examiner further alleges that the term "deionizing agent" is a broad term which can include water. It is not clear how this argument is derived from Yu. Yu discloses compositions containing a neutral active agent and an ionizing agent (*see* the abstract, col. 4, lines 26-35, and the examples). While some of the examples contain water, many of the examples do not contain water. Moreover, for those examples that do contain water, water is present in addition to the ionizing agent. Yu clearly recognizes that water alone is not sufficient to ionize the active agent; an additional agent is necessary to form the salt. For example, Example 1 contains ibuprofen, potassium hydroxide, and water. The combination of sodium hydroxide and water results in hydroxide as the dominant species in solution with little H^+ present in solution. Therefore, the water in Example 1 in Yu cannot act at as a deionizing agent as required by independent claims 1, 14, 18, 19, 38, 40, and 41 and the claims dependent thereon. Yu also does not disclose the concentration of the deionizing agent recited in independent claims 1, 14, 18, 19, 38, 40, and 41 and the claims dependent thereon.

Further, water alone cannot generate the amount of deionizing agent recited in independent claims 1, 14, 18, 19, 38, 40, and 41. At 25°C, the dissociation constant of water, K_w, is 1.0×10^{-14}. Water molecules dissociate into equal amounts of H_3O^+ and ^-OH. Thus, the

concentrations of H_3O^+ and ^-OH are 1.0×10^{-7}. Therefore, water does not dissociate sufficiently to produce the concentration of the H_3O^+ or ^-OH recited in the claims.

Yu does not disclose or suggest a softgel capsule comprising a salt of an acidic or basic active agent and a deionizing agent having the concentration specified in claim 38 and the claims dependent thereon for at least the reasons discussed above.

Accordingly, claims 1-13, 19-21, 38, and 39, as amended, are novel over Yu. New claims 40 and 41 are novel over Yu for at least the reasons discussed above.

Sawyer

Sawyer describes a pharmaceutically acceptable solution containing a medicament and a solvent (abstract). The solvent contains a polymer and an acid salt of a compound having at least three or more carbon atoms (abstract). Sawyer discloses that the salt of the organic acid ionizes the medicament. Ionization is the opposite of deionization, as recited in the pending claims.

The Examiner specifically cited Example 17 in Sawyer. Example 17 is a formulation containing naproxen sodium, polyethylene glycol, potassium hydroxide, and sodium propionate. Potassium hydroxide and sodium propionate are bases, i.e., ionizing agents, which function to maintain naproxen as the sodium salt. The Examiner specifically alleges that because sodium propionate is used as a solution in water (500 g sodium propionate in 700 mL of water), the solution would inherently contain sodium propionate, sodium ions, propionate anions, and propionic acid. The pH of the sodium propionate solution in Example 17 is 9.6, which is

strongly basic. Moreover, this solution is used in combination with a solution of 6.8 g KOH (a strong base) in 100 mL of water. Thus the predominant species in solution will be ^{-}OH and propionate. Therefore, the concentration of H^{+} is well outside the range recited in independent claims 1, 14, 18, 19, 38, 40, and 41. Sawyer does not disclose a salt of an either acidic or basic drug and a deionizing agent as recited in the claims.

Sawyer does not disclose or suggest a softgel capsule comprising a salt of an acidic or basic active agent and a deionizing agent having the concentration specified in claim 38 and the claims dependent thereon for at least the reasons discussed above.

Accordingly, claims 1-13, 19-35, 38, and 39, and new claims 40 and 41, are novel over Sawyer.

Cupps

The Examiner alleges that Example R anticipates the claims. Specifically, the Examiner alleges that Example R contains naproxen sodium and citric acid. The Examiner has not considered Example R in its entirety. Examiner R contains citric acid in combination with sodium citrate. Sodium citrate is present in molar excess to citric acid. Therefore, the predominant species in solution is a base. The concentration of H^{+} is well outside the range recited in independent claims 1, 14, 18, 19, 38, 40, and 41. Cupps does not disclose or suggest a composition containing a salt of an active agent and a deionizing agent as recited in the claims.

Cupps does not disclose or suggest a softgel capsule comprising a salt of an acidic or basic active agent and a deionizing agent having the concentration specified in claim 38 and the claims dependent thereon for at least the reasons discussed above. In fact, the Example cited by the Examiner described an oral solution not a softgel capsule.

Accordingly, claims 1-4, 6, 8-13, 19-22, 24, 26-35, 38, and 39, and new claims 40 and 41, are novel over Cupps.

Rejection Under 35 U.S.C. § 103

Claims 1-4, 6-13, 19-22, and 24-39 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Sawyer, in view of U.S. Patent No. 6,383,515 to McEntee. Applicants respectfully traverse this rejection.

Legal Standard

The starting point for an obviousness determination must be the Supreme Court's decision in *KSR v. Teleflex,* 550 U.S. 398 (2007), which refocuses the determination of whether a claimed invention is obvious back to the process the Court had defined in *Graham v. John Deere Co. of Kansas City*, 383 U.S. 1, 17-18 (1966). There, the Court had held that the obviousness determination should address four factors, all of which must be considered, though not in any prescribed order: (1) the scope and content of the prior art; (2) the level of ordinary skill in the art; (3) the differences between the claimed invention and the prior art; and (4) any secondary considerations suggesting nonobviousness, such as commercial success, failure of others, and

long felt but unmet need. *Id.* The Court cautioned that the fact finder should be careful about reading the teachings of the invention at issue into the prior art, to avoid applying inappropriate hindsight, *ex post* reasoning. *Id. at 36.*

Analysis

Sawyer is discussed above. Sawyer does not disclose or suggest pharmaceutical composition containing the salt of an acidic or basic active agent and a deionizing agent nor a softgel capsule encapsulating the pharmaceutical composition as recited in independent claims 1, 14, 19, 39, 40, and 41 and the claims dependent thereon.

McEntee does not cure the deficiencies of Sawyer.

Sawyer teaches away from the claimed compositions

A reference may be said to teach away when a person of ordinary skill, upon reading the reference, *would be discouraged from following the path set out in the reference, or would be led in a direction divergent from the path that was taken by the applicant* (emphasis added). See *United States v. Adams*, 383 U.S. 39, 52, 148 U.S.P.Q. (BNA) 479, 484, 15 L. Ed. 2d 572, 86 S. Ct. 708 (1966); *W.L. Gore & Assoc., Inc. v. Garlock, Inc.*, 721 F.2d 1540, 1550-51, 220 U.S.P.Q. (BNA) 303, 311 (Fed. Cir. 1983) (the totality of a reference's teachings must be considered), cert. denied, 469 U.S. 851 (1984); *In re Caldwell*, 50 C.C.P.A. 1464, 319 F.2d 254, 256, 138 U.S.P.Q. (BNA) 243, 245 (CCPA 1963).

One of ordinary skill in the art, reading Sawyer, would prepare a composition containing the salt of an active agent and a species which functions to keep the drug ionized by creating a basic environment, not the salt of a drug and deionizing agent which partially deionizes or neutralizes the salt, as recited by the claims. Therefore, one of ordinary skill in the art, reading Sawyer, would be led on a path divergent from the one taken in Sawyer.

Further, modifying Sawyer in the manner suggested by the Examiner would make Sawyer inoperable for its intended purpose, which is improper under 35 U.S.C. § 103, since Sawyer teaches maintaining the ionized form of the drug in the compositions described therein, not partially deionizing or neutralizing the drug as recited in the claims. Accordingly, for at least the reasons discussed above, claims 1-13 and 19-39 are not obvious over Sawyer in view of McEntee.

Allowance of claims 1-4, 6-13, 19-22, and 24-39, as amended, and new claims 40 and 41, is respectfully solicited.

Respectfully submitted,

/Michael J. Terapane, Ph.D., J.D./
Michael J. Terapane, Ph.D., J.D.
Reg. No. 57,633

Date: August 10, 2011

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Electronic Patent Application Fee Transmittal

Application Number:	11367238
Filing Date:	03-Mar-2006
Title of Invention:	Solvent system for enhancing the solubility of pharmaceutical agents
First Named Inventor/Applicant Name:	Nachiappan Chidambaram
Filer:	Michael John Terapane/Candace Andrews
Attorney Docket Number:	BAN 102

Filed as Large Entity

Utility under 35 USC 111(a) Filing Fees

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Basic Filing:				
Pages:				
Claims:				
Miscellaneous-Filing:				
Petition:				
Patent-Appeals-and-Interference:				
Post-Allowance-and-Post-Issuance:				
Extension-of-Time:				
Extension - 2 months with $0 paid	1252	1	490	490

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Miscellaneous:				
		Total in USD ($)		**490**

Electronic Acknowledgement Receipt

EFS ID:	10708752
Application Number:	11367238
International Application Number:	
Confirmation Number:	5524
Title of Invention:	Solvent system for enhancing the solubility of pharmaceutical agents
First Named Inventor/Applicant Name:	Nachiappan Chidambaram
Customer Number:	23579
Filer:	Michael John Terapane/Candace Andrews
Filer Authorized By:	Michael John Terapane
Attorney Docket Number:	BAN 102
Receipt Date:	10-AUG-2011
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File Listing:

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

1	Extension of Time	BAN_102_Petition_for_Two_Month_EOT.pdf	85515 e1f5138ba39d45da7cc2ab230525b599a95b5b31	no	1
Warnings:					
Information:					
2		BAN_102_Amendment_and_Response.pdf	792792 51c3ac677073e148d0f454268d76aadd86c0be10	yes	20

	Multipart Description/PDF files in .zip description		
	Document Description	**Start**	**End**
	Amendment/Req. Reconsideration-After Non-Final Reject	1	1
	Specification	2	2
	Claims	3	10
	Applicant Arguments/Remarks Made in an Amendment	11	20

Warnings:					
Information:					
3	Fee Worksheet (SB06)	fee-info.pdf	30366 43dccd2224099bd721aa443873a2b9d163d03f21	no	2
Warnings:					
Information:					
		Total Files Size (in bytes):	908673		

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

New Applications Under 35 U.S.C. 111

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

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

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

New International Application Filed with the USPTO as a Receiving Office

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

PTO/SB/22 (07-09)
Approved for use through 07/31/2012. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARMENT OF COMMERCE

PETITION FOR EXTENSION OF TIME UNDER 37 CFR 1.136(a) **FY 2009** ***(Fees pursuant to the Consolidated Appropriations Act, 2005 (H.R. 4818).)***	Docket Number (Optional) BAN 102
Application Number 11/367,238	Filed March 3, 2006
For SOLVENT SYSTEM FOR ENHANCING THE SOLUBILITY OF PHARMACEUTICAL AGENTS	
Art Unit 1618	Examiner Jake Minh Vu

This is a request under the provisions of 37 CFR 1.136(a) to extend the period for filing a reply in the above identified application.

The requested extension and fee are as follows (check time period desired and enter the appropriate fee below):

		Fee	Small Entity Fee	
☐	One month (37 CFR 1.17(a)(1))	$130	$65	$
☑	Two months (37 CFR 1.17(a)(2))	$490	$245	$ 490
☐	Three months (37 CFR 1.17(a)(3))	$1110	$555	$
☐	Four months (37 CFR 1.17(a)(4))	$1730	$865	$
☐	Five months (37 CFR 1.17(a)(5))	$2350	$1175	$

☐ Applicant claims small entity status. See 37 CFR 1.27.

☐ A check in the amount of the fee is enclosed.

☐ Payment by credit card. Form PTO-2038 is attached.

☐ The Director has already been authorized to charge fees in this application to a Deposit Account.

☑ The Director is hereby authorized to charge any fees which may be required, or credit any overpayment, to Deposit Account Number 50-3129.

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.

I am the

☐ applicant/inventor.

☐ assignee of record of the entire interest. See 37 CFR 3.71.
Statement under 37 CFR 3.73(b) is enclosed (Form PTO/SB/96).

☑ attorney or agent of record. Registration Number 57,633

☐ attorney or agent under 37 CFR 1.34.
Registration number if acting under 37 CFR 1.34 _____

/Michael J. Terapane, Ph.D., J.D./	August 10, 2011
Signature	Date
Michael J. Terapane, Ph.D., J.D.	404-879-2155
Typed or printed name	Telephone Number

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

☐ Total of _____ forms are submitted.

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
11/367,238	03/03/2006	

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))							
			TOTAL			TOTAL	

* If the difference in column 1 is less than zero, enter "0" in column 2.

APPLICATION AS AMENDED – PART II

AMENDMENT	08/10/2011	(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))	* 36	Minus	** 38	= 0	X $ =		OR	X $52=	0
	Independent (37 CFR 1.16(h))	* 5	Minus	***5	= 0	X $ =		OR	X $220=	0
	☐ Application Size Fee (37 CFR 1.16(s))									
	☐ FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))							OR		
						TOTAL ADD'L FEE		OR	TOTAL ADD'L FEE	0

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

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

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

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

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

Legal Instrument Examiner:
/WILLIAM PHILLIPS/

UNITED STATES PATENT AND TRADEMARK OFFICE

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
11/367,238	03/03/2006	Nachiappan Chidambaram	BAN 102	5524

23579 7590 11/29/2011

Pabst Patent Group LLP
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SUITE 320
ATLANTA, GA 30309

EXAMINER	
VU, JAKE MINH	
ART UNIT	PAPER NUMBER
1618	
MAIL DATE	DELIVERY MODE
11/29/2011	PAPER

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

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

Office Action Summary	Application No.	Applicant(s)	
	11/367,238	CHIDAMBARAM ET AL.	
	Examiner	Art Unit	
	JAKE VU	1618	

-- 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 August 2011*.

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

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

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

Disposition of Claims

5)☒ Claim(s) *1,2,6-14,16-20 and 24-41* is/are pending in the application.

5a) Of the above claim(s) *14 and 16-18* is/are withdrawn from consideration.

6)☐ Claim(s) _____ is/are allowed.

7)☒ Claim(s) *1-2, 6-13, 19-20, 24-41* is/are rejected.

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

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

Application Papers

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

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

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

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

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

Priority under 35 U.S.C. § 119

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

a)☐ All b)☐ Some * c)☐ None of:

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

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

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

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

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Receipt is acknowledged of Applicant's Amendment filed on 08/10/2011.

- Claims 1, 14, 19, 38 have been amended.
- Claims 3-4, 21-22 have been cancelled.
- Claims 40-41 have been added.
- Claims 1-2, 6-14, 16-20, 24-41 are pending in the instant application.
- Claims 14, 16-18 have been previously withdrawn from consideration.

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 1, 19, 40-41 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. This is a new matter rejection.

Claims 1, 19, 40-41 recite the newly amended limitation of "optionally water"; however, the specification as-filed does not provide a written description or set forth the metes and bounds of this phrase. The instant claims now recite limitations which were not clearly disclosed in the specification as-filed and now change the scope of the instant disclosure as-filed. Such limitations recited in the present claims, introduce new

concepts and thus violate the written description requirement of the first paragraph of 35 U.S.C. §112.

Applicant is required to cancel the new matter in the response to this Office action. Alternatively, Applicant is invited to identify sufficient written support in the original specification for the "limitations" indicated above.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-2, 6-13 and 19-20, 24-31, 40-41 rejected under 35 U.S.C. 102(b) as being anticipated by YU et al (5,360,615) **are maintained** and will be discussed in more detail below.

YU teaches a composition comprised of: a salt of a therapeutically active agent, such as diclofenac sodium (see col. 12, Example 8); a deionizing agent, such as 0.2 mole equivalent hydrochloric acid (see col. 12, Example 8), which is a deionizing agent (see Applicant's claim 39); 71.5% of polyethylene glycol with molecular weight of 600 (see col. 12, Example 8); 7.16% of water (see col. 12, Example 8); excipients, such as preservatives (see col. 9, line 34); 4-8% of solubilizers, such as polyvinyl pyrrolidone (see col. 8, line 51-68). Additional limitation includes: softgel capsule (see col. 1, line 20). Note, even though product-by-process claims are limited by and defined by the

process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process. In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985). In this instance, the prior art has every ingredients as claimed by Applicant.

Claims 1-2, 6-13, 19-20, 24-35 are rejected under 35 U.S.C. 102(b) as being anticipated by SAWYER et al (US 6,383,515) **are maintained** and will be discussed in more detail below.

SAWYER teaches a composition comprised of: 21.67% naproxen sodium (see abstract; and col. 14, line 32); deionizing agent, such as 5.88% of sodium propionate in water (see col. 14, line 23 and 35), which would inherently have propionic acid (see col. 4, line 40-44) when the sodium propionate salt goes into solution and is about 0.2-1.0 mole equivalent of naproxen sodium, wherein propionic acid is a deionizing agent (see Applicant's claim 39). Additional disclosures include: 10-70% of polyethylene glycol 400-600 (see col. 3, line 48 - col. 4, line 19); 0-25% of water (see col. 3, line 33; col. 5, line 4-5; col. 14, line 23; and examples); 2% of propylene glycol (see col. 3, line 48-54; col. 8, line 24) or polyvinyl pyrrolidone (see col. 3, line 49); soft gel capsule (see abstract); other organic acids can be used in place of propionic acid, such as citric acid or organic acids with at least 3 carbon atoms (see col. 4, line 31-44). Note, even though product-by-process claims are limited by and defined by the process, determination of

patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process. In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985). In this instance, the prior art has every ingredients as claimed by Applicant.

Claims 1-2, 6, 8-13, 19-20, 24, 26-35, 38-41 rejected under 35 U.S.C. 102(b) as being anticipated by CUPPS et al (US 5,541,210) **are maintained** and will be discussed in more detail below.

CUPPS teaches a composition comprising of: a salt of an active agent, such as 220mg of naproxen sodium (see col. 28, line 66); a deionizing agent, such as 50mg of citric acid (see col. 29, line 12), which is about 0.2-1.0 mole equivalent of naproxen sodium; 3000mg of polyethylene glycol (see col. 29, line 8), which is about 10% by weight; 3800mg of water (see col. 29, line 14), which is about 13% weight; excipients, such as 3000mg of propylene glycol (see col. 29, line 9), which is a solubilizer and is about 10% by weight. Additional disclosures include: preferred composition include softgel capsules (see col. 19, line 4). Note, citric acid is a deionizing agent (see Applicant's claim 39). Note, even though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art,

the claim is unpatentable even though the prior product was made by a different process. In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985). In this instance, the prior art has every ingredients as claimed by Applicant.

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.

Claims 1-2, 6-13, 19-20, 24-41 are rejected under 35 U.S.C. 103(a) as being unpatentable over SAWYER et al (US 6,383,515) in view of McENTEE et al (US 5,885,608) **are maintained** for reasons of record in the previous office action filed on 07/14/2010 and as discussed below.

SAWYER teaches a composition comprised of: 21.67% naproxen sodium (see abstract; and col. 14, line 32); deionizing agent, such as 5.88% of sodium propionate in water (see col. 14, line 23 and 35), which would inherently have propionic acid (see col. 4, line 40-44) when the sodium propionate salt goes into solution and is about 0.2-1.0 mole equivalent of naproxen sodium, wherein propionic acid is a deionizing agent (see Applicant's claim 39). Additional disclosures include: 10-70% of polyethylene glycol 400-600 (see col. 3, line 48 - col. 4, line 19); 0-25% of water (see col. 3, line 33; col. 5, line 4-5; col. 14, line 23; and examples); 2% of propylene glycol (see col. 3, line 48-54; col. 8, line 24) or polyvinyl pyrrolidone (see col. 3, line 49); soft gel capsule (see

abstract); other organic acids can be used in place of propionic acid, such as citric acid or organic acids with at least 3 carbon atoms (see col. 4, line 31-44).

SAWYER does not teach using an organic acid, such as lactic acid.

McENTEE teaches that organic acids, such as citric acid and lactic acid are known in the prior art (see col. 10, line 17-19).

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to incorporate lactic acid or sodium lactate into SAWYER's composition. The person of ordinary skill in the art would have been motivated to make those modifications, because lactic acid is an organic functional equivalent of citric acid, and reasonably would have expected success because SAWYER teaches using organic acids with at least 3 carbons, wherein lactic acid has at least 3 carbons.

The references do not specifically teach adding the ingredients in the amounts claimed by Applicant. The amount of a specific ingredient in a composition is clearly a result effective parameter that a person of ordinary skill in the art would routinely optimize. Optimization of parameters is a routine practice that would be obvious for a person of ordinary skill in the art to employ and reasonably would expect success. It would have been customary for an artisan of ordinary skill to determine the optimal amount of each ingredient to add in order to best achieve the desired results, such as solubility of the active agent. Thus, absent some demonstration of unexpected results from the claimed parameters, this optimization of ingredient amount would have been obvious at the time of Applicant's invention.

Note, even though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process. In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985). In this instance, the prior art has every ingredients as claimed by Applicant.

Note, Applicant's specification has not provided with any increased solubility or bioavailability data.

Response to Arguments

Applicant argues that Yu clearly recognizes that water alone is not sufficient to ionize the active agent; an additional agent is necessary to form the salt. For example, Example 1 contains ibuprofen, potassium hydroxide, and water. The combination of sodium hydroxide and water results in hydroxide as the dominant species in solution with little H+ present in solution. Therefore, the water in Example 1 in Yu cannot act as deionizing agent as required by independent claims 1, 14, 18, 19, 38, 40, and 41 and the claims dependent thereon.

The Examiner finds this argument unpersuasive, because as discussed above, YU teaches a deionizing agent, such as 0.2 mole equivalent of hydrochloric acid (see col. 12, Example 8), which is a deionizing agent by Applicant’s definition (see Applicant's claim 39).

Applicant argues that the pH of the sodium propionate solution in Example 17 is 9.6, which is strongly basic. Moreover, this solution is used in combination with a solution of 6.8 g KOH (a strong base) in 100 mL of water. Thus the predominant species in solution will be -OH and propionate. Therefore, the concentration of H+ is well outside the range recited in independent claims 1, 14, 18, 19, 38, 40, and 41.

The Examiner finds this argument unpersuasive, because nowhere in Example 17 does SAWYER states the pH is 9.6. As a matter of fact, SAWYER teaches the pH is adjusted to provide acceptable pH limits in the softgel (see col. 4, line 59-61), which is an acidic pH of 2.5 to 7.5 (see col. 1, line 54-56; and col. 11, line 30-32), by addition of more propionic acid (see col. 4, line 50-53).

Applicant argues that Example R contains citric acid in combination with sodium citrate. Sodium citrate is present in molar excess to citric acid. Therefore, the predominant species in solution is a base. The concentration of H+ is well outside the range recited in independent claims 1, 14, 18, 19, 38, 40, and 41.

The Examiner finds this argument unpersuasive, because as discussed above, CUPPS teaches using a deionizing agent, such as 50mg of citric acid (see col. 29, line 12), which is about 0.2-1.0 mole equivalent of naproxen sodium, wherein citric acid is a deionizing agent by Applicant's definition (see Applicant's claim 39).

Applicant argues that Sawyer teaches away from the claimed compositions. One of ordinary skill in the art, reading Sawyer, would prepare a composition containing the salt of an active agent and a species which functions to keep the drug ionized by

creating a basic environment, not the salt of a drug and deionizing agent which partially deionizes or neutralizes the salt, as recited by the claims

The Examiner finds this argument unpersuasive, because as discussed above, SAWYER teaches creating an acidic environment, not basic as alleged by Applicant.

Conclusion

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

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

Telephonic Inquiries

Any inquiry concerning this communication or earlier communications from the examiner should be directed to JAKE VU whose telephone number is (571)272-8148. The examiner can normally be reached on Mon-Tue and Thu-Fri 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Hartley can be reached on (571) 272-0616. 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.

/Jake M. Vu/
Primary Examiner, Art Unit 1618

RESPONSE UNDER 37 C.F.R. § 1.116
EXPEDITED PROCEDURE
ART UNIT 1618

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Nachiappan Chidambaram and Aqeel Fatmi

Serial No.: 11/367,238 Art Unit: 1618

Filed: March 3, 2006 Examiner: Jake Minh Vu

For: *SOLVENT SYSTEM FOR ENHANCING THE SOLUBILITY OF PHARMACEUTICAL AGENTS*

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

AMENDMENT AND RESPONSE

Sir:

Responsive to the Office Action mailed on November 29, 2011, please amend the application as follows, and consider the following remarks.

It is believed that no fee is required with this submission. However, should a fee be required, the Commissioner is hereby authorized to charge the fee to Deposit Account No. 50-3129.

Amendment in the Claims

1. (Currently Amended) A pharmaceutical composition comprising

(a) a salt of one or more either acidic or basic pharmaceutically active agents; and

(b) a deionizing agent in an amount from about 0.2 to about 1.0 mole equivalents per mole of the pharmaceutically active agent(s), which at least partially neutralizes the pharmaceutically active agent(s) ~~agent~~; and

(c) polyethylene glycol; ~~and optionally~~

~~(d) water;~~

wherein when the salt is a salt of a weak acid and a strong base, the deionizing agent is a hydrogen ion species and when the salt is a salt of a weak base and a strong acid, the deionizing agent is a hydroxide ion species, and

wherein the pharmaceutically active agent(s) are not amphoteric.

2. (Currently Amended) The composition of claim 1, wherein the one or more pharmaceutically active agents(s) are ~~agent is~~ selected from the group consisting of therapeutically active agents, diagnostic agents, and prophylactic agents.

3. (Canceled)

4. (Canceled)

5. (Canceled)

6. (Currently Amended) The composition of claim 1, wherein the polyethylene glycol is present in an amount from about 10% to about 80% by weight.

7. (Currently Amended) The composition of claim 1, wherein the polyethylene glycol is one or more polyethylene glycols with a molecular weight between 300 and 1500.

8. (Currently Amended) The composition of claim 1, further comprising water.

9. (Currently Amended) The composition of claim 8, wherein water is present in an amount from about 1% to about 18% by weight.

10. (Currently Amended) The composition of claim 1, further comprising one or more excipients.

11. (Previously Presented) The composition of claim 10, wherein the one or more excipients are selected from the group consisting of plasticizers, crystallization inhibitors, wetting agents, bulk filling agents, solubilizers, bioavailability enhancers, solvents, pH-adjusting agents, dyes, preservatives, surfactants, and combinations thereof.

12. (Currently Amended) The composition of claim 11, wherein the solubilizer is selected from the group consisting of glycerin, polyvinylpyrrolidone, propylene glycol, and combinations thereof.

13. (Currently Amended) The composition of claim 12, wherein the solubilizer is present in amount from about 1% to about 10% by weight.

14. (Withdrawn-Currently Amended) A method of making the capsule of claim 19 comprising

(a) mixing a salt of one or more acidic or basic pharmaceutically active agents, a deionizing agent in an amount from about 0.2 to about 1.0 mole equivalents per mole of the

pharmaceutically active agent(s), which at least partially neutralizes the pharmaceutically active agent(s) ~~agent~~, and polyethylene glycol at an appropriate temperature; and

(b) encapsulating the mixture in a softgel capsule,

wherein the one or more pharmaceutically active agent(s) are not amphoteric.

15. (Canceled)

16. (Withdrawn – Currently Amended) The method of claim 14, further comprising water.

17. (Withdrawn – Currently Amended) The method of claim 14, wherein the appropriate temperature is from about 50°C to about 70°C.

18. (Withdrawn) A method of using the pharmaceutical composition of claim 1 or the capsule of claim 19 or 38 comprising

administering to a patient in need thereof an effective amount of the composition of claim 1 or the capsule of claim 19 or 38.

19. (Currently Amended) A softgel capsule comprising a fill material, wherein the fill material comprises

(a) a salt of one or more either acidic or basic pharmaceutically active agents; and

(b) a deionizing agent in an amount from about 0.2 to about 1.0 mole equivalents per mole of the pharmaceutically active agent(s), which at least partially neutralizes the pharmaceutically active agent(s) ~~agent~~; and

(c) polyethylene glycol; ~~and optionally~~

~~(d) water;~~

wherein, when the salt is a salt of a weak acid and a strong base, the deionizing agent is a hydrogen ion species and when the salt is a salt of a weak base and a strong acid, the deionizing agent is a hydroxide ion species, and

wherein the one or more pharmaceutically active agent(s) are not amphoteric.

20. (Currently Amended) The capsule of claim 19, wherein the one or more pharmaceutically active agent(s) are ~~agent is~~ selected from the group consisting of therapeutically active agents, diagnostic agents, and prophylactic agents.

21. (Canceled)

22. (Canceled)

23. (Canceled)

24. (Currently Amended) The capsule of claim 19, wherein the polyethylene glycol is present in an amount from about 10% to about 80% by weight

25. (Currently Amended) The capsule of claim 19, wherein the polyethylene glycol is one or more polyethylene glycols with a molecular weight between 300 and 1500.

26. (Currently Amended) The capsule of claim 19, further comprising water.

27. (Currently Amended) The capsule of claim 26, wherein water is present in an amount from about 1% to about 18% by weight.

28. (Currently Amended) The capsule of claim 19, further comprising one or more excipients.

29. (Currently Amended) The capsule of claim 28, wherein the one or more excipients are selected from the group consisting of plasticizers, crystallization inhibitors, wetting agents,

bulk filling agents, solubilizers, bioavailability enhancers, solvents, pH-adjusting agents, dyes, preservatives, surfactants, and combinations thereof.

30. (Currently Amended) The capsule of claim 29, wherein the solubilizer is selected from the group consisting of glycerin, polyvinylpyrrolidone, propylene glycol and combinations thereof.

31. (Currently Amended) The capsule of claim 29, wherein the solubilizer is present in amount from about 1% to about 10% by weight.

32. (Currently Amended) The composition of claim 1, wherein the pharmaceutically active agent is naproxen sodium and the deionizing agent is a hydrogen ion species.

33. (Currently Amended) The composition of claim 19, wherein the pharmaceutically active agent is naproxen sodium and the deionizing agent is a hydrogen ion species.

34. (Currently Amended) The composition of claim 32, wherein the hydrogen ion species is selected from the group consisting of hydrochloric acid, hydrobromic acid, hydroiodic acid, sulfuric acid, fumaric cid, maleic acid, tartaric acid, methane-, ethane-, and benzene sulfonates, citric acid, malic acid, acetic acid, proprionic acid, pyruvic acid, butanoic acid, and lactic acid.

35. (Currently Amended) The composition of claim 33, wherein the hydrogen ion species is selected from the group consisting of hydrochloric acid, hydrobromic acid, hydroiodic acid, sulfuric acid, fumaric cid, maleic acid, tartaric acid, methane-, ethane-, and benzene sulfonates, citric acid, malic acid, acetic acid, proprionic acid, pyruvic acid, butanoic acid, and lactic acid.

36. (Currently Amended) The composition of claim 34, wherein the hydrogen ion species is lactic acid.

37. (Currently Amended) The composition of claim 35, wherein the hydrogen ion species is lactic acid.

38. (Previously Presented) A softgel capsule comprising a fill material comprising from about 10% to about 80% by weight polyethylene glycol having a molecular weight between 300 and 1500, about 10% to about 50% by weight naproxen sodium, and about 0.2 to about 1.0 moles of a deionizing agent per mole of naproxen sodium, which at least partially neutralizes the naproxen sodium.

39. (Currently Amended) The softgel capsule of claim 38, wherein the deionizing agent is selected from the group consisting of hydrochloric acid, hydrobromic acid, hydroiodic acid, sulfuric acid, fumaric cid, maleic acid, tartaric acid, methane-, ethane-, and benzene sulfonates, citric acid, malic acid, acetic acid, proprionic acid, pyruvic acid, butanoic acid, and lactic acid.

40. (Currently Amended) A pharmaceutical composition prepared by a method comprising

(a) mixing a salt of one or more acidic or basic pharmaceutically active agents;

(b) a deionizing agent in an amount from about 0.2 to about 1.0 mole equivalents per mole of the salt of the pharmaceutically active agent(s), which at least partially neutralizes the salt of pharmaceutically active agent(s) ~~agent~~; and

(c) polyethylene glycol; ~~and optionally~~

~~(d) water~~

wherein when the salt ~~(a)~~ is a salt of a weak ~~week~~ acid and a strong base, the deionizing agent is a hydrogen ion species, and when the salt ~~(a)~~ is the salt of a weak base and a strong acid, the deionizing agent is a hydroxide ion species, and

wherein the pharmaceutically active agent(s) are not amphoteric.

41. (Currently Amended) A softgel capsule prepared by a method comprising

(a) producing a fill material by mixing

(i) a salt of one or more acidic or basic pharmaceutically active agents;

(ii) a deionizing agent in an amount from about 0.2 to about 1.0 mole equivalents per mole of the pharmaceutically active agent(s) to cause partial deionization of the salt of the pharmaceutically active agent(s); and

(iii) polyethylene glycol;~~; and optionally~~

~~(iv) water; and~~

(b) encapsulating the mixture in a softgel capsule;

wherein when the salt ~~(a)~~ is a salt of a weak acid and a strong base, the deionizing agent is a hydrogen ion species, and when the salt ~~(a)~~ is the salt of a weak base and a strong acid, the deionizing agent is a hydroxide ion species, and

wherein the pharmaceutically active agent(s) are not amphoteric.

Remarks

The undersigned would like to thank Examiner Vu for his time during the in person interview on December 28, 2012. During the interview, the undersigned and Examiner Vu discussed the cited art and potential amendments to the claims. The Examiner's comments were instrumental in preparing this response to address all issues that were of concern to the Examiner. As discussed below, the amendments proposed by the undersigned and by the Examiner, particularly with respect to claim scope, have been made.

Claims 1, 2, 6, 7, 14, 19, 20, 24, 25, and 40 have been amended to correct antecedent basis.

Claims 6-10, 12-13, 16-17, 19-20, 24-37, and 39 have been amended to correct punctuation.

These amendments require no additional search on the part of the Examiner, do not raise any new issues, and place the claims in condition for allowance. The M.P.E.P. provides that "any amendment," including an after-final amendment, "that will place the application either in condition for allowance or in better form for appeal may be entered." *See* M.P.E.P. § 714.12. Accordingly, Applicants respectfully request entry of the claim amendments.

In the event this Response does not result in allowance of the claims, the undersigned respectfully requests a telephone interview with Examiner Vu, his supervisor, and a Quality Assurance Specialist (QAS).

Rejections Under 35 U.S.C. § 112, First Paragraph

Claims 1, 19, and 40-41 were rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. Specifically, the Examiner alleges the phrase "optionally water" is not supported by the specification, as filed, and constitutes new matter.

Applicants respectfully disagree. Support for the optional inclusion of water in the claimed formulations can be found in the specification as originally filed, at least in Examples (pages 11-15). Examples 1-7 describe formulations within the scope of the claims which include water. Examples 8-12 describe formulations within the scope of the claims which do not include water. Accordingly, the specification inherently describes formulations that optionally contain water. Therefore, claims 1, 19, and 40-41 satisfy the written description requirement.

The phrase "optionally water" was added to claims 1, 19, and 40-41 in the Amendment and Response filed August 10, 2011, in order to clarify that the deionizing agent present in the pharmaceutical composition is not water. During the interview on December 28, 2012, Examiner Vu indicated that if claims 1, 19, and 40-41 were amended to delete the phrase "optionally water," the Examiner would not construe the deionizing agent to be water.

Therefore, in order to facilitate prosecution, claims 1, 19, and 40-41 were amended to delete the phrase "optionally water." This amendment requires no additional search on the part of the Examiner, does not raise any new issues, directly address a concern raised by the

Examiner in the Office Action mailed November 29, 2011, and places the claims in condition for allowance.

The M.P.E.P. provides that "any amendment," including an after-final amendment, "that will place the application either in condition for allowance or in better form for appeal may be entered." *See* M.P.E.P. § 714.12. Accordingly, Applicants respectfully request entry of this claim amendment. In view of the amendment to claims 1, 19, and 40-41, the Examiner's rejection is moot.

Rejection Under 35 U.S.C. § 102

Claims 1-2, 6-13, 19-20, 24-31, and 40-41 were rejected under 35 U.S.C. § 102(b) as being anticipated by U.S. Patent No. 5,360,615 to Yu ("Yu").

Claims 1-2, 6-13, 19-20, and 24-35 were rejected under 35 U.S.C. § 102(b) as being anticipated by U.S. Patent No. 6,383,515 to Sawyer et al. ("Sawyer").

Claims 1-2, 6, 8-13, 19-20, 24, 26-35, and 38-41 were rejected under 35 U.S.C. § 102(b) as being anticipated by U.S. Patent No. 5,541,210 to Cupps et al ("Cupps").

Applicants respectfully traverse these rejections to the extent that they are applied to the claims, as amended.

Legal Standard

For a rejection of claims to be properly founded under 35 U.S.C. § 102, it must be established that a prior art reference discloses each and every element of the claims and enables one of skill in the field of the invention to make and use the claimed invention. *Xerox Corp. v. 3Com Corp.*, 458 F.3d 1310, 1322 (Fed. Cir. 2006) ("[I]nvalidity by anticipation requires that the

four corners of a single, prior art document describe every element of the claimed invention.") *quoting Advanced Display Sys., Inc. v. Kent State Univ.*, 212 F.3d 1272, 1282 (Fed. Cir. 2000); *Merck & Co. v. Teva Pharmaceuticals USA, Inc.*, 347 F.3d 1367, 1372, 68 USPQ2d 185 (Fed. Cir. 2003) ("An 'anticipating' reference must describe all of the elements and limitations of the claim in a single reference, and enable one of skill in the field of the invention to make and use the claimed invention."); *RCA Corp. v. Applied Digital Data Sys., Inc.*, 730 F.2d 1440, 1444, 221 USPQ 385, 388 (Fed. Cir. 1984) ("Anticipation is established only when a single prior art reference discloses, expressly or under principles of inherency, each and every element of a claimed invention."). A reference that fails to disclose or enable even one limitation will therefore not be found to anticipate, even if the missing limitation could be discoverable through further experimentation.

Analysis

Yu

Yu describes pharmaceutical formulations containing polyethylene glycol, a pharmaceutical agent in the form of the ***free acid or base***, and an ***ionizing agent***.

In contrast, the claims define formulations containing (a) a salt of one or more either acidic or basic pharmaceutically active agents; and (b) a deionizing agent in an amount from 0.2 to 1.0 mole equivalents of the pharmaceutically active agent(s), which at least partially neutralizes the pharmaceutically active agent. In the claimed formulations, the active agent is in the form of a ***salt***, and a ***deionizing agent*** is added to a fill material containing the salt of the active agent.

Yu does not disclose or suggest a formulation containing (a) a salt of one or more either acidic or basic pharmaceutically active agents; and (b) a deionizing agent in an amount from 0.2 to 1.0 mole equivalents of the pharmaceutically active agent(s), as required by the claims. Therefore, Yu cannot anticipate claims 1-2, 6-13, 19-20, 24-31, and 40-41.

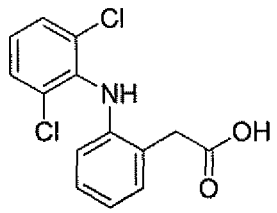
In the Office Action mailed November 29, 2011, the Examiner alleged that "even though product-by-process claims are limited by and defined by the process, determination is based on the product itself." *See* Office Action mailed November 29, 2011, page 3, line 23 to page 4, line 1. The Examiner's arguments in this regard are unclear. The claims, as pending, are not product-by-process claims. Furthermore, as discussed above, the claimed formulations are compositionally distinct from the formulations described by Yu.

The formulation described in Example 8 of Yu is not within the scope of the claims

In the Office Action mailed November 29, 2011, the Examiner alleged that Example 8 of Yu describes a formulation within the scope of the claims. *See* Office Action mailed November 29, 2011, page 3, lines 16-22. Applicants respectfully disagree.

Example 8 of Yu describes a formulation containing diclofenac sodium, polyethylene glycol, and hydrochloric acid. As shown below, diclofenac contains both a basic amine moiety and an acidic carboxylic acid moiety. Accordingly, diclofenac is an ***amphoteric*** active agent.

Therefore, Example 8 of Yu describes a formulation containing the salt of an amphoteric active agent.



Diclofenac

In contrast, the claims specify that the one or more active agents present in the formulation are salts of one or more ***either acidic or basic pharmaceutically active agents***. Diclofenac sodium is not within the scope of these claims, because diclofenac is not exclusively an acid or a base; it is amphoteric. Accordingly, the formulation described in Example 8 of Yu is not within the scope of the claims, as previously pending.

However, to clarify this distinction and facilitate prosecution, claims 1, 14, 19, 40, and 41 were amended to specify that the pharmaceutically active agent(s) are not amphoteric. Support for this amendment can be found in the specification, at least page 3, line 22, where amphoteric active agents are explicitly disclosed. The M.P.E.P. provides that elements which are positively recited in the specification may be explicitly excluded in the claims. See *In re Johnson*, 558 F.2d 1008, 1019, 194 USPQ 187, 196 (CCPA 1977) ("[the] specification, having described the whole, necessarily described the part remaining.").

These amendments require no additional search on the part of the Examiner and do not raise any new issues because the claims, as previously pending, already excluded amphoteric active agents. In addition, these amendments serve to place the claims in condition for

allowance by clarifying claim scope. The M.P.E.P. provides that "any amendment," including an after-final amendment, "that will place the application either in condition for allowance or in better form for appeal may be entered." *See* M.P.E.P. § 714.12. Accordingly, Applicants respectfully request entry of the claim amendments.

For at least these reasons, claims 1-2, 6-13, 19-20, 24-31, and 40-41 are novel over Yu.

Sawyer

Sawyer describes medicinal solutions suitable for encapsulation in sofgel capsules. Col. 1, lines 6-7.

Sawyer is similar in scope to Yu. Sawyer describes formulations containing a low molecular weight polymer, an active agent, and the salt of an organic acid containing at least three carbon atoms (col. 3, lines 23-26). In Sawyer's formulations, the active agent is generally in the form of the ***free acid or base***, and the salt of the organic acid is a base which serves to ***ionize*** the active agent (Col. 4, lines 22-24).

In contrast, the claims define a formulation containing (a) a salt of one or more either acidic or basic pharmaceutically active agents; and (b) a deionizing agent in an amount from 0.2 to 1.0 mole equivalents of the pharmaceutically active agent(s), which at least partially neutralizes the pharmaceutically active agent. In the claimed formulations, the active agent is in the form of a ***salt***, and a ***deionizing agent*** is added to a fill material containing the salt of the active agent.

Sawyer does not disclose or suggest a formulation containing (a) a salt of one or more either acidic or basic pharmaceutically active agents; and (b) a deionizing agent in an amount

from 0.2 to 1.0 mole equivalents of the pharmaceutically active agent(s), as required by the claims. Therefore, Sawyer cannot anticipate claims 1-2, 6-13, 19-20, 24-31, and 40-41.

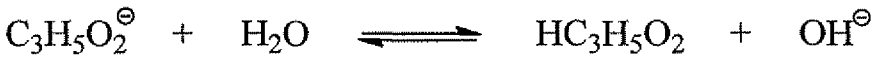
In the Office Action mailed November 29, 2011, the Examiner alleged that "even though product-by-process claims are limited by and defined by the process, determination is based on the product itself." *See* Office Action mailed November 29, 2011, page 4, line 22 to page 5, line 1. The Examiner's arguments in this regard are unclear. The claims, as pending, are not product-by-process claims. Furthermore, as discussed above, the claimed formulations are compositionally distinct from the formulations described by Sawyer.

The formulation described in Example 17 of Sawyer is not within the scope of the claims

In the Office Action mailed November 29, 2011, the Examiner alleged that Example 17 of Sawyer describes a formulation within the scope of the claims. *See* Office Action mailed November 29, 2011, page 4, lines 16-21. Applicants respectfully disagree.

Example 17 describes a solution containing naproxen sodium, polyethylene glycol, potassium hydroxide, and sodium propionate. Potassium hydroxide and sodium propionate are bases, *i.e.*, ionizing agents, which function to maintain naproxen as the sodium salt. The Examiner alleges that because the formulation contains sodium propionate in aqueous solution, the formulation would inherently contain sodium propionate, sodium ions, propionate anions, and propionic acid. However, the Examiner has provided no evidence to demonstrate that propionic acid, if present, would be in an amount between 0.2 to 1.0 mole equivalents of the active agent(s), as required by the claims.

When sodium propionate is added to water, as in the formulation described in Example 17, an equilibrium is established between propionate and propionic acid, as shown below:



However, while trace amounts of propionic acid may be present in the formulation described in Example 17, the amount of propionic acid present in the formulation is far below the 0.2 equivalents required by the claims.

The formulation described in Example 17 contains 0.8153 g sodium propionate (K_b = 7.46 x 10^{-10}) dissolved in 800 mL of water (*i.e.*, an aqueous solution of approximately 0.0106 M sodium propionate). If the impact of other species present in solution (including the naproxen sodium, PEG 300, and potassium hydroxide) on the equilibrium between propionate and propionic acid is ignored, the concentration of propionic acid at equilibrium can be calculated to be approximately 2.7 x 10^{-5} M (corresponding to roughly 2.2 x 10^{-5} moles propionic acid at equilibrium). The formulation in Example 17 of Sawyer contains 3.0033 g (0.0119 moles) of naproxen sodium. Therefore, Example 17 describes a formulation containing only trace amounts of propionic acid (approximately ***0.0018 mole equivalents*** of propionic acid per mole of naproxen sodium). In contrast, the claims require the deionizing agent to be present in an amount ***between 0.2 and 1.0 mole equivalents*** per mole of active agent.

Furthermore, the solution in Example 17 also contains 6.66 mg of potassium hydroxide. The pH of an aqueous solution of approximately 0.0106 M sodium propionate (*i.e.*, the formulation described in Example 17) is approximately 9.6. The addition of potassium hydroxide will make the solution even more basic, driving the equilibrium between propionate

and propionic acid in the direction of propionate. As a result, the actual amount of propionate present in the formulation described in Example 17 will be even less than 0.0018 mole equivalents per mole of naproxen sodium. Therefore, what small amounts of propionic acid may be present in Example 17 of Sawyer are not with the range of between 0.2 and 1.0 mole equivalents per mole of active agent, as required by the claims.

For at least these reasons, claims 1-2, 6-13, 19-20, and 24-35 are novel over Sawyer.

Cupps

Cupps describes 5-(2-imidazolinylamino)benzimidazoles, as well as pharmaceutical compositions containing these compounds (Col. 1, lines 11-15).

In the Office Action mailed November 29, 2011, the Examiner alleged that "even though product-by-process claims are limited by and defined by the process, determination is based on the product itself." *See* Office Action mailed November 29, 2011, page 5, lines 19-21. The Examiner's arguments in this regard are unclear. The claims, as pending, are not product-by-process claims. Furthermore, as discussed below, the claimed formulations are compositionally distinct from the formulations described by Cupps.

The formulation described in Example R of Cupps is not within the scope of the claims

In the Office Action mailed November 29, 2011, the Examiner alleged that Example R of Cupps describes a formulation within the scope of the claims. *See* Office Action mailed November 29, 2011, page 5, lines 11-17. Applicants respectfully disagree.

Example R describes a formulation containing naproxen sodium (220 mg/fl oz), sodium citrate dihydrate (trisodium citrate dihydrate, 150 mg/fl oz), and citric acid (50 mg/fl oz). The

Examiner alleges that this formulation contains between 0.2 and 1.0 mole equivalents of citric acid per mole of active agent, as required by the claims. However, the Examiner has provided no evidence to demonstrate that the citric acid would be present in an amount between 0.2 to 1.0 mole equivalents of the active agent(s), as required by the claims.

Because citric acid is a weak triprotic acid, calculation of the amount of citric acid present in an aqueous solution containing citric acid and trisodium citrate is difficult. In addition, while Example R does contain water (3800 mg/fl oz), the formulation is largely composed of high fructose corn syrup (16000 mg/fl oz), polyethylene glycol (3000 mg/fl oz), propylene glycol (3000 mg/fl oz), and alcohol (2500 mg/fl oz). As a result, calculations of the amount of citric acid present in the formulation at equilibrium, which rely upon equilibrium constants specific for aqueous solutions, may not be accurate. Therefore, only rough approximations for the amount of citric acid in the formulation are possible.

Example R describes a solution containing 50 mg/fl oz of citric acid (approximately 0.0088 M citric acid, $K_{a1} = 7.44 \times 10^{-4}$) and 220 mg/fl oz of naproxen sodium (approximately 0.0295 M naproxen sodium). If the impact of other species in solution on the citric acid equilibrium is ignored and the solution is assumed to be aqueous, the concentration of citric acid at equilibrium can be calculated to be approximately 2.2×10^{-3} M. Therefore, Example R describes a formulation containing approximately ***0.075 mole equivalents*** of citric acid per mole of naproxen sodium. In contrast, the claims require the deionizing agent to be present in an amount ***between 0.2 and 1.0 mole equivalents*** per mole of active agent.

Furthermore, the solution in Example R also contains 150 mg/fl oz of sodium citrate dihydrate (trisodium citrate dihydrate, 0.01725 M). The addition of more than two moles of sodium citrate for every one mole of citric acid will make the solution more basic, driving the equilibrium between citrate and citric acid in the direction of citrate. As a result, the actual amount of citric acid present in the formulation described in Example R will be even less than 0.075 mole equivalents per mole of naproxen sodium. Accordingly, Example R of Cupps does not describe a formulation containing a deionizing agent in an amount between 0.2 and 1.0 mole equivalents per mole of active agent, as required by the claims. Therefore, Cupps cannot anticipate claims 1-2, 6, 8-13, 19-20, 24, 26-35, and 38-41.

For at least these reasons, claims 1-2, 6, 8-13, 19-20, 24, 26-35, and 38-41 are novel over Cupps.

Rejection Under 35 U.S.C. § 103

Claims 1-2, 6-13, 19-20, and 24-41 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Sawyer, in view of U.S. Patent No. 5,885,608 to McEntee ("McEntee").

Applicants respectfully traverse this rejection to the extent that it is applied to the claims, as amended.

Legal Standard

The starting point for an obviousness determination must be the Supreme Court's decision in *KSR v. Teleflex,* 550 U.S. 398 (2007), which focuses the determination of whether a claimed invention is obvious on the process the Court defined in *Graham v. John Deere Co. of Kansas City*, 383 U.S. 1, 17-18 (1966). There, the Court held that the obviousness determination

should address four factors, all of which must be considered, though not in any prescribed order: (1) the scope and content of the prior art; (2) the level of ordinary skill in the art; (3) the differences between the claimed invention and the prior art; and (4) any secondary considerations suggesting nonobviousness, such as commercial success, failure of others, and long felt but unmet need. *Id.* The Court cautioned that the fact finder should be careful about reading the teachings of the invention at issue into the prior art, to avoid applying inappropriate hindsight, *ex post* reasoning. *Id. at 36.*

The Federal Circuit's decisions since KSR reflect an appropriately nuanced obviousness analysis required by *KSR* and *Graham*. The U.S. Patent Office updated its guidelines on September 1, 2010 to reflect the updated case law since *KSR*. *Examination Guidelines Update: Developments in the Obviousness Inquiry After KSR v. Teleflex*, Fed. Reg. 75 (169): 53643-53660 (Sept. 1, 2010) ("the 2010 Obviousness Guidelines").

Obviousness requires all the claim limitations are taught or suggested by the prior art

In making an obviousness rejection under 35 U.S.C. § 103(a), the Examiner has the burden under 35 U.S.C. § 103 to establish a *prima facie* case of obviousness. *In re Warner et al.*, 379 F.2d 1011, 154 U.S.P.Q. 173, 177 (C.C.P.A. 1967); *In re Fine*, 837 F.2d 1071, 1074, 5 U.S.P.Q.2d 1596, 1598-99 (Fed. Cir. 1988). To establish a *prima facie* case of obviousness, the Examiner must first establish that all the claim limitations are taught or suggested by the prior art. *In re Royka*, 490 F.2d 981, 180 U.S.P.Q. 580 (C.C.P.A. 1974); *In re Wilson*, 424 F.2d 1382, 1385, 165 U.S.P.Q. 494, 496 (C.C.P.A. 1970) (holding that all words in a claim must be considered in judging the patentability of that claim against the prior art).

In this context, prior art is not strictly limited to the references being applied in making an obviousness rejection. Rather, the prior art also includes the understanding of one of ordinary skill in the art. However, when relying upon the understanding of one of ordinary skill in the art to arrive at claim limitations not disclosed in the prior art reference (or references when combined), "Office personnel must explain why the difference(s) between the prior art and the claimed invention would have been obvious to one of ordinary skill in the art." *See* M.P.E.P. § 2141.

Analysis

Sawyer is discussed above. Sawyer does not disclose or suggest the claimed compositions.

McEntee describes a method for treating, ameliorating, and/or prevent age-related neurological disorders by administering lipid-soluble thiamine. *Abstract.*

Neither Sawyer nor McEntee disclose or suggest a formulation containing (a) the salt of an acidic or basic active agent, and (b) a deionizing agent in an amount from 0.2 to 1.0 mole equivalents of the pharmaceutically active agent(s), as required by the claims

As discussed above, Sawyer does not disclose or suggest a formulation containing (a) a salt of one or more either acidic or basic pharmaceutically active agents; and (b) a deionizing agent in an amount from 0.2 to 1.0 mole equivalents of the pharmaceutically active agent(s), as required by the claims. McEntee does not cure the deficiencies of Sawyer. McEntee is silent with respect to formulations containing a salt of one or more either acidic or basic pharmaceutically active agents; and (b) a deionizing agent in an amount from 0.2 to 1.0 mole equivalents of the pharmaceutically active agent(s).

Sawyer teaches away from the claimed compositions

A reference may be said to teach away when a person of ordinary skill, upon reading the reference, *would be discouraged from following the path set out in the reference, or would be led in a direction divergent from the path that was taken by the applicant* (emphasis added). See *United States v. Adams*, 383 U.S. 39, 52, 148 U.S.P.Q. (BNA) 479, 484, 15 L. Ed. 2d 572, 86 S. Ct. 708 (1966); *W.L. Gore & Assoc., Inc. v. Garlock, Inc.*, 721 F.2d 1540, 1550-51, 220 U.S.P.Q. (BNA) 303, 311 (Fed. Cir. 1983) (the totality of a reference's teachings must be considered), cert. denied, 469 U.S. 851 (1984); *In re Caldwell*, 50 C.C.P.A. 1464, 319 F.2d 254, 256, 138 U.S.P.Q. (BNA) 243, 245 (CCPA 1963).

As described above, Sawyer describes formulations containing an active agent and the salt of an organic acid which serves as an ***ionizing agent*** (Col. 4, lines 22-24). Sawyer expressly describes that the salt of an organic acid should be added to the formulations to ***ionize*** the active agent (Col. 4, lines 22-24). Accordingly, one of ordinary skill in the art, reading Sawyer, would prepare a composition containing an active agent and a species which functions to keep the drug ionized, not a composition the salt of a drug and deionizing agent designed to deionize the salt of the active agent, as required by the claims. Therefore, one of ordinary skill in the art, reading Sawyer, would be led on a path divergent from the one taken in Sawyer.

For at least these reasons, claims 1-2, 6-13, 19-20, and 24-41 non-obvious over Sawyer in view of McEntee.

Allowance of claims 1-4, 6-13, 19-22, and 24-41, as amended, is respectfully solicited.

Respectfully submitted,

/Michael J. Terapane, Ph.D., J.D./
Michael J. Terapane, Ph.D., J.D.
Reg. No. 57,633

Date: February 28, 2012

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CERTIFICATE OF ELECTRONIC TRANSMISSION UNDER 37 C.F.R. § 1.8

I hereby certify that this correspondence, including any items indicated as attached or included, is being transmitted via electronic transmission via EFS-Web on the date indicated below.

Date: February 28, 2012

Signature: /Candace C. Andrews

Candace C. Andrews

Electronic Acknowledgement Receipt

EFS ID:	12179529
Application Number:	11367238
International Application Number:	
Confirmation Number:	5524
Title of Invention:	Solvent system for enhancing the solubility of pharmaceutical agents
First Named Inventor/Applicant Name:	Nachiappan Chidambaram
Customer Number:	23579
Filer:	Michael John Terapane/Candace Andrews
Filer Authorized By:	Michael John Terapane
Attorney Docket Number:	BAN 102
Receipt Date:	28-FEB-2012
Filing Date:	03-MAR-2006
Time Stamp:	16:06:24
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	no

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1		BAN_102_Amendment_and_Response.pdf	1137764 e88d5e9b0e9d94edba4936bcb43b38f0cd286907	yes	24

	Multipart Description/PDF files in .zip description		
	Document Description	**Start**	**End**
	Amendment After Final	1	1
	Claims	2	8
	Applicant Arguments/Remarks Made in an Amendment	9	24
Warnings:			
Information:			
	Total Files Size (in bytes):	1137764	

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

New Applications Under 35 U.S.C. 111

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

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

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

New International Application Filed with the USPTO as a Receiving Office

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

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

PATENT APPLICATION FEE DETERMINATION RECORD

Substitute for Form PTO-875

Application or Docket Number	Filing Date	☐ To be Mailed
11/367,238	03/03/2006	

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))							
			TOTAL			TOTAL	

* If the difference in column 1 is less than zero, enter "0" in column 2.

APPLICATION AS AMENDED – PART II

AMENDMENT	02/28/2012	(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))	* 34	Minus	** 38	=	X $ =		OR	X $ =	
	Independent (37 CFR 1.16(h))	* 5	Minus	***5	=	X $ =		OR	X $ =	
	☐ Application Size Fee (37 CFR 1.16(s))									
	☐ FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))							OR		
						TOTAL ADD'L FEE		OR	TOTAL ADD'L FEE	

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

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

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

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

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

Legal Instrument Examiner:
/KATRINA . TURNER/

UNITED STATES PATENT AND TRADEMARK OFFICE

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
11/367,238	03/03/2006	Nachiappan Chidambaram	BAN 102	5524

23579 7590 03/01/2012

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EXAMINER	
VU, JAKE MINH	
ART UNIT	PAPER NUMBER
1618	
MAIL DATE	DELIVERY MODE
03/01/2012	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.** 11/367,238	**Applicant(s)** CHIDAMBARAM ET AL.
	Examiner JAKE VU	**Art Unit** 1618

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

THE REPLY FILED 28 February 2012 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 *3* 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: _____.
   Claim(s) withdrawn from consideration: _____.

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: _____.

/Jake M. Vu/
Primary Examiner, Art Unit 1618

Continuation of 3. NOTE: The newly amendment to the independent claims will require further consideration.

RESPONSE UNDER 37 C.F.R. § 1.116
EXPEDITED PROCEDURE
ART UNIT 1618

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Nachiappan Chidambaram and Aqeel Fatmi

Serial No.: 11/367,238 Art Unit: 1618

Filed: March 3, 2006 Examiner: Jake Minh Vu

For: *SOLVENT SYSTEM FOR ENHANCING THE SOLUBILITY OF PHARMACEUTICAL AGENTS*

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

DO NOT ENTER: /J.V./

AMENDMENT AND RESPONSE

Sir:

Responsive to the Office Action mailed on November 29, 2011, please amend the application as follows, and consider the following remarks.

It is believed that no fee is required with this submission. However, should a fee be required, the Commissioner is hereby authorized to charge the fee to Deposit Account No. 50-3129.

RESPONSE UNDER 37 C.F.R. § 1.116
EXPEDITED PROCEDURE
ART UNIT 1618

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Nachiappan Chidambaram and Aqeel Fatmi

Serial No.: 11/367,238 Art Unit: 1618

Filed: March 3, 2006 Examiner: Jake Minh Vu

For: *SOLVENT SYSTEM FOR ENHANCING THE SOLUBILITY OF PHARMACEUTICAL AGENTS*

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

SUBSTITUTE AMENDMENT AND RESPONSE

Sir:

Responsive to the Office Action mailed on November 29, 2011, the Advisory Action mailed on March 1, 2012, and the Examiner's voice mail message on April 28, 2012, please amend the application as follows, and consider the following remarks.

It is believed that no fee is required with this submission. However, should a fee be required, the Commissioner is hereby authorized to charge the fee to Deposit Account No. 50-3129.

Amendment in the Claims

1. (Currently Amended) A pharmaceutical composition comprising

(a) a salt of one or more either acidic or basic pharmaceutically active agents; and

(b) a deionizing agent in an amount from about 0.2 to about 1.0 mole equivalents per mole of the pharmaceutically active agent(s), which at least partially neutralizes the pharmaceutically active agent(s) ~~agent~~; and

(c) polyethylene glycol; ~~and optionally~~

~~(d) water;~~

wherein when the salt is a salt of a weak acid and a strong base, the deionizing agent is a hydrogen ion species and when the salt is a salt of a weak base and a strong acid, the deionizing agent is a hydroxide ion species.

2. (Currently Amended) The composition of claim 1, wherein the one or more pharmaceutically active agents(s) are ~~agent is~~ selected from the group consisting of therapeutically active agents, diagnostic agents, and prophylactic agents.

3. (Canceled)

4. (Canceled)

5. (Canceled)

6. (Currently Amended) The composition of claim 1,wherein the polyethylene glycol is present in an amount from about 10% to about 80% by weight.

7. (Currently Amended) The composition of claim 1, wherein the polyethylene glycol is one or more polyethylene glycols with a molecular weight between 300 and 1500.

8. (Currently Amended) The composition of claim 1, further comprising water.

9. (Currently Amended) The composition of claim 8, wherein water is present in an amount from about 1% to about 18% by weight.

10. (Currently Amended) The composition of claim 1, further comprising one or more excipients.

11. (Previously Presented) The composition of claim 10, wherein the one or more excipients are selected from the group consisting of plasticizers, crystallization inhibitors, wetting agents, bulk filling agents, solubilizers, bioavailability enhancers, solvents, pH-adjusting agents, dyes, preservatives, surfactants, and combinations thereof.

12. (Currently Amended) The composition of claim 11, wherein the solubilizer is selected from the group consisting of glycerin, polyvinylpyrrolidone, propylene glycol, and combinations thereof.

13. (Currently Amended) The composition of claim 12, wherein the solubilizer is present in amount from about 1% to about 10% by weight.

14. (Withdrawn-Currently Amended) A method of making the capsule of claim 19 comprising

(a) mixing a salt of one or more acidic or basic pharmaceutically active agents, a deionizing agent in an amount from about 0.2 to about 1.0 mole equivalents per mole of the pharmaceutically active agent(s), which at least partially neutralizes the pharmaceutically active agent(s) ~~agent~~, and polyethylene glycol at an appropriate temperature; and

(b) encapsulating the mixture in a softgel capsule.

15. (Canceled)

16. (Withdrawn – Currently Amended) The method of claim 14, further comprising water.

17. (Withdrawn – Currently Amended) The method of claim 14, wherein the appropriate temperature is from about 50°C to about 70°C.

18. (Withdrawn) A method of using the pharmaceutical composition of claim 1 or the capsule of claim 19 or 38 comprising

administering to a patient in need thereof an effective amount of the composition of claim 1 or the capsule of claim 19 or 38.

19. (Currently Amended) A softgel capsule comprising a fill material, wherein the fill material comprises

(a) a salt of one or more either acidic or basic pharmaceutically active agents; and

(b) a deionizing agent in an amount from about 0.2 to about 1.0 mole equivalents per mole of the pharmaceutically active agent(s), which at least partially neutralizes the pharmaceutically active agent(s) ~~agent~~; and

(c) polyethylene glycol; ~~and optionally~~

~~(d) water;~~

wherein, when the salt is a salt of a weak acid and a strong base, the deionizing agent is a hydrogen ion species and when the salt is a salt of a weak base and a strong acid, the deionizing agent is a hydroxide ion species.

20. (Currently Amended) The capsule of claim 19, wherein the one or more pharmaceutically active agent(s) are ~~agent is~~ selected from the group consisting of therapeutically active agents, diagnostic agents, and prophylactic agents.

21. (Canceled)

22. (Canceled)

23. (Canceled)

24. (Currently Amended) The capsule of claim 19, wherein the polyethylene glycol is present in an amount from about 10% to about 80% by weight

25. (Currently Amended) The capsule of claim 19, wherein the polyethylene glycol is one or more polyethylene glycols with a molecular weight between 300 and 1500.

26. (Currently Amended) The capsule of claim 19, further comprising water.

27. (Currently Amended) The capsule of claim 26, wherein water is present in an amount from about 1% to about 18% by weight.

28. (Currently Amended) The capsule of claim 19, further comprising one or more excipients.

29. (Currently Amended) The capsule of claim 28, wherein the one or more excipients are selected from the group consisting of plasticizers, crystallization inhibitors, wetting agents, bulk filling agents, solubilizers, bioavailability enhancers, solvents, pH-adjusting agents, dyes, preservatives, surfactants, and combinations thereof.

30. (Currently Amended) The capsule of claim 29, wherein the solubilizer is selected from the group consisting of glycerin, polyvinylpyrrolidone, propylene glycol and combinations thereof.

31. (Currently Amended) The capsule of claim 29, wherein the solubilizer is present in amount from about 1% to about 10% by weight.

32. (Currently Amended) The composition of claim 1, wherein the pharmaceutically active agent is naproxen sodium and the deionizing agent is a hydrogen ion species.

33. (Currently Amended) The composition of claim 19, wherein the pharmaceutically active agent is naproxen sodium and the deionizing agent is a hydrogen ion species.

34. (Currently Amended) The composition of claim 32, wherein the hydrogen ion species is selected from the group consisting of hydrochloric acid, hydrobromic acid, hydroiodic acid, sulfuric acid, fumaric cid, maleic acid, tartaric acid, methane-, ethane-, and benzene sulfonates, citric acid, malic acid, acetic acid, proprionic acid, pyruvic acid, butanoic acid, and lactic acid.

35. (Currently Amended) The composition of claim 33, wherein the hydrogen ion species is selected from the group consisting of hydrochloric acid, hydrobromic acid, hydroiodic acid, sulfuric acid, fumaric cid, maleic acid, tartaric acid, methane-, ethane-, and benzene sulfonates, citric acid, malic acid, acetic acid, proprionic acid, pyruvic acid, butanoic acid, and lactic acid.

36. (Currently Amended) The composition of claim 34, wherein the hydrogen ion species is lactic acid.

37. (Currently Amended) The composition of claim 35, wherein the hydrogen ion species is lactic acid.

38. (Previously Presented) A softgel capsule comprising a fill material comprising from about 10% to about 80% by weight polyethylene glycol having a molecular weight between 300 and 1500, about 10% to about 50% by weight naproxen sodium, and about 0.2 to about 1.0 moles of a deionizing agent per mole of naproxen sodium, which at least partially neutralizes the naproxen sodium.

39. (Currently Amended) The softgel capsule of claim 38, wherein the deionizing agent is selected from the group consisting of hydrochloric acid, hydrobromic acid, hydroiodic acid, sulfuric acid, fumaric cid, maleic acid, tartaric acid, methane-, ethane-, and benzene sulfonates, citric acid, malic acid, acetic acid, proprionic acid, pyruvic acid, butanoic acid, and lactic acid.

40. (Currently Amended) A pharmaceutical composition prepared by a method comprising

(a) mixing a salt of one or more acidic or basic pharmaceutically active agents;

(b) a deionizing agent in an amount from about 0.2 to about 1.0 mole equivalents per mole of the salt of the pharmaceutically active agent(s), which at least partially neutralizes the salt of pharmaceutically active agent(s) ~~agent~~; and

(c) polyethylene glycol;~~; and optionally~~

~~(d) water~~

wherein when the salt ~~(a)~~ is a salt of a weak ~~week~~ acid and a strong base, the deionizing agent is a hydrogen ion species, and when the salt ~~(a)~~ is the salt of a weak base and a strong acid, the deionizing agent is a hydroxide ion species.

41. (Currently Amended) A softgel capsule prepared by a method comprising

(a) producing a fill material by mixing

(i) a salt of one or more acidic or basic pharmaceutically active agents;

(ii) a deionizing agent in an amount from about 0.2 to about 1.0 mole equivalents per mole of the pharmaceutically active agent(s) to cause partial deionization of the salt of the pharmaceutically active agent(s); and

(iii) polyethylene glycol; ~~and optionally~~

~~(iv) water; and~~

(b) encapsulating the mixture in a softgel capsule;

wherein when the salt ~~(a)~~ is a salt of a weak acid and a strong base, the deionizing agent is a hydrogen ion species, and when the salt ~~(a)~~ is the salt of a weak base and a strong acid, the deionizing agent is a hydroxide ion species.

Remarks

The undersigned would like to thank Examiner Vu for his time during the in person interview on December 28, 2012. During the interview, the undersigned and Examiner Vu discussed the cited art and potential amendments to the claims. The Examiner's comments were instrumental in preparing this response to address all issues that were of concern to the Examiner. As discussed below, the amendments proposed by the undersigned and by the Examiner, particularly with respect to claim scope, have been made.

Claims 1, 2, 6, 7, 14, 19, 20, 24, 25, and 40 have been amended to correct antecedent basis.

Claims 6-10, 12-13, 16-17, 19-20, 24-37, and 39 have been amended to correct punctuation.

These amendments require no additional search on the part of the Examiner, do not raise any new issues, and place the claims in condition for allowance. The M.P.E.P. provides that "any amendment," including an after-final amendment, "that will place the application either in condition for allowance or in better form for appeal may be entered." *See* M.P.E.P. § 714.12. Accordingly, Applicants respectfully request entry of the claim amendments.

In the event this Response does not result in allowance of the claims, the undersigned respectfully requests a telephone interview with Examiner Vu, his supervisor, and a Quality Assurance Specialist (QAS).

Rejections Under 35 U.S.C. § 112, First Paragraph

Claims 1, 19, and 40-41 were rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. Specifically, the Examiner alleges the phrase "optionally water" is not supported by the specification, as filed, and constitutes new matter.

Applicants respectfully disagree. Support for the optional inclusion of water in the claimed formulations can be found in the specification as originally filed, at least in Examples (pages 11-15). Examples 1-7 describe formulations within the scope of the claims which include water. Examples 8-12 describe formulations within the scope of the claims which do not include water. Accordingly, the specification inherently describes formulations that optionally contain water. Therefore, claims 1, 19, and 40-41 satisfy the written description requirement.

The phrase "optionally water" was added to claims 1, 19, and 40-41 in the Amendment and Response filed August 10, 2011, in order to clarify that the deionizing agent present in the pharmaceutical composition is not water. During the interview on December 28, 2012, Examiner Vu indicated that if claims 1, 19, and 40-41 were amended to delete the phrase "optionally water," the Examiner would not construe the deionizing agent to be water.

Therefore, in order to facilitate prosecution, claims 1, 19, and 40-41 were amended to delete the phrase "optionally water." This amendment requires no additional search on the part of the Examiner, does not raise any new issues, directly address a concern raised by the

Examiner in the Office Action mailed November 29, 2011, and places the claims in condition for allowance.

The M.P.E.P. provides that "any amendment," including an after-final amendment, "that will place the application either in condition for allowance or in better form for appeal may be entered." *See* M.P.E.P. § 714.12. Accordingly, Applicants respectfully request entry of this claim amendment. In view of the amendment to claims 1, 19, and 40-41, the Examiner's rejection is moot.

Rejection Under 35 U.S.C. § 102

Claims 1-2, 6-13, 19-20, 24-31, and 40-41 were rejected under 35 U.S.C. § 102(b) as being anticipated by U.S. Patent No. 5,360,615 to Yu ("Yu").

Claims 1-2, 6-13, 19-20, and 24-35 were rejected under 35 U.S.C. § 102(b) as being anticipated by U.S. Patent No. 6,383,515 to Sawyer et al. ("Sawyer").

Claims 1-2, 6, 8-13, 19-20, 24, 26-35, and 38-41 were rejected under 35 U.S.C. § 102(b) as being anticipated by U.S. Patent No. 5,541,210 to Cupps et al ("Cupps").

Applicants respectfully traverse these rejections to the extent that they are applied to the claims, as amended.

Legal Standard

For a rejection of claims to be properly founded under 35 U.S.C. § 102, it must be established that a prior art reference discloses each and every element of the claims and enables one of skill in the field of the invention to make and use the claimed invention. *Xerox Corp. v. 3Com Corp.*, 458 F.3d 1310, 1322 (Fed. Cir. 2006) ("[I]nvalidity by anticipation requires that the

four corners of a single, prior art document describe every element of the claimed invention.") *quoting Advanced Display Sys., Inc. v. Kent State Univ.*, 212 F.3d 1272, 1282 (Fed. Cir. 2000); *Merck & Co. v. Teva Pharmaceuticals USA, Inc.*, 347 F.3d 1367, 1372, 68 USPQ2d 185 (Fed. Cir. 2003) ("An 'anticipating' reference must describe all of the elements and limitations of the claim in a single reference, and enable one of skill in the field of the invention to make and use the claimed invention."); *RCA Corp. v. Applied Digital Data Sys., Inc.*, 730 F.2d 1440, 1444, 221 USPQ 385, 388 (Fed. Cir. 1984) ("Anticipation is established only when a single prior art reference discloses, expressly or under principles of inherency, each and every element of a claimed invention."). A reference that fails to disclose or enable even one limitation will therefore not be found to anticipate, even if the missing limitation could be discoverable through further experimentation.

Analysis

Yu

Yu describes pharmaceutical formulations containing polyethylene glycol, a pharmaceutical agent in the form of the ***free acid or base***, and an ***ionizing agent***.

In contrast, the claims define formulations containing (a) a salt of one or more either acidic or basic pharmaceutically active agents; and (b) a deionizing agent in an amount from 0.2 to 1.0 mole equivalents of the pharmaceutically active agent(s), which at least partially neutralizes the pharmaceutically active agent. In the claimed formulations, the active agent is in the form of a ***salt***, and a ***deionizing agent*** is added to a fill material containing the salt of the active agent.

Yu does not disclose or suggest a formulation containing (a) a salt of one or more either acidic or basic pharmaceutically active agents; and (b) a deionizing agent in an amount from 0.2 to 1.0 mole equivalents of the pharmaceutically active agent(s), as required by the claims. Therefore, Yu cannot anticipate claims 1-2, 6-13, 19-20, 24-31, and 40-41.

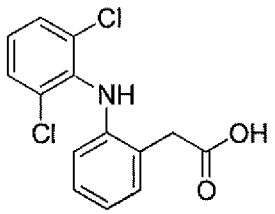
In the Office Action mailed November 29, 2011, the Examiner alleged that "even though product-by-process claims are limited by and defined by the process, determination is based on the product itself." *See* Office Action mailed November 29, 2011, page 3, line 23 to page 4, line 1. The Examiner's arguments in this regard are unclear. The claims, as pending, are not product-by-process claims. Furthermore, as discussed above, the claimed formulations are compositionally distinct from the formulations described by Yu.

The formulation described in Example 8 of Yu is not within the scope of the claims

In the Office Action mailed November 29, 2011, the Examiner alleged that Example 8 of Yu describes a formulation within the scope of the claims. *See* Office Action mailed November 29, 2011, page 3, lines 16-22. Applicants respectfully disagree.

Example 8 of Yu describes a formulation containing diclofenac sodium, polyethylene glycol, and hydrochloric acid. As shown below, diclofenac contains both a basic amine moiety and an acidic carboxylic acid moiety. Accordingly, diclofenac is an ***amphoteric*** active agent.

Therefore, Example 8 of Yu describes a formulation containing the salt of an amphoteric active agent.



Diclofenac

In contrast, the claims specify that the one or more active agents present in the formulation are salts of one or more ***either acidic or basic pharmaceutically active agents***. Diclofenac sodium is not within the scope of these claims, because diclofenac is not exclusively an acid or a base; it is amphoteric. These terms are used in the alternative in the specification as originally filed (page 3, lines 19-23 and page 4, lines 17 and 18). Accordingly, the formulation described in Example 8 of Yu is not within the scope of the claims, as previously pending.

For at least these reasons, claims 1-2, 6-13, 19-20, 24-31, and 40-41 are novel over Yu.

Sawyer

Sawyer describes medicinal solutions suitable for encapsulation in sofgel capsules. Col. 1, lines 6-7.

Sawyer is similar in scope to Yu. Sawyer describes formulations containing a low molecular weight polymer, an active agent, and the salt of an organic acid containing at least three carbon atoms (col. 3, lines 23-26). In Sawyer's formulations, the active agent is generally in the form of the ***free acid or base***, and the salt of the organic acid is a base which serves to ***ionize*** the active agent (Col. 4, lines 22-24).

In contrast, the claims define a formulation containing (a) a salt of one or more either acidic or basic pharmaceutically active agents; and (b) a deionizing agent in an amount from 0.2 to 1.0 mole equivalents of the pharmaceutically active agent(s), which at least partially neutralizes the pharmaceutically active agent. In the claimed formulations, the active agent is in the form of a ***salt***, and a ***deionizing agent*** is added to a fill material containing the salt of the active agent.

Sawyer does not disclose or suggest a formulation containing (a) a salt of one or more either acidic or basic pharmaceutically active agents; and (b) a deionizing agent in an amount from 0.2 to 1.0 mole equivalents of the pharmaceutically active agent(s), as required by the claims. Therefore, Sawyer cannot anticipate claims 1-2, 6-13, 19-20, 24-31, and 40-41.

In the Office Action mailed November 29, 2011, the Examiner alleged that "even though product-by-process claims are limited by and defined by the process, determination is based on the product itself." *See* Office Action mailed November 29, 2011, page 4, line 22 to page 5, line 1. The Examiner's arguments in this regard are unclear. The claims, as pending, are not product-by-process claims. Furthermore, as discussed above, the claimed formulations are compositionally distinct from the formulations described by Sawyer.

The formulation described in Example 17 of Sawyer is not within the scope of the claims

In the Office Action mailed November 29, 2011, the Examiner alleged that Example 17 of Sawyer describes a formulation within the scope of the claims. *See* Office Action mailed November 29, 2011, page 4, lines 16-21. Applicants respectfully disagree.

Example 17 describes a solution containing naproxen sodium, polyethylene glycol, potassium hydroxide, and sodium propionate. Potassium hydroxide and sodium propionate are bases, *i.e.*, ionizing agents, which function to maintain naproxen as the sodium salt. The Examiner alleges that because the formulation contains sodium propionate in aqueous solution, the formulation would inherently contain sodium propionate, sodium ions, propionate anions, and propionic acid. However, the Examiner has provided no evidence to demonstrate that propionic acid, if present, would be in an amount between 0.2 to 1.0 mole equivalents of the active agent(s), as required by the claims.

When sodium propionate is added to water, as in the formulation described in Example 17, an equilibrium is established between propionate and propionic acid, as shown below:

However, while trace amounts of propionic acid may be present in the formulation described in Example 17, the amount of propionic acid present in the formulation is far below the 0.2 equivalents required by the claims.

The formulation described in Example 17 contains 0.8153 g sodium propionate (K_b = 7.46 x 10^{-10}) dissolved in 800 mL of water (*i.e.*, an aqueous solution of approximately 0.0106 M sodium propionate). If the impact of other species present in solution (including the naproxen sodium, PEG 300, and potassium hydroxide) on the equilibrium between propionate and propionic acid is ignored, the concentration of propionic acid at equilibrium can be calculated to be approximately 2.7 x 10^{-5} M (corresponding to roughly 2.2 x 10^{-5} moles propionic acid at equilibrium). The formulation in Example 17 of Sawyer contains 3.0033 g (0.0119 moles) of

naproxen sodium. Therefore, Example 17 describes a formulation containing only trace amounts of propionic acid (approximately ***0.0018 mole equivalents*** of propionic acid per mole of naproxen sodium). In contrast, the claims require the deionizing agent to be present in an amount ***between 0.2 and 1.0 mole equivalents*** per mole of active agent.

Furthermore, the solution in Example 17 also contains 6.66 mg of potassium hydroxide. The pH of an aqueous solution of approximately 0.0106 M sodium propionate (*i.e.*, the formulation described in Example 17) is approximately 9.6. The addition of potassium hydroxide will make the solution even more basic, driving the equilibrium between propionate and propionic acid in the direction of propionate. As a result, the actual amount of propionate present in the formulation described in Example 17 will be even less than 0.0018 mole equivalents per mole of naproxen sodium. Therefore, what small amounts of propionic acid may be present in Example 17 of Sawyer are not with the range of between 0.2 and 1.0 mole equivalents per mole of active agent, as required by the claims.

For at least these reasons, claims 1-2, 6-13, 19-20, and 24-35 are novel over Sawyer.

Cupps

Cupps describes 5-(2-imidazolinylamino)benzimidazoles, as well as pharmaceutical compositions containing these compounds (Col. 1, lines 11-15).

In the Office Action mailed November 29, 2011, the Examiner alleged that "even though product-by-process claims are limited by and defined by the process, determination is based on the product itself." *See* Office Action mailed November 29, 2011, page 5, lines 19-21. The Examiner's arguments in this regard are unclear. The claims, as pending, are not product-by-

process claims. Furthermore, as discussed below, the claimed formulations are compositionally distinct from the formulations described by Cupps.

The formulation described in Example R of Cupps is not within the scope of the claims

In the Office Action mailed November 29, 2011, the Examiner alleged that Example R of Cupps describes a formulation within the scope of the claims. *See* Office Action mailed November 29, 2011, page 5, lines 11-17. Applicants respectfully disagree.

Example R describes a formulation containing naproxen sodium (220 mg/fl oz), sodium citrate dihydrate (trisodium citrate dihydrate, 150 mg/fl oz), and citric acid (50 mg/fl oz). The Examiner alleges that this formulation contains between 0.2 and 1.0 mole equivalents of citric acid per mole of active agent, as required by the claims. However, the Examiner has provided no evidence to demonstrate that the citric acid would be present in an amount between 0.2 to 1.0 mole equivalents of the active agent(s), as required by the claims.

Because citric acid is a weak triprotic acid, calculation of the amount of citric acid present in an aqueous solution containing citric acid and trisodium citrate is difficult. In addition, while Example R does contain water (3800 mg/fl oz), the formulation is largely composed of high fructose corn syrup (16000 mg/fl oz), polyethylene glycol (3000 mg/fl oz), propylene glycol (3000 mg/fl oz), and alcohol (2500 mg/fl oz). As a result, calculations of the amount of citric acid present in the formulation at equilibrium, which rely upon equilibrium constants specific for aqueous solutions, may not be accurate. Therefore, only rough approximations for the amount of citric acid in the formulation are possible.

Example R describes a solution containing 50 mg/fl oz of citric acid (approximately 0.0088 M citric acid, $K_{a1} = 7.44 \times 10^{-4}$) and 220 mg/fl oz of naproxen sodium (approximately 0.0295 M naproxen sodium). If the impact of other species in solution on the citric acid equilibrium is ignored and the solution is assumed to be aqueous, the concentration of citric acid at equilibrium can be calculated to be approximately 2.2×10^{-3} M. Therefore, Example R describes a formulation containing approximately ***0.075 mole equivalents*** of citric acid per mole of naproxen sodium. In contrast, the claims require the deionizing agent to be present in an amount ***between 0.2 and 1.0 mole equivalents*** per mole of active agent.

Furthermore, the solution in Example R also contains 150 mg/fl oz of sodium citrate dihydrate (trisodium citrate dihydrate, 0.01725 M). The addition of more than two moles of sodium citrate for every one mole of citric acid will make the solution more basic, driving the equilibrium between citrate and citric acid in the direction of citrate. As a result, the actual amount of citric acid present in the formulation described in Example R will be even less than 0.075 mole equivalents per mole of naproxen sodium. Accordingly, Example R of Cupps does not describe a formulation containing a deionizing agent in an amount between 0.2 and 1.0 mole equivalents per mole of active agent, as required by the claims. Therefore, Cupps cannot anticipate claims 1-2, 6, 8-13, 19-20, 24, 26-35, and 38-41.

For at least these reasons, claims 1-2, 6, 8-13, 19-20, 24, 26-35, and 38-41 are novel over Cupps.

Rejection Under 35 U.S.C. § 103

Claims 1-2, 6-13, 19-20, and 24-41 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Sawyer, in view of U.S. Patent No. 5,885,608 to McEntee ("McEntee").

Applicants respectfully traverse this rejection to the extent that it is applied to the claims, as amended.

Legal Standard

The starting point for an obviousness determination must be the Supreme Court's decision in *KSR v. Teleflex,* 550 U.S. 398 (2007), which focuses the determination of whether a claimed invention is obvious on the process the Court defined in *Graham v. John Deere Co. of Kansas City*, 383 U.S. 1, 17-18 (1966). There, the Court held that the obviousness determination should address four factors, all of which must be considered, though not in any prescribed order: (1) the scope and content of the prior art; (2) the level of ordinary skill in the art; (3) the differences between the claimed invention and the prior art; and (4) any secondary considerations suggesting nonobviousness, such as commercial success, failure of others, and long felt but unmet need. *Id.* The Court cautioned that the fact finder should be careful about reading the teachings of the invention at issue into the prior art, to avoid applying inappropriate hindsight, *ex post* reasoning. *Id. at 36.*

The Federal Circuit's decisions since KSR reflect an appropriately nuanced obviousness analysis required by *KSR* and *Graham*. The U.S. Patent Office updated its guidelines on September 1, 2010 to reflect the updated case law since *KSR*. *Examination Guidelines Update:*

Developments in the Obviousness Inquiry After KSR v. Teleflex, Fed. Reg. 75 (169): 53643-53660 (Sept. 1, 2010) ("the 2010 Obviousness Guidelines").

Obviousness requires all the claim limitations are taught or suggested by the prior art

In making an obviousness rejection under 35 U.S.C. § 103(a), the Examiner has the burden under 35 U.S.C. § 103 to establish a *prima facie* case of obviousness. *In re Warner et al.*, 379 F.2d 1011, 154 U.S.P.Q. 173, 177 (C.C.P.A. 1967); *In re Fine*, 837 F.2d 1071, 1074, 5 U.S.P.Q.2d 1596, 1598-99 (Fed. Cir. 1988). To establish a *prima facie* case of obviousness, the Examiner must first establish that all the claim limitations are taught or suggested by the prior art. *In re Royka*, 490 F.2d 981, 180 U.S.P.Q. 580 (C.C.P.A. 1974); *In re Wilson*, 424 F.2d 1382, 1385, 165 U.S.P.Q. 494, 496 (C.C.P.A. 1970) (holding that all words in a claim must be considered in judging the patentability of that claim against the prior art).

In this context, prior art is not strictly limited to the references being applied in making an obviousness rejection. Rather, the prior art also includes the understanding of one of ordinary skill in the art. However, when relying upon the understanding of one of ordinary skill in the art to arrive at claim limitations not disclosed in the prior art reference (or references when combined), "Office personnel must explain why the difference(s) between the prior art and the claimed invention would have been obvious to one of ordinary skill in the art." *See* M.P.E.P. § 2141.

Analysis

Sawyer is discussed above. Sawyer does not disclose or suggest the claimed compositions.

McEntee describes a method for treating, ameliorating, and/or prevent age-related neurological disorders by administering lipid-soluble thiamine. *Abstract.*

Neither Sawyer nor McEntee disclose or suggest a formulation containing (a) the salt of an acidic or basic active agent, and (b) a deionizing agent in an amount from 0.2 to 1.0 mole equivalents of the pharmaceutically active agent(s), as required by the claims

As discussed above, Sawyer does not disclose or suggest a formulation containing (a) a salt of one or more either acidic or basic pharmaceutically active agents; and (b) a deionizing agent in an amount from 0.2 to 1.0 mole equivalents of the pharmaceutically active agent(s), as required by the claims. McEntee does not cure the deficiencies of Sawyer. McEntee is silent with respect to formulations containing a salt of one or more either acidic or basic pharmaceutically active agents; and (b) a deionizing agent in an amount from 0.2 to 1.0 mole equivalents of the pharmaceutically active agent(s).

Sawyer teaches away from the claimed compositions

A reference may be said to teach away when a person of ordinary skill, upon reading the reference, *would be discouraged from following the path set out in the reference, or would be led in a direction divergent from the path that was taken by the applicant* (emphasis added). See *United States v. Adams*, 383 U.S. 39, 52, 148 U.S.P.Q. (BNA) 479, 484, 15 L. Ed. 2d 572, 86 S. Ct. 708 (1966); *W.L. Gore & Assoc., Inc. v. Garlock, Inc.*, 721 F.2d 1540, 1550-51, 220 U.S.P.Q. (BNA) 303, 311 (Fed. Cir. 1983) (the totality of a reference's teachings must be considered), cert. denied, 469 U.S. 851 (1984); *In re Caldwell*, 50 C.C.P.A. 1464, 319 F.2d 254, 256, 138 U.S.P.Q. (BNA) 243, 245 (CCPA 1963).

As described above, Sawyer describes formulations containing an active agent and the salt of an organic acid which serves as an ***ionizing agent*** (Col. 4, lines 22-24). Sawyer expressly describes that the salt of an organic acid should be added to the formulations to ***ionize*** the active agent (Col. 4, lines 22-24). Accordingly, one of ordinary skill in the art, reading Sawyer, would prepare a composition containing an active agent and a species which functions to keep the drug ionized, not a composition the salt of a drug and deionizing agent designed to deionize the salt of the active agent, as required by the claims. Therefore, one of ordinary skill in the art, reading Sawyer, would be led on a path divergent from the one taken in Sawyer.

For at least these reasons, claims 1-2, 6-13, 19-20, and 24-41 non-obvious over Sawyer in view of McEntee.

Allowance of claims 1-4, 6-13, 19-22, and 24-41, as amended, is respectfully solicited.

Respectfully submitted,

/Michael J. Terapane, Ph.D., J.D./
Michael J. Terapane, Ph.D., J.D.
Reg. No. 57,633

Date: April 30, 2012

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CERTIFICATE OF ELECTRONIC TRANSMISSION UNDER 37 C.F.R. § 1.8

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Date: April 30, 2012

Signature: /Candace C. Andrews

Candace C. Andrews

Electronic Acknowledgement Receipt

EFS ID:	12662636
Application Number:	11367238
International Application Number:	
Confirmation Number:	5524
Title of Invention:	Solvent system for enhancing the solubility of pharmaceutical agents
First Named Inventor/Applicant Name:	Nachiappan Chidambaram
Customer Number:	23579
Filer:	Michael John Terapane/Candace Andrews
Filer Authorized By:	Michael John Terapane
Attorney Docket Number:	BAN 102
Receipt Date:	30-APR-2012
Filing Date:	03-MAR-2006
Time Stamp:	15:44:32
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	no

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1		BAN_102_Substitute_Amendment_and_Response.pdf	1093896 f34bc05f77939e2f910591f7331eede1c2ffba88	yes	24

	Multipart Description/PDF files in .zip description		
	Document Description	**Start**	**End**
	Amendment After Final	1	1
	Claims	2	8
	Applicant Arguments/Remarks Made in an Amendment	9	24
Warnings:			
Information:			
	Total Files Size (in bytes):	1093896	

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

New Applications Under 35 U.S.C. 111

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

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

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

New International Application Filed with the USPTO as a Receiving Office

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

RESPONSE UNDER 37 C.F.R. § 1.116
EXPEDITED PROSECUTION
ART UNIT 1618

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Nachiappan Chidambaram and Aqeel Fatmi

Serial No.: 11/367,238 Art Unit: 1618

Filed: March 3, 2006 Examiner: Jake Minh Vu

For: *SOLVENT SYSTEM FOR ENHANCING THE SOLUBILITY OF PHARMACEUTICAL AGENTS*

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

TRANSMITTAL OF NOTICE OF APPEAL UNDER 37 C.F.R. § 41.31

Sir:

Responsive to the Advisory Action mailed March 1, 2012, Applicants submit a Notice of Appeal under 37 C.F.R. § 41.31. A Petition for a Two-Month extension of time is submitted with this Notice of Appeal extending the time to respond to April 29, 2012. The Commissioner is authorized to charge the sum of $1,180 (i.e., $620 the fee for the Notice of Appeal and $560, the fee for the Petition for a Two-Month Extension of Time) for a large entity to Deposit Account 50-3129.

It is believed that no additional fee is required with this submission. However, should any additional fee be required, the Commissioner is hereby authorized to charge the fee to Deposit Account No. 50-3129.

Respectfully submitted,

/Michael J. Terapane, Ph.D., J.D./
Michael J. Terapane, Ph.D., J.D.
Reg. No. 57,633

Date: April 30, 2012

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CERTIFICATE OF ELECTRONIC TRANSMISSION UNDER 37 C.F.R. § 1.8

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Date: April 30, 2012

/Candace C. Andrews/
Candace C. Andrews

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

NOTICE OF APPEAL FROM THE EXAMINER TO THE BOARD OF PATENT APPEALS AND INTERFERENCES

Docket Number (Optional): BAN 102

I hereby certify that this correspondence is being facsimile transmitted to the USPTO or deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to "Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450" [37 CFR 1.8(a)]
on _____

Signature _____

Typed or printed name _____

In re Application of: Nachiappan Chidambaram

Application Number	Filed
11/367,238	March 3, 2006

For: Solvent System for Enhancing the Solubility of Pharmaceutical Agents

Art Unit	Examiner
1618	Jake Minh Vu

Applicant hereby **appeals** to the Board of Patent Appeals and Interferences from the last decision of the examiner.

The fee for this Notice of Appeal is (37 CFR 41.20(b)(1)) $ 620

☐ Applicant claims small entity status. See 37 CFR 1.27. Therefore, the fee shown above is reduced by half, and the resulting fee is: $ _____

☐ A check in the amount of the fee is enclosed.

☐ Payment by credit card. Form PTO-2038 is attached.

☐ The Director has already been authorized to charge fees in this application to a Deposit Account.

☑ The Director is hereby authorized to charge any fees which may be required, or credit any overpayment to Deposit Account No. 50-3129 .

☑ A petition for an extension of time under 37 CFR 1.136(a) (PTO/SB/22) is enclosed.

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

I am the

☐ applicant/inventor.

☐ assignee of record of the entire interest. See 37 CFR 3.71. Statement under 37 CFR 3.73(b) is enclosed. (Form PTO/SB/96)

☑ attorney or agent of record. Registration number 57,633

☐ attorney or agent acting under 37 CFR 1.34. Registration number if acting under 37 CFR 1.34. _____

/Michael J. Terapane, Ph.D., J.D./
Signature

Michael J. Terapane, Ph.D., J.D.
Typed or printed name

404-879-2155
Telephone number

April 30, 2012
Date

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

☐ *Total of _____ forms are submitted.

This collection of information is required by 37 CFR 41.31. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11, 1.14 and 41.6. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

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

PTO/SB/22 (09-11)
Approved for use through 07/31/2012. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARMENT OF COMMERCE

PETITION FOR EXTENSION OF TIME UNDER 37 CFR 1.136(a)	Docket Number (Optional) BAN 102
Application Number 11/367,238	Filed March 3, 2006
For SOLVENT SYSTEM FOR ENHANCING THE SOLUBILITY OF PHARMACEUTICAL AGENTS	
Art Unit 1618	Examiner Jake Minh Vu

This is a request under the provisions of 37 CFR 1.136(a) to extend the period for filing a reply in the above identified application.

The requested extension and fee are as follows (check time period desired and enter the appropriate fee below):

		Fee	Small Entity Fee	
☐	One month (37 CFR 1.17(a)(1))	$150	$75	$
☑	Two months (37 CFR 1.17(a)(2))	$560	$280	$ 560
☐	Three months (37 CFR 1.17(a)(3))	$1270	$635	$
☐	Four months (37 CFR 1.17(a)(4))	$1980	$990	$
☐	Five months (37 CFR 1.17(a)(5))	$2690	$1345	$

☐ Applicant claims small entity status. See 37 CFR 1.27.

☐ A check in the amount of the fee is enclosed.

☑ Payment by credit card. Form PTO-2038 is attached.

☐ The Director has already been authorized to charge fees in this application to a Deposit Account.

☑ The Director is hereby authorized to charge any fees which may be required, or credit any overpayment, to Deposit Account Number 50-3129.

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.

I am the

☐ applicant/inventor.

☐ assignee of record of the entire interest. See 37 CFR 3.71.
Statement under 37 CFR 3.73(b) is enclosed (Form PTO/SB/96).

☑ attorney or agent of record. Registration Number 57,633

☐ attorney or agent under 37 CFR 1.34.
Registration number if acting under 37 CFR 1.34 _____

/Michael J. Terapane, Ph.D., J.D./	April 30, 2012
Signature	Date
Michael J. Terapane, Ph.D., J.D.	404-879-2155
Typed or printed name	Telephone Number

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

☐ Total of _____ forms are submitted.

Electronic Patent Application Fee Transmittal

Application Number:	11367238
Filing Date:	03-Mar-2006
Title of Invention:	Solvent system for enhancing the solubility of pharmaceutical agents
First Named Inventor/Applicant Name:	Nachiappan Chidambaram
Filer:	Michael John Terapane/Candace Andrews
Attorney Docket Number:	BAN 102

Filed as Large Entity

Utility under 35 USC 111(a) Filing Fees

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Basic Filing:				
Pages:				
Claims:				
Miscellaneous-Filing:				
Petition:				
Patent-Appeals-and-Interference:				
Notice of appeal	1401	1	620	620
Post-Allowance-and-Post-Issuance:				
Extension-of-Time:				

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Extension - 2 months with $0 paid	1252	1	560	560
Miscellaneous:				
			Total in USD ($)	**1180**

Electronic Acknowledgement Receipt

EFS ID:	12664116
Application Number:	11367238
International Application Number:	
Confirmation Number:	5524
Title of Invention:	Solvent system for enhancing the solubility of pharmaceutical agents
First Named Inventor/Applicant Name:	Nachiappan Chidambaram
Customer Number:	23579
Filer:	Michael John Terapane/Candace Andrews
Filer Authorized By:	Michael John Terapane
Attorney Docket Number:	BAN 102
Receipt Date:	30-APR-2012
Filing Date:	03-MAR-2006
Time Stamp:	16:13:08
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	Credit Card
Payment was successfully received in RAM	$1180
RAM confirmation Number	3572
Deposit Account	503129
Authorized User	ANDREWS,CANDACE C
The Director of the USPTO is hereby authorized to charge indicated fees and credit any overpayment as follows: Charge any Additional Fees required under 37 C.F.R. Section 1.16 (National application filing, search, and examination fees)	

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Miscellaneous Incoming Letter	BAN_102_Transmittal_of_Notice_of_Appeal.pdf	70633 8f483bcba6f60afae9b2bf32b4b71baa656d35ec	no	2
Warnings:					
Information:					
2	Notice of Appeal Filed	BAN_102_Notice_of_Appeal.pdf	84438 f4ca437e7c5d7054be59d2b340a15ddb05eae171	no	1
Warnings:					
Information:					
3	Extension of Time	BAN_102_Petition_for_Two_Month_EOT.pdf	85880 51315cec01261cab797f0e49b25177429d19355f	no	1
Warnings:					
Information:					
4	Fee Worksheet (SB06)	fee-info.pdf	31871 2142adf6df546f2c51a3ef77e6862ebeb269d1e8	no	2
Warnings:					
Information:					
		Total Files Size (in bytes):	272822		

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

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

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

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

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

PATENT APPLICATION FEE DETERMINATION RECORD

Substitute for Form PTO-875

Application or Docket Number	Filing Date	☐ To be Mailed
11/367,238	03/03/2006	

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

AMENDMENT	04/30/2012	(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))	* 30	Minus	** 38	=	X $ =		OR	X $ =	
	Independent (37 CFR 1.16(h))	* 5	Minus	*** 5	=	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:
/EVERETT WILLIAMS/

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
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www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
11/367,238	03/03/2006	Nachiappan Chidambaram	BAN 102	5524

23579 7590 05/18/2012

Pabst Patent Group LLP
1545 PEACHTREE STREET NE
SUITE 320
ATLANTA, GA 30309

EXAMINER	
VU, JAKE MINH	
ART UNIT	**PAPER NUMBER**
1618	
MAIL DATE	**DELIVERY MODE**
05/18/2012	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.** *11/367,238*	**Applicant(s)** CHIDAMBARAM ET AL.
	Examiner JAKE VU	**Art Unit** 1618

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

THE REPLY FILED 30 April 2012 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

NO NOTICE OF APPEAL FILED

1. ☐ The reply was filed after a final rejection. No Notice of Appeal has been filed. 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 if this is a utility or plant application. Note that RCEs are not permitted in design applications. 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.
   c) ☐ A prior Advisory Action was mailed more than 3 months after the mailing date of the final rejection in response to a first after-final reply filed within 2 months of the mailing date of the final rejection. The current period for reply expires months from the mailing date of *the prior Advisory Action* or SIX MONTHS from the mailing date of the final rejection, whichever is earlier.
   Examiner Note: If box 1 is checked, check either box (a), (b) or (c). ONLY CHECK BOX (b) WHEN THIS ADVISORY ACTION IS THE FIRST RESPONSE TO APPLICANT'S FIRST AFTER-FINAL REPLY WHICH WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. ONLY CHECK BOX (c) IN THE LIMITED SITUATION SET FORTH UNDER BOX (c). 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) or (c) 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 *30 April 2012*. 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 amendments 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 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.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after 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 the 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 of 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: See Continuation Sheet.
12. ☐ Note the attached Information *Disclosure Statement*(s). (PTO/SB/08) Paper No(s). _____
13. ☐ Other: _____.

STATUS OF CLAIMS

14. The status of the claim(s) is (or will be) as follows:
    Claim(s) allowed: .
    Claim(s) objected to: .
    Claim(s) rejected: 1,2,6-13,19,20 and 24-41.
    Claim(s) withdrawn from consideration: 14 and 16-18.

/Jake M. Vu/
Primary Examiner, Art Unit 1618

Continuation of 11. does NOT place the application in condition for allowance because: The request for another interview is denied, since applicant has 2 interviews already. The 112 rejection is withdrawn in view of applicant's amendment to fix the new matter issue. The 102 and 103 rejections are maintained. Applicant argued that YU does not teach a formulation containing (a) a salt of one or more either acidic or basic pharmaceutically active agents; and (b) a deionizing agent in an amount from 0.2 to 1.0 mole equivalents of the pharmaceutically active agent(s), as required by the claims. The Examiner finds this argument YU teaches a composition comprised of: a salt of a therapeutically active agent, such as diclofenac sodium (see col. 12, Example 8); a deionizing agent, such as 0.2 mole equivalent hydrochloric acid (see col. 12, Example 8), which is a deionizing agent (see Applicant's claim 39). Applicant argues that the Examiner alleged that "even though product-by-process claims are limited by and defined by the process, determination is based on the product itself." See Office Action mailed November 29, 2011, page 3, line 23 to page 4, line 1. The Examiner's arguments in this regard are unclear. The claims, as pending, are not product-by-process claims. The Examiner request Applicant to see claims 40-41, which are product-by-process claims. Applicant argues that diclofenac contains both a basic amine moiety and an acidic carboxylic acid moiety. Accordingly, diclofenac is an amphoteric active agent. In contrast, the claims specify that the one or more active agents present in the formulation are salts of one or more either acidic or basic pharmaceutically active agents. Diclofenac sodium is not within the scope of these claims, because diclofenac is not exclusively an acid or a base; it is amphoteric. The Examiner finds this argument unpersuasive, because an amphoteric has both a basic amine moiety and an acidic carboxylic acid moiety; thus, would read on an acid or a base. As discuss in the previous office action, SAWYER teaches a composition comprised of: 21.67% naproxen sodium (see abstract; and col. 14, line 32); deionizing agent, such as 5.88% of sodium propionate in water (see col. 14, line 23 and 35), which would inherently have propionic acid (see col. 4, line 40-44) when the sodium propionate salt goes into solution and is about 0.2-1.0 mole equivalent of naproxen sodium, wherein propionic acid is a deionizing agent (see Applicant's claim 39). Applicant argues that the pH of the sodium propionate solution in Example 17 is 9.6, which is strongly basic. Moreover, this solution is used in combination with a solution of 6.8 g KOH (a strong base) in 100 mL of water. Thus the predominant species in solution will be -OH and propionate. Therefore, the concentration of H+ is well outside the range recited in independent claims 1, 14, 18, 19, 38, 40, and 41.

The Examiner finds this argument unpersuasive, because nowhere in Example 17 does SAWYER states the pH is 9.6. As a matter of fact, SAWYER teaches the pH is adjusted to provide acceptable pH limits in the softgel (see col. 4, line 59-61), which is an acidic pH of 2.5 to 7.5 (see col. 1, line 54-56; and col. 11, line 30-32), by addition of more propionic acid (see col. 4, line 50-53). The Examiner finds Applicant's other argument unpersuasive, because as discussed in the previous office action, CUPPS teaches using a deionizing agent, such as 50mg of citric acid (see col. 29, line 12), which is about 0.2-1.0 mole equivalent of naproxen sodium, wherein citric acid is a deionizing agent by Applicant's definition (see Applicant's claim 39).

Applicant argues that Sawyer teaches away from the claimed compositions because Sawyer describes formulations containing an active agent and the salt of an organic acid which serves as an ionizing agent (Col. 4, lines 22-24). Sawyer expressly describes that the salt of an organic acid should be added to the formulations to ionize the active agent (Col. 4, lines 22-24). Accordingly, one of ordinary skill in the art, reading Sawyer, would prepare a composition containing an active agent and a species which functions to keep the drug ionized, not a composition the salt of a drug and deionizing agent designed to deionize the salt of the active agent, as required by the claims. Therefore, one of ordinary skill in the art, reading Sawyer, would be led on a path divergent from the one taken in Sawyer. The Examiner finds this argument unpersuasive, because applicant is entitled to be his or her own lexicographer. In this case, Applicant calls hydrochloric acid and proprionic acid a deionizing agent, wherein SAWYER teaches using propionic acid. Note, most of Applicant's argument have been discussed in the previous office action..

RESPONSE UNDER 37 C.F.R. § 1.116
EXPEDITED PROCEDURE
ART UNIT 1618

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Nachiappan Chidambaram and Aqeel Fatmi

Serial No.: 11/367,238 Art Unit: 1618

Filed: March 3, 2006 Examiner: Jake Minh Vu

For: *SOLVENT SYSTEM FOR ENHANCING THE SOLUBILITY OF PHARMACEUTICAL AGENTS*

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

OK TO ENTER: /J.V./

SUBSTITUTE AMENDMENT AND RESPONSE

Sir:

Responsive to the Office Action mailed on November 29, 2011, the Advisory Action mailed on March 1, 2012, and the Examiner's voice mail message on April 28, 2012, please amend the application as follows, and consider the following remarks.

It is believed that no fee is required with this submission. However, should a fee be required, the Commissioner is hereby authorized to charge the fee to Deposit Account No. 50-3129.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Appellants: Nachiappan Chidambaram and Aqeel Fatmi

Serial No.: 11/367,238 Art Unit: 1618

Filed: March 3, 2006 Examiner: Jake Minh Vu

For: *SOLVENT SYSTEM FOR ENHANCING THE SOLUBILITY OF PHARMACEUTICAL AGENTS*

Mail Stop: Appeal Brief Patents
Commissioner for Patents
P.O. Box 1450
Washington, D.C. 20231

APPEAL BRIEF

Sir:

This is an appeal from the rejection of claims 1, 2, 6-13, 19, 20, and 24-41, in the Office Action mailed on March 18, 2012, in the above-identified patent application. A Notice of Appeal was filed April 30, 2012. The Commissioner is hereby authorized to charge $770.00, the fee for filing an Appeal Brief and a one month extension of time for a large entity, to Deposit Account No. 50-3129.

It is believed that no additional fee is required with this submission. However, should an additional fee be required, the Commissioner is hereby authorized to charge the fee to Deposit Account No. 50-3129.

(1) REAL PARTY IN INTEREST

The real party in interest of this application is Banner Pharmacaps Inc.

(2) RELATED APPEALS AND INTERFERENCES

There are no related appeals or interferences known to the appellant, the undersigned, or appellant's assignee which directly affects, which would be directly affected by, or which would have a bearing on, the Board's decision in this appeal.

(3) STATUS OF CLAIMS ON APPEAL

Claims 1, 2, 6-13, 19, 20, and 24-41 are pending, rejected and on appeal. Claims 14 and 16-18 have been withdrawn from consideration. The text of each claim on appeal, as pending, is set forth in the Claim Appendix to this Appeal Brief.

(4) STATUS OF AMENDMENTS

The claims were last amended in the Amendment and Response filed on April 30, 2012. The Claims Appendix to this Appeal Brief sets forth the claims on appeal.

(5) SUMMARY OF THE CLAIMED SUBJECT MATTER

Independent claim 1 defines a pharmaceutical composition (pg. 3, lines 13-14) including (a) a salt of one or more acidic or basic pharmaceutically active agents (pg. 3, line 15; pg.4, line 15 through pg. 6, line 8; pg. 9, line 3; Examples 1-12); (b) a deionizing agent (pg. 3, line 16; pg. 6, lines 10-28; pg. 9, line 4; Examples 1-12); and (c) polyethylene glycol (pg. 7, lines 11-16; pg. 9, line 4; pg. 9, lines 9-10; Examples 1-12). The deionizing agent is present in an amount from 0.2 to 1.0 mole equivalents per mole of the active agent (pg. 3, line 16; pg. 6, lines 15-16; pg. 9, lines 7-8; Examples 1-12) and partially neutralizes the pharmaceutically active agent (pg. 3, lines 17-21; pg. 4, lines 16-20; pg. 10, lines 10-11; Examples 1-12). When the salt is of a weak acid

and strong base, the deionizing agent is a hydrogen ion species (pg. 6, lines 11-13; Examples 1-12); and when the salt is of a weak base and a strong acid, the deionizing agent is a hydroxide ion species (pg. 6, lines 13-15).

Independent claim 19 defines a softgel capsule containing a fill material (pg. 3, lines 13-15; pg. 10, lines 7-25, pg. 11, lines 2-5) where the fill material contains (a) a salt of one or more acidic or basic pharmaceutically active agents (pg. 3, line 15; pg.4, line 15 through pg. 6, line 8; pg. 9, line 3; Examples 1-12); (b) a deionizing agent (pg. 3, line 16; pg. 6, lines 10-28; pg. 9, line 4; Examples 1-12); and (c) polyethylene glycol (pg. 7, lines 11-16; pg. 9, line 4; pg. 9, lines 9-10; Examples 1-12). The deionizing agent is present in an amount from 0.2 to 1.0 mole equivalents per mole of the active agent (pg. 3, line 16; pg. 6, lines 15-16; pg. 9, lines 7-8; Examples 1-12) and partially neutralizes the pharmaceutically active agent (pg. 3, lines 17-21; pg. 4, lines 16-20; pg. 10, lines 10-11; Examples 1-12). When the salt is of a weak acid and strong base, the deionizing agent is a hydrogen ion species (pg. 6, lines 11-13; Examples 1-12); and when the salt is of a weak base and a strong acid, the deionizing agent is a hydroxide ion species (pg. 6, lines 13-15).

Independent claim 38 defines a softgel capsule (pg. 10, lines 7-19) containing a fill material containing from about 10% to 80% by weight polyethylene glycol (pg. 7, lines 11-14; pg. 9, line 4; pg. 9, lines 9-10; Examples 1-12); from about 10% to about 50% by weight naproxen sodium (pg. 5, lines 3; Examples 1-12); and about 0.2 to 1.0 moles of deionizing agent per mole of naproxen sodium (pg. 3, line 16; pg. 6, lines 15-16; pg. 9, lines 7-8; Examples 1-12). The polyethylene glycol has a molecular weight between 300 and 1500 (pg. 7, lines 14-15;

Examples 1-12). The deionizing agent partially neutralizes the naproxen sodium (pg. 3, lines 17-21; pg. 4, lines 16-20; pg. 10, lines 10-11; Examples 1-12).

Independent claim 40 defines a pharmaceutical composition (pg. 3, lines 13-14) prepared by a method (pg. 9, lines 1-12) of mixing (a) a salt of one or more acidic or basic pharmaceutically active agents (pg. 3, line 15; pg.4, line 15 through pg. 6, line 8; pg. 9, line 3; Examples 1-12); (b) a deionizing agent (pg. 3, line 16; pg. 6, lines 10-28; pg. 9, line 4; Examples 1-12); and (c) polyethylene glycol (pg. 7, lines 11-16; pg. 9, line 4; pg. 9, lines 9-10; Examples 1-12). The deionizing agent is present in an amount from 0.2 to 1.0 mole equivalents per mole of the active agent (pg. 3, line 16; pg. 6, lines 15-16; pg. 9, lines 7-8; Examples 1-12) and partially neutralizes the pharmaceutically active agent (pg. 3, lines 17-21; pg. 4, lines 16-20; pg. 10, lines 10-11; Examples 1-12). When the salt is of a weak acid and strong base, the deionizing agent is a hydrogen ion species (pg. 6, lines 11-13; Examples 1-12); and when the salt is of a weak base and a strong acid, the deionizing agent is a hydroxide ion species (pg. 6, lines 13-15).

Independent claim 41 defines a softgel capsule prepared by a method of (a) producing a fill material (pg. 9, lines 2-12); and (b) encapsulating the fill material in a softgel capsule (pg. 3, lines 13-14; pg. 10, lines 7-19). The fill material is prepared by mixing (a) a salt of one or more acidic or basic pharmaceutically active agents (pg. 3, line 15; pg.4, line 15 through pg. 6, line 8; pg. 9, line 3; Examples 1-12); (b) a deionizing agent (pg. 3, line 16; pg. 6, lines 10-28; pg. 9, line 4; Examples 1-12); and (c) polyethylene glycol (pg. 7, lines 11-16; pg. 9, line 4; pg. 9, lines 9-10; Examples 1-12). The deionizing agent is present in an amount from 0.2 to 1.0 mole equivalents per mole of the active agent (pg. 3, line 16; pg. 6, lines 15-16; pg. 9, lines 7-8; Examples 1-12) and partially neutralizes the pharmaceutically active agent (pg. 3, lines 17-21; pg. 4, lines 16-20;

pg. 10, lines 10-11; Examples 1-12). When the salt is of a weak acid and strong base, the deionizing agent is a hydrogen ion species (pg. 6, lines 11-13; Examples 1-12); and when the salt is of a weak base and a strong acid, the deionizing agent is a hydroxide species (pg. 6, lines 13-15).

All dependent claims depend from claim 1, unless otherwise noted.

Dependent claim 2 requires the pharmaceutically active agent be selected from the group consisting of therapeutically active agents, diagnostic agents, and prophylactic agents (pg. 3 lines 26 through pg. 4, line 14).

Dependent claim 6 requires the polyethylene glycol is present in an amount from about 10% to 80% by weight (pg. 7, lines 13-14; pg. 9, lines 9-10; Examples 1-12).

Dependent claim 7 requires the polyethylene glycol is one or more polyethylene glycols with a molecular weight between 300 and 1500 (pg. 7, lines 14-15; Examples 1-12).

Dependent claim 8 requires the composition further contain water (pg. 7, lines 11-12; pg. 9, lines 3-5; Examples 1-12).

Dependent claim 9, dependent from claim 8, requires the water is present between about 1% and about 18% by weight (pg. 7, line 14; pg. 9, lines 8-10; Examples 1-12).

Dependent claim 10 requires the composition further contain one or more excipients (pg. 7, lines 5-10; pg. 7, lines 17-18; Examples 1-12).

Dependent claim 11, dependent from claim 10, requires the excipient is selected from the group consisting of plasticizers, crystallization inhibitors, wetting agents, bulk filling agents, solubilizers, bioavailability enhancers, solvents, pH-adjusting agents, dyes, preservatives, surfactants, and combinations thereof (pg. 7, lines 6-10; pg. 7, lines 17-18; Examples 1-12).

Dependent claim 12, dependent from claim 11, requires the solubilizer is selected from the group consisting of glycerin, polyvinylpyrrolidone, propylene glycol, and combinations thereof (pg. 7, lines 17-18; Examples 1-12).

Dependent claim 13, dependent from claim 12, requires the solubilizer is present in an amount from about 1% to about 10% by weight (Examples 1-12).

Dependent claim 20, dependent from claim 19, requires the one or more pharmaceutically active agent(s) are selected from the group consisting of therapeutically active agents, diagnostic agents, and prophylactic agents (pg. 3 lines 26 through pg. 4, line 14).

Dependent claim 24, dependent from claim 19, requires the polyethylene glycol is present in an amount from about 10% to about 80% by weight (pg. 7, lines 13-14; pg. 9, lines 9-10; Examples 1-12).

Dependent claim 25, dependent from claim 19, requires the polyethylene glycol is one or more polyethylene glycols with a molecular weight between 300 and 1500 (pg. 7, lines 14-15; Examples 1-12).

Dependent claim 26, dependent from claim 19, requires the capsule further contain water (pg. 7, lines 11-12; pg. 9, lines 3-5; Examples 1-12).

Dependent claim 27, dependent from claim 26, requires the water is present in an amount from about 1% to about 18% by weight (pg. 7, line 14; pg. 9, lines 8-10; Examples 1-12).

Dependent claim 28, dependent from claim 19, requires the capsule further comprise one or more excipients (pg. 7, lines 5-10; pg. 7, lines 17-18; Examples 1-12).

Dependent claim 29, dependent from claim 28, requires the one or more excipients is selected from the group consisting of plasticizers, crystallization inhibitors, wetting agents, bulk

filling agents, solubilizers, bioavailability enhancers, solvents, pH-adjusting agents, dyes, preservatives, surfactants, and combinations thereof (pg. 7, lines 6-10; pg. 7, lines 17-18; Examples 1-12).

Dependent claim 30, dependent from claim 29, requires the solubilizer is selected from the group consisting of glycerin, polyvinylpyrrolidone, propylene glycol and combinations thereof (pg. 7, lines 17-18; Examples 1-12).

Dependent claim 31, dependent from claim 29, requires the solubilizer is present in an amount from about 1% to about 10% by weight (Examples 1-12).

Dependent claim 32 requires the pharmaceutically active agent is naproxen sodium and the deionizing agent is a hydrogen ion species (pg. 5, line 3; pg. 6, lines 11-13; Examples 1-12).

Dependent claim 33, dependent from claim 19, requires pharmaceutically active agent is naproxen sodium and the deionizing agent is a hydrogen ion species (pg. 5, line 3; pg. 6, lines 11-13; Examples 1-12).

Dependent claim 34, dependent from claim 32, requires the hydrogen ion species is selected from the group consisting of hydrochloric acid, hydrobromic acid, hydroiodic acid, sulfuric acid, fumaric cid, maleic acid, tartaric acid, methane, ethane, and benzene sulfonates, citric acid, malic acid, acetic acid, proprionic acid, pyruvic acid, butanoic acid, and lactic acid (pg. 6, lines 17-21, Examples 1-12).

Dependent claim 35, dependent from claim 33, requires the hydrogen ion species is selected from the group consisting of hydrochloric acid, hydrobromic acid, hydroiodic acid, sulfuric acid, fumaric cid, maleic acid, tartaric acid, methane, ethane, and benzene sulfonates,

citric acid, malic acid, acetic acid, proprionic acid, pyruvic acid, butanoic acid, and lactic acid (pg. 6, lines 17-21, Examples 1-12).

Dependent claim 36, dependent from claim 34, requires the hydrogen ion species is lactic acid (pg. 6, lines 21; Examples 7-12).

Dependent claim 37, dependent from claim 35, requires the hydrogen ion species is lactic acid (pg. 6, lines 21; Examples 7-12).

Depend claim 39, dependent from claim 38, requires the deionizing agent is selected from the group consisting of hydrochloric acid, hydrobromic acid, hydroiodic acid, sulfuric acid, fumaric cid, maleic acid, tartaric acid, methane, ethane, and benzene sulfonates, citric acid, malic acid, acetic acid, proprionic acid, pyruvic acid, butanoic acid, and lactic acid (pg. 6, lines 17-21, Examples 1-12).

(6) GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

The issues present on appeal are whether:

(i) claims 1, 2, 6-13, 19, 20, 24-31, 40, and 41 are anticipated under 35 U.S.C. § 102(b) by U.S. Patent No. 5,360,615 to Yu ("Yu");

(ii) claims 1, 2, 6-13, 19, 20, and 24-35 are anticipated under 35 U.S.C. § 102(b) by U.S. Patent No. 6,383,515 to Sawyer et al. ("Sawyer");

(iii) claims 1, 2, 6, 8-13, 19, 20, 24, 26-35, and 38-41 are anticipated under 35 U.S.C. § 102(b) by U.S. Patent No. 5,541,210 to Cupps et al. ("Cupps");

(iv) claims 1, 2, 6-13, 19, 20, and 24-41 are obvious under 35 U.S.C. § 103(a) over Sawyer in view of U.S. Patent No. 5,885,608 to McEntee ("McEntee").

(7) ARGUMENTS

The Claimed Invention

The claimed invention describes pharmaceutical formulations which can be encapsulated in soft or hard shell capsules. The formulations contain the salt of one or more acidic or basic active agents, and 0.2-1.0 mole equivalents of a de-ionizing agent per mole of the active agent(s) to partially de-ionize (neutralize) the salt of the active agent resulting in enhanced bioavailability and decreased amounts of polyethylene glycol (PEG) esters. Decreasing or preventing the formation of PEG esters is important in pharmaceutical formulations because PEG ester formation is known to adversely affect the efficacy of some active ingredients, including naproxen sodium.

Independent claims 1, 19, and 38 are not product-by-process claims

In the Office Action mailed November 29, 2011, the Examiner alleged that "even though product-by-process claims are limited by and defined by the process, determination is based on the product itself." See Office Action mailed November 29, 2011, page 3, line 23 to page 4, line 1. The Examiner's arguments in this regard are unclear. Independent claims 1, 19, and 38 are product claims, ***not product-by-process claims***. The claims do not contain any process steps. The phrase in question, discussed below, is a functional limitation which further defines the deionizing agent. Therefore, there remains a heavy burden on the Examiner to establish that the prior art expressly, implicitly, or inherently discloses each and every element of the claims.

Independent claims 1, 19, and 38 require a deionizing agent in a specific amount. The claims also state that the deionizing agent "at least partially neutralizes the pharmaceutically active agent." This is a functional limitation, not a process step as alleged by the Examiner. This

is supported by the holding in *In re Barr*, 444 F.2d 588 (CCPA 1971). In *In re Barr*, it was held that the limitation used to define a radical on a chemical compound as "incapable of forming a dye with said oxidizing developing agent" although functional, was perfectly acceptable because it set definite boundaries on the patent protection sought. *In re Barr*, 444 F.2d 588, 170 USPQ 33 (CCPA 1971). The functional limitation at issue in *In re Barr* is analogous to the functional limitation in the present claims in that the limitation defines the reactivity or lack of reactivity of a component in the formulation. The functional limitation in question sets definite boundaries on the patent protection being sought.

A functional limitation must be evaluated and considered, just like any other limitation of the claim, for what it fairly conveys to a person of ordinary skill in the pertinent art in the context in which it is used. In *Innova/Pure Water Inc. v. Safari Water Filtration Sys. Inc.*, 381 F.3d 1111, 1117-20, 72 USPQ2d 1001, 1006-08 (Fed. Cir. 2004).

The functional limitation that the deionizing agent "at least partially neutralizes the pharmaceutically active agent" is a distinguishing feature of the claims. As will be discussed in detail below, even if an acid (hydrogen ion species) is present in a composition, the presence of a strong or stronger base, such as hydroxide ion or citrate, will likely render the acid incapable of satisfying the functional limitation, i.e., partial neutralization of the active agent. This is due to the fact that the basic species are stronger bases than the conjugate base of the acidic active agent and thus are protonated before the conjugate base of the acidic active agent.

Rejections under 35 U.S.C § 102(b)

Legal Standard

"A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987).

The fact that a certain result or characteristic may occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic. *In re Rijckaert*, 9 F.3d 1531, 1534, 28 USPQ2d 1955, 1957 (Fed. Cir. 1993) (reversed rejection because inherency was based on what would result due to optimization of conditions, not what was necessarily present in the prior art); *In re Oelrich*, 666 F.2d 578, 581-82, 212 USPQ 323, 326 (CCPA 1981). "To establish inherency, the extrinsic evidence 'must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill. ***Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient***.' " *In re Robertson*, 169 F.3d 743, 745, 49 USPQ2d 1949, 1950-51 (Fed. Cir. 1999) (citations omitted).

For at least the reasons discussed below, the Examiner has failed to provide any, let alone strong, rationale or evidence that the prior art expressly, implicitly, or inherently discloses each and every element of claims 1, 2, 6-13, 19, 20, and 24-39. Accordingly, claims 1, 2, 6-13, 19, 20, and 24-39 are novel over the prior art cited by the Examiner.

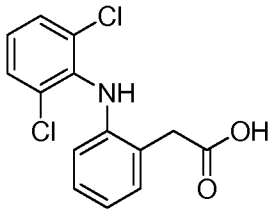
U. S. Patent No. 5,360,615 to Yu ("Yu")

Scope and context of the prior art

Yu describes pharmaceutical formulations containing polyethylene glycol, a pharmaceutical agent in the form of the ***free acid or base***, and ***an ionizing agent***. *Abstract* and col. 4, lines 25-35.

In the Office Action mailed November 29, 2011, the Examiner alleged that Example 8 of Yu describes a formulation within the scope of the claims. *See* Office Action mailed November 29, 2011, page 3, lines 16-22. Appellants respectfully disagree.

Example 8 of Yu describes a formulation containing diclofenac sodium, polyethylene glycol, and hydrochloric acid. As shown below, diclofenac contains both a basic amine moiety and an acidic carboxylic acid moiety.



Diclofenac

Therefore, Diclofenac is an ***amphoteric*** active agent. Example 8 of Yu describes a formulation containing the salt of an amphoteric active agent.

Claims 1, 2, 6-13, 19, 20, and 24-31 are novel over Yu

MPEP § 2173.05(a) states "Consistent with the well-established axiom in patent law that a patentee or applicant is free to be his or her own lexicographer, a patentee or applicant may use terms in a manner contrary to or inconsistent with one or more of their ordinary meanings if the

written description clearly redefines the terms. See, e.g., *Process Control Corp. v. HydReclaim Corp.*, 190 F.3d 1350, 1357, 52 USPQ2d 1029, 1033 (Fed. Cir. 1999)

The claims specify that the one or more active agents present in the formulation are salts of one or more ***either acidic or basic pharmaceutically active agents***. The present application classifies active agents as acidic, basic, or amphoteric (pg. 4, lines 15-16). The specification reads, "A first class of drugs is selected based on inclusion in the molecule of a weakly acidic, basic or amphoteric group that can form a salt." The use of the disjunctive "or" clearly differentiates the three groups. Diclofenac sodium is not within the scope of the claims, because diclofenac is not exclusively an acid or a base. It is amphoteric.

Moreover, the embodiment in Example 8 is not effective as a pharmaceutical composition. As discussed in the Amendment and Response filed on May 3, 2010, it is known in the art that strong acids, such as hydrochloric acid, catalyze the cyclization of diclofenac sodium to an indolinone derivative (see Figure 1 of Palomo, et al., *J. Pharm Biomed. Anal.*, 21: 83-94 (1999) copy of which are enclosed with this Appeal Brief). Palomo states that the cyclized indolinone is pharmaceutically inactive. Therefore, such a formulation is not a pharmaceutical composition.

For at least the reasons discussed above, Yu does not disclose or suggest the elements of claims 1, 2, 6-13, 19, 20, and 24-31. Accordingly, claims 1, 2, 6-13, 19, 20, and 24-31 are novel over Yu.

Independent claims 40 and 41 are novel over Yu

Example VIII in Yu describes a formulation prepared by mixing an amphiphilic active agent, diclofenac sodium, with hydrochloric acid. As discussed above, diclofenac sodium is not an acidic or basic active agent as required in claims 40 and 41. Yu does not disclose or suggest mixing the salt of an acidic or basic active agent with a deionizing agent in the amount defined in claims 40 and 41, wherein the deionizing agent at least partially deionizes the salt of the acidic or basic active agent. Moreover, as discussed above, it is known in the art that strong acids, such as hydrochloric acid, catalyze the cyclization of diclofenac sodium to an indolinone derivative, which is pharmaceutically inactive.

Yu does not disclose or suggest the elements of claims 40 and 41. Accordingly, claims 40 and 41 are novel over Yu.

U. S. Patent No. 6,383,515 to Sawyer et al. ("Sawyer")

Scope and context of the prior art

Sawyer describes solutions suitable for encapsulation in softgel capsules (col. 1, lines 6-7). Sawyer describes formulations containing a low molecular weight polymer, an active agent, and the salt of an organic acid containing at least three carbon atoms (col. 3, lines 23-26). The active agent is generally in the form of the ***free acid or base***, and the salt of the organic acid is a base which serves to ***ionize*** the active agent, when the active agent is an acid (Col. 4, lines 22-24).

Claims 1, 2, 6-13, 19, 20, and 24-35 *are novel over Sawyer*

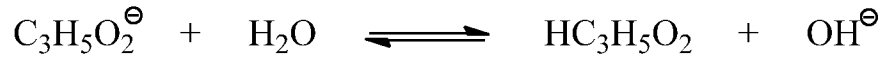
Claim 1 defines a formulation containing (a) a salt of one or more either acidic or basic pharmaceutically active agents; and (b) a deionizing agent in an amount from 0.2 to 1.0 mole

equivalents of the pharmaceutically active agent(s), which at least partially neutralizes the pharmaceutically active agent. In the claimed formulations, the active agent is in the form of a ***salt***, and a ***deionizing agent*** is added to a fill material containing the salt of the active agent to partially neutralize the salt of the active agent.

In the Office Action mailed November 29, 2011, the Examiner alleged that Example 17 of Sawyer describes a formulation within the scope of the claims. *See* Office Action mailed November 29, 2011, page 4, lines 16-21. Appellants respectfully disagree.

Example 17 describes a solution containing naproxen sodium, polyethylene glycol, potassium hydroxide, and sodium propionate. Potassium hydroxide and sodium propionate are bases, *i.e.*, ionizing agents, which function to maintain naproxen as the sodium salt. The Examiner alleges that because the formulation contains sodium propionate in aqueous solution, the formulation would inherently contain propionic acid. However, the Examiner has provided no evidence to demonstrate that propionic acid is present in an amount between 0.2 to 1.0 mole equivalents of the active agent(s), as required by the claims.

When sodium propionate is added to water, as in the formulation described in Example 17, an equilibrium is established between propionate and propionic acid, as shown below:



The formulation described in Example 17 contains 0.8153 g sodium propionate (K_b = 7.46 x 10^{-10}) dissolved in 800 mL of water (*i.e.*, an aqueous solution of approximately 0.0106 M sodium propionate). If the impact of other species present in solution on the equilibrium between propionate and propionic acid is ignored, the concentration of propionic acid at

equilibrium is calculated to be approximately 2.7 x 10^{-5} M (corresponding to roughly 2.2 x 10^{-5} moles propionic acid at equilibrium). The formulation in Example 17 of Sawyer contains 3.0033 g (0.0119 moles) of naproxen sodium. Therefore, Example 17 describes a formulation containing only trace amounts of propionic acid, approximately ***0.0018 mole equivalents*** of propionic acid per mole of naproxen sodium. In contrast, the claims require the deionizing agent to be present in an amount ***between 0.2 and 1.0 mole equivalents*** per mole of active agent.

Furthermore, the solution in Example 17 also contains 6.66 mg of potassium hydroxide. The pH of an aqueous solution of approximately 0.0106 M sodium propionate (*i.e.*, the formulation described in Example 17) is approximately 9.6. The addition of potassium hydroxide will make the solution even more basic, driving the equilibrium between propionate and propionic acid in the direction of propionate. As a result, the actual amount of propionate present in the formulation described in Example 17 will be ***even less than 0.0018 mole equivalents per mole of naproxen sodium***. Therefore, what small amounts of propionic acid may be present in Example 17 of Sawyer are not with the range of between 0.2 and 1.0 mole equivalents per mole of active agent, as required by Appellants' claims.

Moreover, to the extent any propionic acid is formed, it does not meet the functional limitation in claim 1 that it partially deionizes the salt of the active agent. In Example 17, the potassium hydroxide is a prototypical strong base, with a pK_b of approximately 0.5. The naproxen sodium, on the other hand, is a weak base with a pK_b of approximately 9.8. The potassium hydroxide is present in excess compared to propionate by more than a factor of 10. Therefore, any propionic acid which forms will be consumed through reaction with hydroxide. No propionic acid will remain to react with the conjugate base of the active agent.

Appellants note that the Examiner has repeatedly alleged that the sodium propionate in Example 17, at equilibrium, generates propionic acid in the amounts specified in the claims. Appellants also note, however, that this allegation has ignored the effect of sodium hydroxide on the equilibrium. Moreover, the Examiner has failed to provide any evidence that the allegation is accurate, even when explicitly requested to do so by the Appellants. Appellants have shown through the calculations above that the amount of propionic acid formed, regardless of whether or not one considers the effect of the potassium hydroxide, is not with the range specified in the claims.

In the basic solutions disclosed by Sawyer, the concentration of propionic acid is at least two orders of magnitude lower than the 0.2 to 1.0 mole equivalents specified in independent claims 1 and 19. Furthermore, in these basic conditions, the propionic acid in Example 17 of Sawyer does not meet the functional limitation that the deionizing agent at least partially neutralizes the active agents, as specified in independent claims 1 and 19. The Examiner has failed to provide basis in fact or technical reasoning to the contrary and in support of inherency. "In relying upon the theory of inherency, the Examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art." See *Ex parte Levy*, 17 USPQ2d 1461, 1464 (Bd. Pat. App. & Inter. 1990). Accordingly, claims 1, 2, 6-13, 19, 20, and 24-35 are novel over Sawyer.

Claims 32 and 33 are novel over Sawyer

Claims 32 and 33 depend from claims 1 and 19, respectively, and specify that the salt of the active agent is naproxen sodium and the deionizing agent is a hydrogen ion species.

As discussed above, Example 17 in Sawyer does not disclose or suggest a pharmaceutical composition comprising naproxen sodium and a deionizing agent. Example 17 discloses a composition containing naproxen sodium, sodium propionate, and potassium hydroxide. Sodium propionate and potassium hydroxide are ionizing agents. Appellants have demonstrated that even ignoring the contribution of potassium hydroxide, at equilibrium the theoretical amount of propionic acid in solution is at least two orders of magnitude less than what is specified in independent claims 1 and 19. When one includes the contribution of potassium hydroxide, the pH of the composition is significantly more basic which drives the equilibrium further to the left and results in even less propionic acid in solution. The excess potassium hydroxide in solution will also serve to prevent the neutralization of the active agent by any propionic acid present. Sawyer does not disclose or suggest, explicitly or inherently, the elements of claims 32 and 33. Accordingly, claims 32 and 33 are novel over Sawyer.

Claims 34 and 35 are novel over Sawyer

Claims 34 and 35 depend from claims 32 and 33, respectively, and further define the hydrogen ion species as selected from the members of the Markush group in claims 34 and 35. Example 17 in Sawyer discloses a composition containing naproxen sodium, sodium propionate, and potassium hydroxide. None of the hydrogen ion species specified in claims 34 and 35 are in the list of ingredients in Example 17. As discussed above, to the extent any citric acid forms during mixing, the amount of citric acid is at least two, and likely more than two, orders of magnitude less than the amount specified in claims 1 and 19, from which claims 34 and 35 depend. Sawyer does not disclose or suggest, explicitly or inherently, the elements of claims 34 and 35. Accordingly, claims 34 and 35 are novel over Sawyer.

Claims 36 and 37 are novel over Sawyer

Claims 36 and 37 depend from claims 32 and 33 specifically and specify that the hydrogen ion species is lactic acid. Example 17 in Sawyer discloses a composition containing naproxen sodium, sodium propionate, and potassium hydroxide. Lactic acid is not in the list of ingredients in Example 17. Moreover, lactic acid cannot form from any of the ingredients in Example 17. Sawyer does not disclose or suggest, explicitly or inherently, the elements of claims 36 and 37. Accordingly, claims 36 and 37 are novel over Sawyer.

Claims 38 and 39 are novel over Sawyer

Claims 38 and 39 are drawn to a softgel capsule comprising naproxen sodium, PEG, and 0.2-1.0 mole equivalents of a deionizing agent per mole of naproxen sodium. Example 17 discloses a solution. Example 17 does not disclose or suggest that the solution was encapsulated in a soft gel capsule as required by claims 38 and 39.

Example 17 discloses a composition containing naproxen sodium, sodium propionate, and potassium hydroxide. Sodium propionate and potassium hydroxide are ionizing agents. Appellants have demonstrated that even ignoring the contribution of potassium hydroxide, at equilibrium the theoretical amount of propionic acid in solution is at least two orders of magnitude less than what is specified in independent claim 38. When one includes the contribution of potassium hydroxide, the pH of the composition is significantly more basic which drives the equilibrium further to the left and results in even less propionic acid in solution. The excess potassium hydroxide in solution will also serve to prevent the neutralization of the active agent by any propionic acid present. Sawyer does not disclose or suggest, explicitly or

inherently, the elements of claims 38 and 39. Accordingly, claims 38 and 39 are novel over Sawyer.

U. S. Patent No. 5,541,210 to Cupps et al. ("Cupps")

Please note that the claims do not stand or fall together. The claims have been argued separately with respect to the prior art to identify the differences shared in common as well as additional differences.

Scope and context of the prior art

Cupps describes 5-(2-imidazolinylamino)benzimidazoles, as well as pharmaceutical compositions containing these compounds (Col. 1, lines 11-15). In the Office Action mailed November 29, 2011, the Examiner alleged that Example R of Cupps describes a formulation within the scope of the claims. *See* Office Action mailed November 29, 2011, page 5, lines 11-17. Appellants respectfully disagree.

Example R describes a formulation containing naproxen sodium (220 mg/fl oz), sodium citrate dihydrate (trisodium citrate dihydrate, 150 mg/fl oz), and citric acid (50 mg/fl oz). The Examiner alleges that this formulation contains between 0.2 and 1.0 mole equivalents of citric acid per mole of active agent, as required by the claims. However, the Examiner has provided no evidence to demonstrate that the citric acid would be present in an amount between 0.2 to 1.0 mole equivalents of the active agent(s), as required by the claims, even when explicitly requested to do so by the Appellants.

Claims 1, 2, 6, 8-13, 19, 20, 24, 26-31, and 41 are novel over Cupps

Because citric acid is a weak triprotic acid, calculation of the amount of citric acid present in an aqueous solution containing citric acid and trisodium citrate is difficult. In

addition, while Example R does contain water (3800 mg/fl oz), the formulation is largely composed of high fructose corn syrup (16000 mg/fl oz), polyethylene glycol (3000 mg/fl oz), propylene glycol (3000 mg/fl oz), and alcohol (2500 mg/fl oz). Therefore, only rough approximations for the amount of citric acid in the formulation are possible.

Example R describes a solution containing 50 mg/fl oz of citric acid (approximately 0.0088 M citric acid, $K_{a1} = 7.44 \times 10^{-4}$) and 220 mg/fl oz of naproxen sodium (approximately 0.0295 M naproxen sodium). If the impact of other species in solution on the citric acid equilibrium is ignored and the solution is assumed to be aqueous, the concentration of citric acid at equilibrium is calculated to be approximately 2.2×10^{-3} M. Therefore, Example R describes a formulation containing approximately ***0.075 mole equivalents*** of citric acid per mole of naproxen sodium. In contrast, the claims require the deionizing agent to be present in an amount ***between 0.2 and 1.0 mole equivalents*** per mole of active agent.

Furthermore, the solution in Example R also contains 150 mg/fl oz of sodium citrate dihydrate (trisodium citrate dihydrate, 0.01725 M). The addition of more than two moles of sodium citrate for every one mole of citric acid will make the solution more basic, driving the equilibrium between citrate and citric acid in the direction of citrate. As a result, the actual amount of citric acid present in the formulation described in Example R will be significantly less than 0.075 mole equivalents per mole of naproxen sodium. Accordingly, Example R of Cupps does not describe a formulation containing a deionizing agent in an amount between 0.2 and 1.0 mole equivalents per mole of active agent, as required by the claims. Therefore, Cupps cannot anticipate claims 1-2, 6, 8-13, 19-20, 24, 26-31, and 41.

For at least these reasons, claims 1-2, 6, 8-13, 19-20, 24, 26-31, and 41 are novel over Cupps.

Claims 32-35 are novel over Cupps

Claims 32 and 33 depend from claims 1 and 19, respectively, and specify that the salt of the active agent is naproxen sodium and the deionizing agent is a hydrogen ion species. Claims 34 and 35 depend from claims 32 and 33, respectively, and further define the hydrogen ion species.

Example R describes a formulation containing naproxen sodium (220 mg/fl oz), sodium citrate dihydrate (trisodium citrate dihydrate, 150 mg/fl oz), and citric acid (50 mg/fl oz). The Examiner alleges that this formulation contains between 0.2 and 1.0 mole equivalents of citric acid per mole of active agent, as required by the claims.

As discussed above, Example R in Cupps does not disclose or suggest a pharmaceutical composition comprising naproxen sodium and a deionizing agent present in an amount ***between 0.2 and 1.0 mole equivalents*** per mole of the active agent. As outlined above, Example R describes a formulation containing less than approximately ***0.075 mole equivalents*** of citric acid per mole of naproxen sodium. The Examiner has not provided reasoning or sound argument to demonstrate a concentration of at least 0.2 mole equivalents as required by the claims.

Cupps does not disclose or suggest, explicitly or inherently, the elements of claims 32-35. Accordingly, claims 32-35 are novel over Sawyer.

Claims 38 and 39 are novel over Cupps

Claims 38 and 39 are drawn to a softgel capsule comprising naproxen sodium, PEG, and 0.2-1.0 mole equivalents of a deionizing agent per mole of naproxen sodium. Example R in

Cupps describes a formulation for administration as a liquid dosage form (column 28, lines 56-61). Example R does not disclose or suggest the claimed capsules. Cupps does not disclose or suggest every element of claims 38 and 39. For at least these reasons and the reasons discussed above with respect to claims 32-35, claims 38 and 39 are novel over Cupps.

Rejections under 35 U.S.C § 103(a)

claims 1, 2, 6-13, 19, 20, and 24-41 were rejected as obvious under 35 U.S.C. § 103(a) over Sawyer in view of U.S. Patent No. 5,885,608 to McEntee ("McEntee").

Legal Standard

The starting point for an obviousness determination is the Supreme Court's decision in *KSR International Co. v. Teleflex, Inc.,* 550 U.S. 398 (2007), which refocuses the determination of whether a claimed invention is obvious back to the process the Court had defined in *Graham v. John Deere Co. of Kansas City*, 383 U.S. 1, 17–18 (1966). There, the Court had held that the obviousness determination should address four factors, all of which must be considered, though not in any prescribed order: (1) the scope and content of the prior art; (2) the level of ordinary skill in the art; (3) the differences between the claimed invention and the prior art; and (4) any secondary considerations suggesting nonobviousness, such as commercial success, failure of others, and long felt but unmet need. *Id.* The Court cautioned that the fact finder should be careful about reading the teachings of the invention at issue into the prior art, to avoid applying inappropriate hindsight, *ex post* reasoning. *Id.* at 36.

In *KSR*, the Court also warned against the use of hindsight analysis in making an obviousness determination. The Court stated, "A factfinder should be aware, of course, of the distortion caused by hindsight bias and must be cautious of arguments reliant upon *ex post*

reasoning." *KSR*, 550 U.S. at 421, citing *Graham*, 383 U.S. at 36 (warning against a "temptation to read into the prior art the teachings of the invention in issue" and instructing courts to "'guard against slipping into the use of hindsight'" (quoting M*onroe Auto Equipment Co. v. Heckethorn Mfg. & Supply Co.*, 332 F.2d 406, 412, 141 U.S.P.Q. 549 (6th Cir. 1964))).

A *Prima Facie* case of obviousness is established when the following three criteria are met: (1) suggestion or motivation either in the references themselves or in the knowledge generally available to one of ordinary skill in the art to combine or modify the teaching in the references; (2) there must be a reasonable expectation of success; and (3) the references must teach all limitation in the claim. MPEP § 4142.

Sawyer in view of McEntee

Scope and context of the prior art

Sawyer does not disclose or suggest the claimed compositions for at least the reasons discussed above.

McEntee describes a method for treating, ameliorating, and/or preventing age-related neurological disorders by administering lipid-soluble thiamine. *Abstract*.

Claims 1, 2, 6-13, 19, 20, and 24-41 are non-obvious over Sawyer in light of McEntee

As discussed above, Sawyer does not disclose or suggest a formulation containing (a) a salt of one or more either acidic or basic pharmaceutically active agents; and (b) a deionizing agent in an amount from 0.2 to 1.0 mole equivalents of the pharmaceutically active agent(s), as required by the claims. McEntee does not cure the deficiencies of Sawyer. McEntee is silent with respect to formulations containing a salt of one or more either acidic or basic

pharmaceutically active agents; and (b) a deionizing agent in an amount from 0.2 to 1.0 mole equivalents of the pharmaceutically active agent(s).

Allowance of all pending claims 1, 2, 6-13, 19, 20, and 24-41 is earnestly solicited.

Respectfully submitted,

/Michael J. Terapane, Ph.D., J.D./
Michael J. Terapane, Ph.D., J.D.
Reg. No. 31,284

Date: July 30, 2012

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Claims Appendix

1. (Previously presented) A pharmaceutical composition comprising

(a) a salt of one or more either acidic or basic pharmaceutically active agents; and

(b) a deionizing agent in an amount from about 0.2 to about 1.0 mole equivalents per mole of the pharmaceutically active agent(s), which at least partially neutralizes the pharmaceutically active agent(s); and

(c) polyethylene glycol;

wherein when the salt is a salt of a weak acid and a strong base, the deionizing agent is a hydrogen ion species and when the salt is a salt of a weak base and a strong acid, the deionizing agent is a hydroxide ion species.

2. (Previously presented) The composition of claim 1, wherein the one or more pharmaceutically active agents(s) are selected from the group consisting of therapeutically active agents, diagnostic agents, and prophylactic agents.

6. (Previously presented) The composition of claim 1, wherein the polyethylene glycol is present in an amount from about 10% to about 80% by weight.

7. (Previously presented) The composition of claim 1, wherein the polyethylene glycol is one or more polyethylene glycols with a molecular weight between 300 and 1500.

8. (Previously presented) The composition of claim 1, further comprising water.

9. (Previously presented) The composition of claim 8, wherein water is present in an amount from about 1% to about 18% by weight.

10. (Previously presented) The composition of claim 1, further comprising one or more excipients.

11. (Previously Presented) The composition of claim 10, wherein the one or more excipients are selected from the group consisting of plasticizers, crystallization inhibitors, wetting agents, bulk filling agents, solubilizers, bioavailability enhancers, solvents, pH-adjusting agents, dyes, preservatives, surfactants, and combinations thereof.

12. (Previously presented) The composition of claim 11, wherein the solubilizer is selected from the group consisting of glycerin, polyvinylpyrrolidone, propylene glycol, and combinations thereof.

13. (Previously presented) The composition of claim 12, wherein the solubilizer is present in amount from about 1% to about 10% by weight.

14. (Withdrawn) A method of making the capsule of claim 19 comprising

(a) mixing a salt of one or more acidic or basic pharmaceutically active agents, a deionizing agent in an amount from about 0.2 to about 1.0 mole equivalents per mole of the pharmaceutically active agent(s), which at least partially neutralizes the pharmaceutically active agent(s), and polyethylene glycol at an appropriate temperature; and

(b) encapsulating the mixture in a softgel capsule.

16. (Withdrawn) The method of claim 14, further comprising water.

17. (Withdrawn) The method of claim 14, wherein the appropriate temperature is from about 50°C to about 70°C.

18. (Withdrawn) A method of using the pharmaceutical composition of claim 1 or the capsule of claim 19 or 38 comprising

administering to a patient in need thereof an effective amount of the composition of claim 1 or the capsule of claim 19 or 38.

19. (Previously presented) A softgel capsule comprising a fill material, wherein the fill material comprises

(a) a salt of one or more either acidic or basic pharmaceutically active agents; and

(b) a deionizing agent in an amount from about 0.2 to about 1.0 mole equivalents per mole of the pharmaceutically active agent(s), which at least partially neutralizes the pharmaceutically active agent(s); and

(c) polyethylene glycol;

wherein, when the salt is a salt of a weak acid and a strong base, the deionizing agent is a hydrogen ion species and when the salt is a salt of a weak base and a strong acid, the deionizing agent is a hydroxide ion species.

20. (Previously presented) The capsule of claim 19, wherein the one or more pharmaceutically active agent(s) are selected from the group consisting of therapeutically active agents, diagnostic agents, and prophylactic agents.

24. (Previously presented) The capsule of claim 19, wherein the polyethylene glycol is present in an amount from about 10% to about 80% by weight

25. (Previously presented) The capsule of claim 19, wherein the polyethylene glycol is one or more polyethylene glycols with a molecular weight between 300 and 1500.

26. (Previously presented) The capsule of claim 19, further comprising water.

27. (Previously presented) The capsule of claim 26, wherein water is present in an amount from about 1% to about 18% by weight.

28. (Previously presented) The capsule of claim 19, further comprising one or more excipients.

29. (Previously presented) The capsule of claim 28, wherein the one or more excipients are selected from the group consisting of plasticizers, crystallization inhibitors, wetting agents, bulk filling agents, solubilizers, bioavailability enhancers, solvents, pH-adjusting agents, dyes, preservatives, surfactants, and combinations thereof.

30. (Previously presented) The capsule of claim 29, wherein the solubilizer is selected from the group consisting of glycerin, polyvinylpyrrolidone, propylene glycol and combinations thereof.

31. (Previously presented) The capsule of claim 29, wherein the solubilizer is present in amount from about 1% to about 10% by weight.

32. (Previously presented) The composition of claim 1, wherein the pharmaceutically active agent is naproxen sodium and the deionizing agent is a hydrogen ion species.

33. (Previously presented) The composition of claim 19, wherein the pharmaceutically active agent is naproxen sodium and the deionizing agent is a hydrogen ion species.

34. (Previously presented) The composition of claim 32, wherein the hydrogen ion species is selected from the group consisting of hydrochloric acid, hydrobromic acid, hydroiodic acid, sulfuric acid, fumaric cid, maleic acid, tartaric acid, methane-, ethane-, and benzene sulfonates, citric acid, malic acid, acetic acid, proprionic acid, pyruvic acid, butanoic acid, and lactic acid.

35. (Previously presented) The composition of claim 33, wherein the hydrogen ion species is selected from the group consisting of hydrochloric acid, hydrobromic acid, hydroiodic acid, sulfuric acid, fumaric cid, maleic acid, tartaric acid, methane-, ethane-, and benzene

sulfonates, citric acid, malic acid, acetic acid, proprionic acid, pyruvic acid, butanoic acid, and lactic acid.

36. (Previously presented) The composition of claim 34, wherein the hydrogen ion species is lactic acid.

37. (Previously presented) The composition of claim 35, wherein the hydrogen ion species is lactic acid.

38. (Previously Presented) A softgel capsule comprising a fill material comprising from about 10% to about 80% by weight polyethylene glycol having a molecular weight between 300 and 1500, about 10% to about 50% by weight naproxen sodium, and about 0.2 to about 1.0 moles of a deionizing agent per mole of naproxen sodium, which at least partially neutralizes the naproxen sodium.

39. (Previously presented) The softgel capsule of claim 38, wherein the deionizing agent is selected from the group consisting of hydrochloric acid, hydrobromic acid, hydroiodic acid, sulfuric acid, fumaric cid, maleic acid, tartaric acid, methane-, ethane-, and benzene sulfonates, citric acid, malic acid, acetic acid, proprionic acid, pyruvic acid, butanoic acid, and lactic acid.

40. (Previously presented) A pharmaceutical composition prepared by a method comprising

(a) mixing a salt of one or more acidic or basic pharmaceutically active agents;

(b) a deionizing agent in an amount from about 0.2 to about 1.0 mole equivalents per mole of the salt of the pharmaceutically active agent(s), which at least partially neutralizes the salt of pharmaceutically active agent(s); and

(c) polyethylene glycol;

wherein when the salt is a salt of a weak acid and a strong base, the deionizing agent is a hydrogen ion species, and when the salt is the salt of a weak base and a strong acid, the deionizing agent is a hydroxide ion species, and

wherein the pharmaceutically active agent(s) are not amphoteric.

41. (Previously presented) A softgel capsule prepared by a method comprising

(a) producing a fill material by mixing

(i) a salt of one or more acidic or basic pharmaceutically active agents;

(ii) a deionizing agent in an amount from about 0.2 to about 1.0 mole equivalents per mole of the pharmaceutically active agent(s) to cause partial deionization of the salt of the pharmaceutically active agent(s); and

(iii) polyethylene glycol;

(b) encapsulating the mixture in a softgel capsule;

wherein when the salt is a salt of a weak acid and a strong base, the deionizing agent is a hydrogen ion species, and when the salt is the salt of a weak base and a strong acid, the deionizing agent is a hydroxide ion species.

Evidence Appendix

(1) Palomo, et al., *J. Pharm Biomed. Anal.*, 21: 83-94 (1999)

Related Proceedings Appendix

None

Electronic Patent Application Fee Transmittal

Application Number:	11367238
Filing Date:	03-Mar-2006
Title of Invention:	Solvent system for enhancing the solubility of pharmaceutical agents
First Named Inventor/Applicant Name:	Nachiappan Chidambaram
Filer:	Michael John Terapane/Allyson Romain
Attorney Docket Number:	BAN 102

Filed as Large Entity

Utility under 35 USC 111(a) Filing Fees

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Basic Filing:				
Pages:				
Claims:				
Miscellaneous-Filing:				
Petition:				
Patent-Appeals-and-Interference:				
Notice of appeal	1401	1	620	620
Post-Allowance-and-Post-Issuance:				
Extension-of-Time:				

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Extension - 1 month with $0 paid	1251	1	150	150
Miscellaneous:				
			Total in USD ($)	**770**

Electronic Acknowledgement Receipt

EFS ID:	13367265
Application Number:	11367238
International Application Number:	
Confirmation Number:	5524
Title of Invention:	Solvent system for enhancing the solubility of pharmaceutical agents
First Named Inventor/Applicant Name:	Nachiappan Chidambaram
Customer Number:	23579
Filer:	Michael John Terapane/Allyson Romain
Filer Authorized By:	Michael John Terapane
Attorney Docket Number:	BAN 102
Receipt Date:	30-JUL-2012
Filing Date:	03-MAR-2006
Time Stamp:	15:05:04
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	Credit Card
Payment was successfully received in RAM	$770
RAM confirmation Number	1620
Deposit Account	503129
Authorized User	ROMAIN,ALLYSON

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

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File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Extension of Time	BAN_102_Petition_for_Two_Month_EOT_July12.pdf	39472 e85d1addf2d17fef4439eb05fafcd5dc4167d4c1	no	1
Warnings:					
Information:					
2	Appeal Brief Filed	BAN_102_Appeal_Brief_July12.pdf	222833 cb313cbb4f23bbcc76573d2eaa0c87eb7dfef921	no	33
Warnings:					
Information:					
3	Non Patent Literature	Palomo_et_al.pdf	832554 629223f8eefc5fd8a355861cd0c66dd939dc9762	no	12
Warnings:					
Information:					
4	Fee Worksheet (SB06)	fee-info.pdf	31864 7729d613ffa69e2e56f990888b31e7fb2c1bd67f	no	2
Warnings:					
Information:					
		Total Files Size (in bytes):	1126723		

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

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

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

PTO/SB/22 (09-11)
Approved for use through 07/31/2012. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARMENT OF COMMERCE

PETITION FOR EXTENSION OF TIME UNDER 37 CFR 1.136(a)	Docket Number (Optional) BAN 102
Application Number 11/367,238	Filed March 3, 2006
For Solvent System For Enhancing The Solubility Of Pharmaceutical Agents	
Art Unit 1618	Examiner Jake Minh Vu

This is a request under the provisions of 37 CFR 1.136(a) to extend the period for filing a reply in the above identified application.

The requested extension and fee are as follows (check time period desired and enter the appropriate fee below):

		Fee	Small Entity Fee	
☑	One month (37 CFR 1.17(a)(1))	$150	$75	$ 150.00
☐	Two months (37 CFR 1.17(a)(2))	$560	$280	$
☐	Three months (37 CFR 1.17(a)(3))	$1270	$635	$
☐	Four months (37 CFR 1.17(a)(4))	$1980	$990	$
☐	Five months (37 CFR 1.17(a)(5))	$2690	$1345	$

☐ Applicant claims small entity status. See 37 CFR 1.27.

☐ A check in the amount of the fee is enclosed.

☑ Payment by credit card. Form PTO-2038 is attached.

☐ The Director has already been authorized to charge fees in this application to a Deposit Account.

☑ The Director is hereby authorized to charge any fees which may be required, or credit any overpayment, to Deposit Account Number 50-3129.

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.

I am the

☐ applicant/inventor.

☐ assignee of record of the entire interest. See 37 CFR 3.71.
Statement under 37 CFR 3.73(b) is enclosed (Form PTO/SB/96).

☑ attorney or agent of record. Registration Number 31,284

☐ attorney or agent under 37 CFR 1.34.
Registration number if acting under 37 CFR 1.34 _____

/Michael J. Terapane/ — Signature

July 30, 2012 — Date

Michael J. Terapane, Ph.D., J.D. — Typed or printed name

404-879-2155 — Telephone Number

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

☐ Total of _____ forms are submitted.

This collection of information is required by 37 CFR 1.136(a). The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11 and 1.14. This collection is estimated to take 6 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
11/367,238	03/03/2006	Nachiappan Chidambaram	BAN 102	5524

23579 7590 10/12/2012

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ATLANTA, GA 30309

EXAMINER	
VU, JAKE MINH	
ART UNIT	**PAPER NUMBER**
1618	
MAIL DATE	**DELIVERY MODE**
10/12/2012	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.

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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 11/367,238
Filing Date: March 03, 2006
Appellant(s): CHIDAMBARAM ET AL.

Michael J. Terapane
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed 07/30/2012 appealing from the Office action mailed 11/29/2011.

(1) Real Party in Interest

The examiner has no comment on the statement, or lack of statement, identifying by name the real party in interest 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 following is a list of claims that are rejected and pending in the application:

Claims 1, 2, 6-13, 19, 20, 24-41 are pending, rejected an on appeal. Claims 14 and 16-18 have been withdrawn from consideration.

(4) Status of Amendments After Final

The examiner has no comment on the appellant's statement of the status of amendments after final rejection contained in the brief.

(5) Summary of Claimed Subject Matter

The examiner has no comment on the summary of claimed subject matter contained in the brief.

(6) Grounds of Rejection to be Reviewed on Appeal

The examiner has no comment on the appellant's statement of the grounds of rejection to be reviewed on appeal. Every ground of rejection set forth in the Office action from which the appeal is taken (as modified by any advisory actions) is being maintained by the examiner except for the grounds of rejection (if any) listed under the subheading "WITHDRAWN REJECTIONS." New grounds of rejection (if any) are provided under the subheading "NEW GROUNDS OF REJECTION."

(7) Claims Appendix

The examiner has no comment on the copy of the appealed claims contained in the Appendix to the appellant's brief.

(8) Evidence Relied Upon

US 5,360,615	YU	11-1994
US 6,383,515	SAWYER	5-2002
US 5,541,210	CUPPS	7-1996
US 5,885,608	MCENTEE	3-1999

(9) Grounds of Rejection

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

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-2, 6-13 and 19-20, 24-31, 40-41 are rejected under 35 U.S.C. 102(b) as being anticipated by YU et al (5,360,615).

YU teaches a composition comprised of: a salt of a therapeutically active agent, such as diclofenac sodium (see col. 12, Example 8); a deionizing agent, such as 0.2 mole equivalent hydrochloric acid (see col. 12, Example 8), which is a deionizing agent (see Appellant's claim 39); 71.5% of polyethylene glycol with molecular weight of 600 (see col. 12, Example 8); 7.16% of water (see col. 12, Example 8); excipients, such as preservatives (see col. 9, line 34); 4-8% of solubilizers, such as polyvinyl pyrrolidone (see col. 8, line 51-68). Additional limitation includes: softgel capsule (see col. 1, line 20). Note, even though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process. In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985). In this instance, the prior art has every ingredients as claimed by Appellant.

Claims 1-2, 6-13, 19-20, 24-35 are rejected under 35 U.S.C. 102(b) as being anticipated by SAWYER et al (US 6,383,515).

SAWYER teaches a composition comprised of: 21.67% naproxen sodium (see abstract; and col. 14, line 32); deionizing agent, such as 5.88% of sodium propionate in water (see col. 14, line 23 and 35), which would inherently have propionic acid (see col. 4, line 40-44) when the sodium propionate salt goes into solution and is about 0.2-1.0 mole equivalent of naproxen sodium, wherein propionic acid is a deionizing agent (see Appellant's claim 39). Additional disclosures include: 10-70% of polyethylene glycol 400-600 (see col. 3, line 48 - col. 4, line 19); 0-25% of water (see col. 3, line 33; col. 5, line 4-5; col. 14, line 23; and examples); 2% of propylene glycol (see col. 3, line 48-54; col. 8, line 24) or polyvinyl pyrrolidone (see col. 3, line 49); soft gel capsule (see abstract); other organic acids can be used in place of propionic acid, such as citric acid or organic acids with at least 3 carbon atoms (see col. 4, line 31-44). Note, even though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process. In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985). In this instance, the prior art has every ingredients as claimed by Appellant.

Claims 1-2, 6, 8-13, 19-20, 24, 26-35, 38-41 rejected under 35 U.S.C. 102(b) as being anticipated by CUPPS et al (US 5,541,210).

CUPPS teaches a composition comprising of: a salt of an active agent, such as 220mg of naproxen sodium (see col. 28, line 66); a deionizing agent, such as 50mg of citric acid (see col. 29, line 12), which is about 0.2-1.0 mole equivalent of naproxen sodium; 3000mg of polyethylene glycol (see col. 29, line 8), which is about 10% by weight; 3800mg of water (see col. 29, line 14), which is about 13% weight; excipients, such as 3000mg of propylene glycol (see col. 29, line 9), which is a solubilizer and is about 10% by weight. Additional disclosures include: preferred composition include softgel capsules (see col. 19, line 4). Note, citric acid is a deionizing agent (see Appellant's claim 39). Note, even though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process. In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985). In this instance, the prior art has every ingredients as claimed by Appellant.

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.

Claims 1-2, 6-13, 19-20, 24-41 are rejected under 35 U.S.C. 103(a) as being unpatentable over SAWYER et al (US 6,383,515) in view of McENTEE et al (US 5,885,608).

SAWYER teaches a composition comprised of: 21.67% naproxen sodium (see abstract; and col. 14, line 32); deionizing agent, such as 5.88% of sodium propionate in water (see col. 14, line 23 and 35), which would inherently have propionic acid (see col. 4, line 40-44) when the sodium propionate salt goes into solution and is about 0.2-1.0 mole equivalent of naproxen sodium, wherein propionic acid is a deionizing agent (see Appellant's claim 39). Additional disclosures include: 10-70% of polyethylene glycol 400-600 (see col. 3, line 48 - col. 4, line 19); 0-25% of water (see col. 3, line 33; col. 5, line 4-5; col. 14, line 23; and examples); 2% of propylene glycol (see col. 3, line 48-54; col. 8, line 24) or polyvinyl pyrrolidone (see col. 3, line 49); soft gel capsule (see abstract); other organic acids can be used in place of propionic acid, such as citric acid or organic acids with at least 3 carbon atoms (see col. 4, line 31-44).

SAWYER does not teach using an organic acid, such as lactic acid.

McENTEE teaches that organic acids, such as citric acid and lactic acid are known in the prior art (see col. 10, line 17-19).

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to incorporate lactic acid or sodium lactate into SAWYER's composition. The person of ordinary skill in the art would have been motivated to make those modifications, because lactic acid is an organic functional equivalent of citric acid,

and reasonably would have expected success because SAWYER teaches using organic acids with at least 3 carbons, wherein lactic acid has at least 3 carbons.

The references do not specifically teach adding the ingredients in the amounts claimed by Appellant. The amount of a specific ingredient in a composition is clearly a result effective parameter that a person of ordinary skill in the art would routinely optimize. Optimization of parameters is a routine practice that would be obvious for a person of ordinary skill in the art to employ and reasonably would expect success. It would have been customary for an artisan of ordinary skill to determine the optimal amount of each ingredient to add in order to best achieve the desired results, such as solubility of the active agent. Thus, absent some demonstration of unexpected results from the claimed parameters, this optimization of ingredient amount would have been obvious at the time of Appellant's invention.

Note, even though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process. In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985). In this instance, the prior art has every ingredients as claimed by Appellant.

Note, Appellant's specification has not provided with any increased solubility or bioavailability data.

(10) Response to Argument

Appellant argues that independent claims 1, 19, and 38 are product claims, not product-by-process claims.

The Examiner finds this argument unpersuasive, because the product-by-process is in reference to claims 40 and 41 as clarified in the advisory action filed on 05/18/2012. Claims 40 and 41 are product-by-process claims.

Appellant argues the claims specify that the one or more active agents present in the formulation are salts of one or more either acidic or basic pharmaceutically active agents. The present application classifies active agents as acidic, basic, or amphoteric (pg. 4, lines 15-16). The specification reads, "A first class of drugs is selected based on inclusion in the molecule of a weakly acidic, basic or amphoteric group that can form a salt." The use of the disjunctive "or" clearly differentiates the three groups. Diclofenac sodium is not within the scope of the claims, because diclofenac is not exclusively an acid or a base. It is amphoteric.

The Examiner finds this argument unpersuasive, because an amphoteric drug is an acidic or basic depending on the pH environment. Appellant's claims recite "either acidic or basic", wherein an amphoteric drug can be literally either acidic or basic. Appellant's claims as written still reads on an amphoteric drug. See Figure 1 of Palomo, et ai., J Pharm Biomed. Anal., 21: 83-94 (1999) copy of which are enclosed with the Appeal Brief, wherein the final compound does not have an acidic carboxylic acid group.

Appellant argues that it is known in the art that strong acids, such as hydrochloric acid, catalyze the cyclization of diclofenac sodium to an indolinone derivative (see

Figure 1 of Palomo, et ai., J Pharm Biomed. Anal., 21: 83-94 (1999) copy of which are enclosed with this Appeal Brief). Palomo states that the cyclized indolinone is pharmaceutically inactive. Therefore, such a formulation is not a pharmaceutical composition.

The Examiner finds this argument unpersuasive, because Palomo states "the diclofenac sodium undergoes an intramolecular cyclization under the acidic conditions (Fig. 1) found in gastric juices, which can cause its inactivation, so it is recommended to take it after meals" (see Palomo at pg. 84, 2nd column). YU does not teach putting the diclofenac sodium into a bin of gastric juices, which is practically pure acid; thus, it would be premature to allege that YU's diclofenac composition is not active with only a small amount of HCl diluted with 5-6 times the amount of water (see YU, col. 12 at Example VIII) and over 10 times the amount of diclofenac sodium. Additionally, Appellant disclosed that diclofenac could be used as the drug (see Specification pg. 4, line 30). By Appellant's argument, Appellant is arguing that Appellant's independent claims fail the scope of enablement since it reads on diclofenac and a hydrochloric acid recited in Appellant's claim 34.

Appellant argues that Yu does not disclose or suggest mixing the salt of an acidic or basic active agent with a deionizing agent in the amount defined in claims 40 and 41, wherein the deionizing agent at least partially deionizes the salt of the acidic or basic active agent.

The Examiner finds this argument unpersuasive, because as discussed above, YU teaches using a deionizing agent, such as 0.2 mole equivalent hydrochloric acid

(see col. 12, Example 8), which is a deionizing agent (see Appellant's claim 39), wherein it would have inherently partially deionizes some of the diclofenac sodium.

Appellant argues that the Examiner has provided no evidence to demonstrate that propionic acid is present in an amount between 0.2 to 1.0 mole equivalents of the active agent(s), as required by the claims. The formulation described in Example 17 contains 0.8153 g sodium propionate (K_b = 7.46 x 10^{-10}) dissolved in 800 mL of water (i.e., an aqueous solution of approximately 0.0106 M sodium propionate). If the impact of other species present in solution on the equilibrium between propionate and propionic acid is ignored, the concentration of propionic acid at equilibrium is calculated to be approximately 2.7 x 10-5 M (corresponding to roughly 2.2 x 10^{-5} moles propionic acid at equilibrium). The formulation in Example 17 of Sawyer contains 3.0033 g (0.0119 moles) of naproxen sodium. Therefore, Example 17 describes a formulation containing only trace amounts of propionic acid, approximately 0.0018 mole equivalents of propionic acid per mole of naproxen sodium. In contrast, the claims require the deionizing agent to be present in an amount between 0.2 and 1.0 mole equivalents per mole of active agent. Furthermore, the solution in Example 17 also contains 6.66 mg of potassium hydroxide. The pH of an aqueous solution of approximately 0.0106 M sodium propionate (i. e., the formulation described in Example 17) is approximately 9.6. The addition of potassium hydroxide will make the solution even more basic, driving the equilibrium between propionate and propionic acid in the direction of propionate. As a result, the actual amount of propionate present in the formulation described in Example 17 will be even less than 0.0018 mole equivalents per mole of naproxen sodium.

Therefore, what small amounts of propionic acid may be present in Example 17 of Sawyer are not with the range of between 0.2 and 1.0 mole equivalents per mole of active agent, as required by Appellants' claims.

The Examiner finds this argument unpersuasive, because Appellant used K_b instead of K_a in calculating the amount of propionic acid (see Appellant's argument on page 21 of the Appeal Brief, in which the K_a value is used for CUPPS reference). Appellant's calculation using K_b value actually calculated the amount of sodium proprionate. K_b is used to find the amount of base, which is propionate sodium, and K_a is used to find the amount of dissociated acid, in this case, propionic acid. The K_a value for sodium proprionate is $1 \times 10^{-4.87}$. However, there is no need to calculate using the K_a value, since Appellant have already calculated the amount of sodium proprionate in the solution to be 2.2×10^{-5} moles. The total amount of sodium proprionate = (the amount of propionic acid in the solution) plus (the amount of sodium proprionate in the solution). In this case, the total amount of sodium proprionate is 0.106M, which is 0.00848 moles, since the volume of water is 800mL; and the amount of sodium proprionate in the solution is 2.2×10^{-5} moles. Placing these values into the equation gives us: 0.00848 moles of sodium proprionate = (the amount of propionic acid in the solution) plus (2.2×10^{-5} moles of sodium proprionate in the solution). Calculating for propionic acid in the solution = (0.00848 moles of sodium proprionate) minus (2.2×10^{-5} moles of sodium proprionate in the solution) = 0.008458 moles of propionic acid in the solution. Thus, the mole equivalent of propionic acid per mole of naproxen sodium is 0.71 (this value is calculated by 0.008458 divided by 0.0119 moles of naproxen

sodium), which is between about 0.2 and 1.0 mole equivalent. Note, nowhere in Example 17 does SAWYER states the pH is 9.6. As a matter of fact, SAWYER teaches the pH in solution is adjusted to provide acceptable pH limits in the softgel (see col. 4, line 59-61) to be an acidic pH of 2.5 to 7.5 (see col. 1, line 54-56; and col. 11, line 30-32), by addition of more propionic acid (see col. 4, line 50-53). Note, Appellant's independent claims 1 and 19 fall completely without calculating for proprionic acid, since the broad scope of "deionizing agents" of these claims can read on proprionate sodium, in which proprionate sodium can "partially neutralize the pharmaceutically active agent" and is in the amount of 0.00848 moles and would have 0.712 moles equivalent to the active agent.

Appellant argues that the Examiner has repeatedly alleged that the sodium propionate in Example 17, at equilibrium, generates propionic acid in the amounts specified in the claims. Appellants also note, however, that this allegation has ignored the effect of sodium hydroxide on the equilibrium. Moreover, the Examiner has failed to provide any evidence that the allegation is accurate, even when explicitly requested to do so by the Appellants. Appellants have shown through the calculations above that the amount of propionic acid formed, regardless of whether or not one considers the effect of the potassium hydroxide, is not with the range specified in the claims. When one includes the contribution of potassium hydroxide, the pH of the composition is significantly more basic which drives the equilibrium further to the left and results in even less propionic acid in solution.

The Examiner finds this argument unpersuasive, because Appellant calculated incorrectly by using K_b instead of K_a as discussed above. As for the sodium hydroxide, Appellant assumes this will make the environment basic and push the equilibrium toward the left; however, as discussed above, SAWYER specifically teaches the composition to be in an acid pH; thus, the equilibrium would be pushed toward more propionic acid.

Appellant argues that none of the hydrogen ion species specified in claims 34 and 35 are in the list of ingredients in Example 17.

The Examiner finds this argument unpersuasive, because as discussed above, sodium propionate in water (see col. 14, line 23 and 35), which would inherently dissolve and become propionic acid in an acidic environment, wherein SAWYER teaches the pH is adjusted to provide acceptable pH limits in the softgel (see col. 4, line 59-61) to be an acidic pH of 2.5 to 7.5 (see col. 1, line 54-56; and col. 11, line 30-32), by addition of more propionic acid (see col. 4, line 50-53). Thus, additional propionic acid is added if needed to maintain an acidic environment.

Appellant argues that claims 36 and 37 depend from claims 32 and 33 specifically and specify that the hydrogen ion species is lactic acid. Example 17 in Sawyer discloses a composition containing naproxen sodium, sodium propionate, and potassium hydroxide. Lactic acid is not in the list of ingredients in Example 17. Moreover, lactic acid cannot form from any of the ingredients in Example 17. Sawyer does not disclose or suggest, explicitly or inherently, the elements of claims 36 and 37. Accordingly, claims 36 and 37 are novel over Sawyer.

The Examiner finds this argument moot, because claims 36 and 37 are not §102 rejected by SAWYER.

Appellant argues that Example 17 does not disclose or suggest that the solution was encapsulated in a soft gel capsule as required by claims 38 and 39.

The Examiner finds this argument moot, because claims 36 and 37 are not §102 rejected by SAWYER; however, as discussed above, SAWYER teaches the putting the solution into a soft gel capsule (see abstract) and the teaching of SAWYER is not limited to the examples, or else, Appellant's claims would be limited to Appellant's examples.

Appellant argues that Example R [in the CUPPS reference] describes a solution containing 50 mg/fl oz of citric acid (approximately 0.0088 M citric acid, Ka1 = 7.44 x 10-4) and 220 mg/fl oz of naproxen sodium (approximately 0.0295 M naproxen sodium). If the impact of other species in solution on the citric acid equilibrium is ignored and the solution is assumed to be aqueous, the concentration of citric acid at equilibrium is calculated to be approximately 2.2 x 10-3 M. Therefore, Example R describes a formulation containing approximately 0.075 mole equivalents of citric acid per mole of naproxen sodium. In contrast, the claims require the deionizing agent to be present in an amount between 0.2 and 1.0 mole equivalents per mole of active agent. Furthermore, the solution in Example R also contains 150 mg/fl oz of sodium citrate dihydrate (trisodium citrate dihydrate, 0.01725 M). The addition of more than two moles of sodium citrate for every one mole of citric acid will make the solution more basic, driving the equilibrium between citrate and citric acid in the direction of citrate. As a

result, the actual amount of citric acid present in the formulation described in Example R will be significantly less than 0.075 mole equivalents per mole of naproxen sodium.

The Examiner finds this argument unpersuasive, because Appellant's claims recite "about 0.2 and about 1.0 mole equivalent", wherein 0.075 mole is about 0.1 mole, which is about 0.2 mole. Furthermore, the cirtrate in trisodium citrate dihydrate would increase the amount of citric acid.

Appellant argues that Example R does not disclose or suggest the claimed capsules.

The Examiner finds this argument moot, because as discussed above, CUPPS teaches the preferred composition include softgel capsules (see col. 19, line 4) and the teaching of CUPPS is not limited to the examples, or else, Appellant's claims would be limited to Appellant's examples.

Appellant argues that Sawyer does not disclose or suggest the claimed compositions for at least the reasons discussed above.

The Examiner finds this argument unpersuasive for at least the reasons discussed above, wherein Sawyer does discloses a formulation containing (a) a salt of one or more either acidic or basic pharmaceutically active agents; and (b) a deionizing agent in an amount from 0.2 to 1.0 mole equivalents of the pharmaceutically active agent(s), as required by the claims. Even if the references do not specifically teach adding the ingredients in the amounts as claimed by Appellant, the amount of specific ingredients in a composition is clearly a result effective parameter that a person of ordinary skill in the art would routinely optimize. Optimization of parameters is a routine

practice that would be obvious for a person of ordinary skill in the art to employ and reasonably would expect success. It would have been customary for an artisan of ordinary skill to determine the optimal amount of each ingredient to add in order to best achieve the desired results, such as solubility of the active agent. Thus, absent some demonstration of unexpected results from the claimed parameters, this optimization of ingredient amount would have been obvious at the time of Appellant's invention.

Note, Appellant's specification has not provided with any increased solubility or bioavailability data that shows the criticality of a deionizing agent in an amount from 0.2 to 1.0 mole equivalents of the pharmaceutically active agent, wherein Appellant's title is "Solvent system for enhancing the solubility of pharmaceutical agents".

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

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

Respectfully submitted,

/Jake M. Vu/

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

By: Nachiappan Chidambaram and Aqeel Fatmi

Serial No.: 11/367,238 Art Unit: 1618

Filed: March 3, 2006 Examiner: Jake Minh Vu

For: *SOLVENT SYSTEMS FOR ENHANCING SOLUBILITY OF PHARMACEUTICAL AGENTS*

Mail Stop: Appeal Brief Patents
Commissioner for Patents
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Alexandria, VA 22313-1450

REPLY BRIEF

Sir:

This is a reply to the Examiner's Answer mailed October 12, 2012 in the above-identified application. Submitted with this Reply Brief is a Request for Oral Hearing. A credit card payment in the amount of $1,260.00, the fee under 37 C.F.R. § 41.20(b)(3) for a Request for Oral Hearing for a large entity, is made electronically.

It is believed that no additional fee is required with this submission. However, should an additional fee be required, the Commissioner is hereby authorized to charge the fee to Deposit Account No. 50-3129.

(6) Grounds of Rejection to Be Reviewed

The issues present on appeal are whether:

(i) claims 1, 2, 6-13, 19, 20, 24-31, 40, and 41 are anticipated under 35 U.S.C. § 102(b) by U.S. Patent No. 5,360,615 to Yu ("Yu");

(ii) claims 1, 2, 6-13, 19, 20, and 24-35 are anticipated under 35 U.S.C. § 102(b) by U.S. Patent No. 6,383,515 to Sawyer et al. ("Sawyer");

(iii) claims 1, 2, 6, 8-13, 19, 20, 24, 26-35, and 38-41 are anticipated under 35 U.S.C. § 102(b) by U.S. Patent No. 5,541,210 to Cupps et al. ("Cupps");

(iv) claims 1, 2, 6-13, 19, 20, and 24-41 are obvious under 35 U.S.C. § 103(a) over Sawyer in view of U.S. Patent No. 5,885,608 to McEntee ("McEntee").

(8) Argument

Appellants affirm all arguments made in the Appeal Brief.

Rejections under 35 U.S.C. 102(b)

Claims 1, 2, 6-13, 19, 20, 24-31, 40, and 41 are novel over Yu

The Examiner continues to prohibit Applicants from acting as their own lexicographer

The present application classifies active agents as acidic, basic, or amphoteric (pg. 4, lines 15-16). The specification reads, "A first class of drugs is selected based on inclusion in the molecule of a weakly acidic, basic or amphoteric group that can form a salt." The use of the disjunctive "or" clearly differentiates the three groups.

In the Examiner's answer, the Examiner alleges that Applicants' arguments in the Appeal Brief regarding the scope of the term "acidic" and "basic" are "...unpersuasive

because an amphoteric drug is acidic or basic depending on the pH environment. Applicants' claims recite either acidic or basic, wherein an amphoteric drug can be literally either acidic or basic. Appellants' claims as written still read on an amphoteric drug" (see page 10, 4th paragraph).

The Examiner is imposing his definition of what the terms should mean and ignoring the use of the terms clearly established by the Applicants in the application as originally filed.

The use of "or" makes it clear that Applicants intended to distinguish between compounds containing only acidic functional groups (i.e., acidic agents), compounds containing only basic functional groups (i.e., basic agents), and compounds containing both acidic and basic functional groups (i.e., amphoteric agents). The compounds are distinguished by the presence or absence of certain functional groups, not how the functional groups behave at a certain pH.

The fact that the Examiner may consider an amphoteric active agent to be an acidic or basic active agent is irrelevant. The Examiner must use the terms in the claims in the manner that the Applicant defines, even if it is contrary to or inconsistent with one or more of their ordinary meanings, if the written description clearly redefines the terms. The Examiner has provided no evidence to refute that Applicants' have acted as their own lexicographer. As shown above, the application as filed clearly distinguishes between acidic, basic, and amphoteric active agents. Diclofenac sodium is not within the scope of the claims because diclofenac is not exclusively an acid or a base as required by the claims.

The Examiner mischaracterizes the evidence in Palomo

The Examiner alleges that the arguments regarding Palomo are unpersuasive because Palomo teaches that diclofenac sodium cyclizes under the acidic conditions found in gastric juices and that Yu does not teach putting the diclofenac sodium into a bin of gastric juices, which is practically pure acid. Therefore, the Examiner alleges, it is premature to allege that Yu's diclofenac composition is not active with only a small amount of HCl diluted with 5-6 time the amount of water (page 11, 1st full paragraph).

The argument above is indicative of the Examiner's repeated insistence of stating his own judgments/beliefs as fact, even in the face of evidence to the contrary. It is well known in the art that the pH of the stomach is approximately 1.5-3.5 (see the enclosed description of gastric acid, which is provided to address an argument newly raised by the Examiner in the Examiner's Answer). Therefore, the cyclization of diclofenac sodium occurs at a pH of 1.5-3.5. The pH of the formulation in Example VIII is 2.8, which is between 1.5 and 3.5. Therefore, it is reasonable to conclude that diclofenac sodium would cyclize in the formulation described in Example VIII in Yu.

Claims 40 and 41 are novel over Yu

Yu discloses combining the active agent in free acid or free base form with an agent, which ionizes (i.e., forms the salt) the active agent. In contrast, claims 40 and 41 requires that a salt of an acidic or basic active agent is mixed with a deionizing agent. The claimed products are not the same because in Yu, the free acid or free base is always in excess and therefore the free acid or free base is the predominant species. In contrast, in claims 40 and 41, the salt is always in excess and therefore the salt of the acidic or

basic active agent is the predominant species. Accordingly, the product defined in claims 40 and 41 is not the same as, or obvious over, the products described in Yu.

For at least the reasons discussed above, Yu does not disclose or suggest each and every element of claims 1, 2, 6-13, 19, 20, and 24-31. Accordingly, claims 1, 2, 6-13, 19, 20, and 24-31 are novel over Yu.

Claims 1, 2, 6-13, 19, 20, and 24-35 are novel over Sawyer

Applicants' use of K_b in the calculation of the concentration of propionic acid is correct

The Examiner alleges that the use of K_b in calculating the concentration of propionic acid in Example 17 in Sawyer is incorrect. Applicants respectfully disagree.

Propionic acid is a weak acid with a K_a of ~1.34×10^{-5}. Propionate is the corresponding conjugate base of propionic acid. Acid-base chemistry teaches that the K_a of a weak acid and the K_b of its conjugate base are related by the equation

$$K_a \times K_b = K_w,$$

where K_w is the ionic constant of water and has a value of approximately 1.0×10^{-14} at room temperature. Therefore, the K_b of propionate can be calculated to be 7.46×10^{-10} based solely upon the equation above and the K_a of propionic acid. Accordingly, when calculating either the propionic acid concentration or the propionate concentration one may use either the K_a of the acid or the K_b of the conjugate base as long as the equations are set up appropriately. The Examiner's arguments neglect the fact that K_a and K_b are not independent quantities but are related through the expression above. Applicant elected to use K_b since the conjugate base, not the acid, was added to the formulation in Sawyer's Example 17.

The equation for determining the concentration of propionic acid based upon the K_b is below:

$$K_b = [\text{propionic acid}][OH^-]/[\text{propionate}]$$

The concentrations can also be calculated using K_a and the equation below:

$$K_a=[\text{propionate}][H^+]/[\text{propionic acid}].$$

The Examiner also alleges that the total amount of sodium propionate is equal to the sum of the amount of propionic acid in solution plus the amount of sodium propionate. This is incorrect. Propionic acid and sodium propionate are different chemical species. In fact, sodium propionate is the salt of the conjugate base while propionic acid is an acid. One cannot simply add their concentrations to determine the concentration of either propionic acid or propionate in solution.

The Volume of Water in Example 17 is not 800 mL

In reviewing the calculations done previously by Applicants and the Examiner, Applicants and the Examiner inadvertently used the incorrect volume. The 800 mL corresponds to the volume of water used to prepare the initial stock solutions of potassium hydroxide and sodium propionate. The relevant portion (column 14, first paragraph) of Sawyer reads, "The potassium hydroxide was added as a solution of 6.8 g KOH in 100 mls of water. The sodium propionate was added as a solution of 500 g sodium propionate in 700 mls of water." Were the total volumes of both solutions added to the formulation, there would be 6.8 g KOH and 500 g of sodium propionate in the formulation. Table 17 indicates that only 6.66 mg of KOH and 0.8153 g of sodium propionate were added to the formulation using these stock solutions.

Using the information provided in Table 17, the amount of water present from the KOH solution is determined by:

$$(6.66 \text{ mg KOH}) \times (100 \text{ mL } H_2O / 6.8 \text{ g KOH}) \times (1 \text{ g} / 1000 \text{ mg})$$

giving a volume of 0.0979 mL of water from the KOH solution.

The volume of water added from the sodium propionate solution is calculated by:

$$(0.8153 \text{ g sodium propionate}) \times (700 \text{ mL } H_2O / 500 \text{ g sodium propionate})$$

giving a volume of 1.14142 mL of water from the sodium propionate solution. The total volume of water is therefore only 1.23932 mL.

The concentration of propionic acid is essentially zero

In Example 17 of Sawyer both a strong base (6.66 mg KOH) and a weak base (0.8153 g sodium propionate) are added to the formulation, with a volume of water equal to 1.23932 mL. KOH is a strong base that will completely dissociate in water. Therefore, to a first approximation the pH can be determined from the concentration of KOH. KOH has a molecular weight of 56.1056 g/mol. Therefore, the concentration of KOH dissolved in solution is calculated as:

$$(6.66 \text{ mg KOH} / 1.23932 \text{ mL } H_2O) \times (1 \text{ mol KOH}/56.1056 \text{ g KOH}) \times$$

$$(1000 \text{ mg}/1\text{g}) \times (1000 \text{ mL} / 1 \text{ L}),$$

giving a solution that is 0.09578 M. The pH of a 0.09578M KOH solution is calculated as

$$pH = 14.0 - pOH = 14.0 + \log [OH^-] = 14.0 + \log (0.09578) = 14.0\text{-}1.02 = 12.98.$$

The only additional information needed to calculate the concentration of propionic acid is the amount of sodium propionate added to the solution. As only sodium propionate is added (not propionic acid), conservation of mass requires that the sum of the concentration of sodium propionate and the concentration of propionic acid in

solution must be equal to the initial concentration of sodium propionate that is dissolved. The initial concentration of sodium propionate dissolved in the solution is calculated using the 0.8153 g of sodium propionate dissolved in 1.23932 mL of water and a molecular weight of 96.060 g/mol for sodium propionate. This gives a concentration added of 6.84844 M.

$$[\text{propionic acid}] + [\text{propionate}] = 6.84844\ \text{M}$$

Using this information, one can use either the equation for the K_a of propionic acid or the equation for the K_b of propionate to calculate the concentration of propionic acid in solution. Using the equation for the K_b, one finds:

$$K_b = [\text{propionic acid}][OH^-]/[\text{propionate}]$$

$$7.46\times10^{-10} = [\text{propionic acid}]\ [0.09578] / (6.84844 - [\text{propionic acid}])$$

$$[\text{propionic acid}] = 5.3\times10^{-8}\ \text{M}.$$

Using the equation for the Ka, one finds:

$$K_a = [\text{propionate}][H^+]/[\text{propionic acid}].$$

$$1.34\times10^{-5} = (6.84844 - [\text{propionic acid}])\ [10^{-12.98}]/[\text{propionic acid}]$$

$$[\text{propionic acid}] = 5.3\times10^{-8}\ \text{M}.$$

A 1.23932 mL solution that is 5.3×10^{-8} M propionic acid contains only about 6.5×10^{-11} moles of propionic acid. This concentration of propionic acid accounts for the effect of potassium hydroxide in the formulation. The 6.5×10^{-11} moles of propionic acid and 0.0119 moles naproxen sodium gives a ratio of propionic acid to active agent that is only 5.5×10^{-9}, well below the value required by the claims.

The Examiner misconstrues the teachings of Sawyer

The Examiner alleges that Sawyer teaches that the solutions described therein must be adjusted to provide acceptable pH limits in the softgel capsule. Applicants respectfully disagree.

Col. 1, lines 54-56 states that "Softgels are also somewhat sensitive to pH, and generally require a pH in the encapsulated liquid from about 2.5 to about 7.5." However, this statement is in the background of the application and there is no teaching or suggestion in the detailed description that this range is adopted in the formulations described therein, let alone for formulations that are encapsulated. For example, several of the formulations in the working examples were not adjusted for pH (see examples 1-10 and 17). At col. 14, lines 37-45, Sawyer discloses that several of the solutions were incorporated into softgel capsules.

Col. 4, lines 54-56 states that "The pH of this propionate solution may be adjusted by the addition of small amounts of propionic acid, usually no more than about 1-2% by weight of the propionate solution." The statement says "may"; it does not state that the pH is or must be adjusted as alleged by the Examiner. The passage in Example 11 (col. 11, lines 30-32) cited by the Examiner states that "the pH of the sodium propionate solution was adjusted from 9.1 to 7.1 by the addition of a small amount of undiluted propionic acid." The formulation in Table 11 contains only acetaminophen in the form of the free base. There is no salt of an active agent as required by claim 1 and therefore no deionizing agent. Even if one could argue that there is a deionizing agent, which there is not, the Examiner has not shown that this adjustment in the pH results in an amount of deionizing agent having a concentration in the range specified in claim 1.

Finally, the Examiner has repeatedly cited Sawyer's Example 17 as anticipating claim 1 and the above-referenced claims dependent thereon. However, Example 17 does not disclose or suggest adding an acid, such as propionic acid, to adjust the pH. The Examiner is reading into Example 17 a limitation that is explicitly omitted.

For at least the reasons discussed above, Claims 1, 2, 6-13, 19, 20, and 24-35 are novel over Sawyer.

Claims 1, 2, 6, 8-13, 19, 20, 24, 26-35, and 38-41 are novel over Cupps

The Examiner fails to show how 0.075 is within the range of 0.2 to 1.0 and ignores the presence of the base trisodium citrate dihydrate

In the Examiner's Answer, the Examiner correctly notes that the concentration of citric acid in Cupps's Example R is 0.075 mole equivalents, which is outside the range specified in Applicants' claim 1. The Examiner then goes on to suggest that 0.075 is about 0.1, which is about 0.2. The Examiner has provided no basis to support this conclusion. The difference between 0.2 and 0.075 is a factor of approximately 2.7. Even if one were to accept the Examiner's argument that 0.075 is about 0.1, which Applicants reject, the minimum value in the range in claim 1 is still twice as much. While the term "about" is not explicitly disclosed in the application, courts have generally construed to the term to be plus or minus 10%. Using this as a guide, the minimum value of the range in claim 1 is 0.18, which is 2.4 times the calculated amount of citric acid in Cupp's Example R and 1.8 times the 0.1 alleged by the Examiner.

More importantly, the Examiner ignores the presence of sodium citrate dihydrate in Cupp's Example R. As discussed in the Appeal Brief, the solution in Example R also contains 150 mg/fl. oz. of sodium citrate dihydrate (trisodium citrate dihydrate, 0.01725

M). The combination of citric acid and trisodium citrate dihydrate forms a citrate buffer system, the pH of which may be approximated from readily available tables. An example is enclosed of a table obtained from the Sigma-Aldrich website (first table on page 3).

The addition of more than two moles of sodium citrate for every one mole of citric acid will result in a pH of approximately 5.0 -5.5. Assuming a pH of approximately 5 (i.e., more acidic) and using the values for the $K_{a1}=7.5\times10^{-4}$, $K_{a2}=1.7\times10^{-5}$, $K_{a3}=5.0\times10^{-7}$ for citric acid and the corresponding equations, the calculated concentration of citric acid is 1.36×10^{-4} M. This gives an amount of citric acid that corresponds to approximately 0.005 mole equivalents.

Accordingly, Example R of Cupps does not describe a formulation containing a deionizing agent in an amount between 0.2 and 1.0 mole equivalents per mole of active agent, as required by the claims. Therefore, Cupps cannot anticipate claims 1-2, 6, 8-13, 19-20, 24, 26-31, and 41.

Rejections under 35 U.S.C. 103(a)

Claims 1, 2, 6-13, 19, 20, and 24-41 are not obvious Sawyer in view of McEntee

Sawyer describes solvent systems for enhancing solubility (abstract). The solvent system contains a low weight polymeric material, such as PEG (col. 3, line 27 to col. 4, line 19) and a salt of an organic acid (col. 4, lines 20-22). Sawyer explicitly states "The salt helps to ionize the medicament..". Sawyer discloses that "the salt (of the organic acid) is added to help dissolve the medicament. It appears that if the salt is added too quickly, ionization of medicament does not take place and the material does not form a successful solution."

Sawyer is concerned with formulations containing a neutral active agent, particularly acetaminophen, which is ionized during formation of the solution. There is no teaching or suggestion of deionizing or neutralizing the active agent. In fact, any such interpretation is in direct contrast to the teachings of Sawyer. Therefore, the amount of the deionizing agent is not a result effective parameter that one of ordinary skill in the art would optimize in order to deionize the agent, where Sawyer explicitly teaches to ionize the agent. Accordingly, Sawyer teaches away from the claimed compositions.

The Examiner cites McEntee for teaching that citric acid and lactic acid are known in the art. McEntee describes a method for treating, ameliorating, and/or preventing age-related neurological disorders by administering lipid-soluble thiamine. *Abstract*. McEntee does not disclose or suggest formulations containing a salt of one or more either acidic or basic pharmaceutically active agents; and (b) a deionizing agent in an amount from 0.2 to 1.0 mole equivalents of the pharmaceutically active agent(s). Further, McEntee does not teach or suggest that citric acid or lactic acid should be used in such a formulation. Therefore, McEntee does not cure the deficiencies of Sawyer. Accordingly, claims 1, 2, 6-13, 19, 20, and 24-41 are not obvious over Sawyer in view of McEntee.

For the foregoing reasons, Appellant submits that claims 1, 2, 6-13, 19, 20, and 24-41 are patentable.

Respectfully submitted,

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Date:	**December 12, 2012**
Signature:	**/Cindy Phillips/**
Name:	**Cindy Phillips**

Evidence

1. Description of Gastric Juices

2. pH table from Sigma-Aldrich catalog showing pH of various citric acid/citrate buffering systems

Gastric acid

From Wikipedia, the free encyclopedia

Gastric acid is a digestive fluid, formed in the stomach. It has a pH of 1.5 to 3.5 and is composed of hydrochloric acid (HCl) (around 0.5%, or 5000 parts per million), and large quantities of potassium chloride (KCl) and sodium chloride (NaCl). The acid plays a key role in digestion of proteins, by activating digestive enzymes, and making ingested proteins unravel so that digestive enzymes can break down the long chains of amino acids.

Gastric acid is produced by cells lining the stomach, which are coupled to systems to increase acid production when needed. Other cells in the stomach produce bicarbonate, a base, to buffer the fluid, ensuring that it does not become too acidic. These cells also produce mucus, which forms a viscous physical barrier to prevent gastric acid from damaging the stomach. Cells in the beginning of the small intestine, or duodenum, further produce large amounts of bicarbonate to completely neutralize any gastric acid that passes further down into the digestive tract.

The presence of gastric acid in the stomach and its function in digestion was first characterized by United States Army surgeon William Beaumont around 1830. Beaumont was able to study the stomach action of fur trapper Alexis St. Martin due to the latter's gastric fistula.

Contents

Physiology

Gastric acid is produced by parietal cells (also called oxyntic cells) in the stomach. Its secretion is a complex and relatively energetically expensive process. Parietal cells contain an extensive secretory network (called canaliculi) from which the gastric acid is secreted into the lumen of the stomach. These cells are part of epithelial fundic glands in the gastric mucosa. The pH of gastric acid is 1.35 to 3.5 [1] in the human stomach lumen, the acidity being maintained by the proton pump H^+/K^+ ATPase. The parietal cell releases bicarbonate into the blood stream in the process, which causes a temporary rise of pH in the blood, known as alkaline tide.

The resulting highly acidic environment in the stomach lumen causes proteins from food to lose their characteristic folded structure (or denature). This exposes the protein's peptide bonds. The chief cells of the stomach secrete enzymes for protein breakdown (inactive pepsinogen and rennin). Hydrochloric acid activates pepsinogen into the enzyme pepsin, which then helps digestion by breaking the bonds linking amino acids, a process known as proteolysis. In addition, many microorganisms have their growth inhibited by such an acidic environment, which is helpful to prevent infection.

Secretion

Gastric acid secretion happens in several steps. Chloride and hydrogen ions are secreted separately from the cytoplasm

of parietal cells and mixed in the canaliculi. Gastric acid is then secreted into the lumen of the oxyntic gland and gradually reaches the main stomach lumen. The exact manner in which the secreted acid reaches the stomach lumen is controversial, as acid must first cross the relatively pH neutral gastric mucus layer.

Chloride and sodium ions are secreted actively from the cytoplasm of the parietal cell into the lumen of the canaliculus. This creates a negative potential of -40 mV to -70 mV across the parietal cell membrane that causes potassium ions and a small number of sodium ions to diffuse from the cytoplasm into the parietal cell canaliculi.

The enzyme carbonic anhydrase catalyses the reaction between carbon dioxide and water to form carbonic acid. This acid immediately dissociates into hydrogen and bicarbonate ions. The hydrogen ions leave the cell through H^+/K^+ ATPase antiporter pumps.

At the same time sodium ions are actively reabsorbed. This means that the majority of secreted K^+ and Na^+ ions return to the cytoplasm. In the canaliculus, secreted hydrogen and chloride ions mix and are secreted into the lumen of the oxyntic gland.

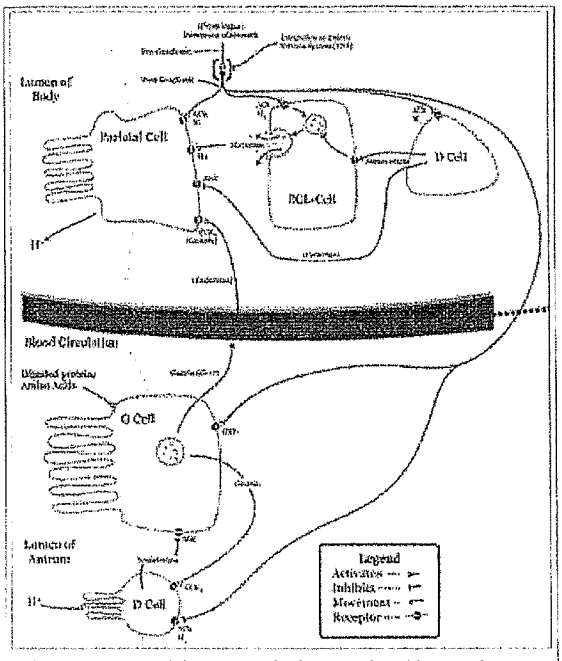

Diagram summarising control of stomach **acid** secretion, emphasising interaction between the *body* and *antrum*.

The highest concentration that gastric acid reaches in the stomach is 160 mM in the canaliculi. This is about 3 million times that of arterial blood, but almost exactly isotonic with other bodily fluids. The lowest pH of the secreted acid is 0.8,[2] but the acid is diluted in the stomach lumen to a pH between 1 and 3.

There are three phases in the secretion of gastric acid:

1. The basal phase: A small amount of acid is always being secreted into the stomach. The three following phases increase the secretion rate in order to digest a meal.
2. The cephalic phase: Thirty percent of the total gastric acid secretions to be produced is stimulated by anticipation of eating and the smell or taste of food. This signalling occurs from higher centres in the brain through the Vagus Nerve. It activates parietal cells to release acid and ECL cells to release histamine. The Vagus nerve also releases Gastrin Releasing Peptide onto G cells. Finally, it also inhibits somatostatin release from D cells.[3]
3. The gastric phase: About fifty percent of the total acid for a meal is secreted in this phase. Acid secretion is stimulated by distension of the stomach and by amino acids present in the food. Caffeine and calcium may also stimulate parietal cells to secrete acid though this has not been proven.
4. The intestinal phase: The remaining 10% of acid is secreted when chyme enters the small intestine, and is stimulated by small intestine distension and by amino acids. The duodenal cells release entero-oxyntin which acts on parietal cells without affecting gastrin.[4]

There is also a small continuous basal secretion of gastric acid between meals of usually less than 10 mEq/hour.[5]

Regulation of secretion

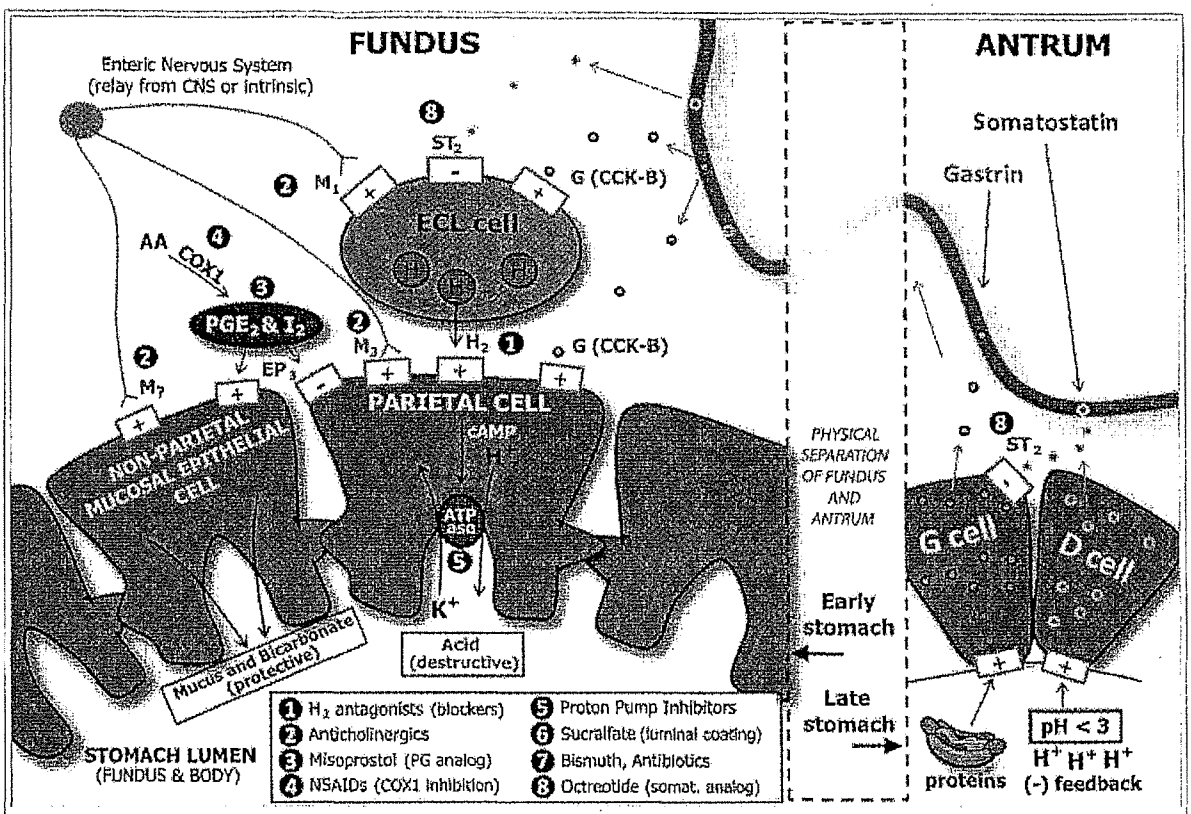

Diagram depicting the major determinants of gastric acid secretion, with inclusion of drug targets for peptic ulcer disease (PUD) and gastroesophageal reflux disease (GERD).

Gastric acid production is regulated by both the autonomic nervous system and several hormones. The parasympathetic nervous system, via the vagus nerve, and the hormone gastrin stimulate the parietal cell to produce gastric acid, both directly acting on parietal cells and indirectly, through the stimulation of the secretion of the hormone histamine from enterochromaffine-like cells (ECL). Vasoactive intestinal peptide, cholecystokinin, and secretin all inhibit production.

The production of gastric acid in the stomach is tightly regulated by positive regulators and negative feedback mechanisms. Four types of cells are involved in this process: parietal cells, G cells, D cells and enterochromaffine-like cells. Besides this, the endings of the vagus nerve (CN X) and the intramural nervous plexus in the digestive tract influence the secretion significantly.

Nerve endings in the stomach secrete two stimulatory neurotransmitters: acetylcholine and gastrin-releasing peptide. Their action is both direct on parietal cells and mediated through the secretion of gastrin from G cells and histamine from enterochromaffine-like cells. Gastrin acts on parietal cells directly and indirectly too, by stimulating the release of histamine.

The release of histamine is the most important positive regulation mechanism of the secretion of gastric acid in the stomach. Its release is stimulated by gastrin and acetylcholine and inhibited by somatostatin.

Neutralization

In the duodenum, gastric acid is neutralized by sodium bicarbonate. This also blocks gastric enzymes that have their optima in the acid range of pH. The secretion of sodium bicarbonate from the pancreas is stimulated by secretin. This polypeptide hormone gets activated and secreted from so-called S cells in the mucosa of the duodenum and jejunum

when the pH in duodenum falls below 4.5 to 5.0. The neutralization is described by the equation:

$$HCl + NaHCO_3 \rightarrow NaCl + H_2CO_3$$

The carbonic acid rapidly equilibrates with carbon dioxide and water through catalysis by carbonic anhydrase enzymes bound to the gut epithelial lining[6], leading to a net release of carbon dioxide gas within the lumen associated with neutralisation. In the absorptive upper intestine, such as the duodenum, both the dissolved carbon dioxide and carbonic acid will tend to equilibrate with the blood, leading to most of the gas produced on neutralisation being exhaled through the lungs.

Role in disease

In hypochlorhydria and achlorhydria, there is low or no gastric acid in the stomach, potentially leading to problems as the disinfectant properties of the gastric lumen are decreased. In such conditions, there is greater risk of infections of the digestive tract (such as infection with *Vibrio* or *Helicobacter* bacteria).

In Zollinger–Ellison syndrome and hypercalcemia, there are increased gastrin levels, leading to excess gastric acid production, which can cause gastric ulcers.

In diseases featuring excess vomiting, patients develop hypochloremic metabolic alkalosis (decreased blood acidity by H^+ and chlorine depletion).

Pharmacology

The proton pump enzyme is the target of proton pump inhibitors, used to increase gastric pH (and hence decrease stomach acidity) in diseases that feature excess acid. H_2 antagonists indirectly decrease gastric acid production. Antacids neutralize existing acid.

History

The role of gastric acid in digestion was established in the 1820s and 1830s by William Beaumont on Alexis St. Martin, who, as a result of an accident, had a fistula (hole) in his stomach, which allowed Beaumont to observe the process of digestion and to extract gastric acid, verifying that acid played a crucial role in digestion.[7]

See also

- Stomach
- Digestion
- Gastroesophageal reflux disease
- Discovery and development of proton pump inhibitors

Notes

1. ^ Marieb EN, Hoehn K (2010). *Human anatomy & physiology*. San Francisco: Benjamin Cummings. ISBN 0-8053-9591-1.
2. ^ Guyton, Arthur C.; John E. Hall (2006). *Textbook of Medical Physiology* (11 ed.). Philadelphia: Elsevier Saunders. p. 797. ISBN 0-7216-0240-1.
3. ^ Lecture, "Function of the Stomach and Small Intestine" Deakin University School of Medicine - October 15, 2012
4. ^ Lecture, "Function of the Stomach and Small Intestine" Deakin University School of Medicine - October 15, 2012
5. ^ Page 192 in: Elizabeth D Agabegi; Agabegi, Steven S. (2008). *Step-Up to Medicine (Step-Up Series)*. Hagerstwon, MD: Lippincott Williams & Wilkins. ISBN 0-7817-7153-6.
6. ^ http://www.ncbi.nlm.nih.gov/pubmed/2506730
7. ^ Harré, R. (1981). *Great Scientific Experiments*. Phaidon (Oxford). pp. 39 – 47. ISBN 0-7148-2096-2.

External links

- The Parietal Cell: Mechanism of Acid Secretion at vivo.colostate.edu (http://www.vivo.colostate.edu/hbooks/pathphys/digestion/stomach/parietal.html)
- First Principles of Gastroenterology. Chapter 6. *Salena B. J., Hunt R. H.* The Stomach and Duodenum (http://www.gastroresource.com/GITextbook/en/chapter6/6-3.htm)
- "Gastric juice (http://web.archive.org/web/20090616022448/http://www.mercksource.com/pp/us/cns/cns_hl_dorlands_split.jsp?pg=/ppdocs/us/common/dorlands/dorland/nine/000953077.htm) " at *Dorland's Medical Dictionary*
- Physiology at MCG *6/6ch4/s6ch4_9 (http://web.archive.org/web/20080401093403/http://www.lib.mcg.edu/edu/eshuphysio/program/section6/6ch4/s6ch4_9.htm)*

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Useful pH Ranges of Selected Biological Buffers (25 °C, 0.1M)

Buffers	Useful pH Range	pKa (at 20)	pKa (at 25)	pKa (at 37)	Reagent Grade	BPC Grade	Ultra Grade
MES	5.5–6.7	6.16	6.10	5.97	M8250	M2933	M5287
Bis-Tris	5.8–7.2	n/a	6.50	6.36	B9754	B4429	B7535
ADA	6.0–7.2	6.65	6.59	6.46	A9883	n/a	A8074
aces	6.1–7.5	6.88	6.78	6.54	A9758	A3594	A7949
PIPES	6.1–7.5	6.80	6.76	6.66	P6757	P1851	P8203
MOPSO	6.2–7.6	n/a	6.90	6.75	M8389	n/a	n/a
Bis-Tris Propane	6.3–9.5	n/a	6.8, 9.0	n/a	B6755	B4679	B9410
BES	6.4–7.8	7.17	7.09	6.90	B9879	B4554	B6420
MOPS	6.5–7.9	7.28	7.20	7.02	M1254	M3183	M5162
TES	6.8–8.2	7.50	7.40	7.16	T1375	T5691	T6541
HEPES	6.8–8.2	7.55	7.48	7.31	H3375	H4034	H7273
DIPSO	7.0–8.2	n/a	7.60	7.35	D9648	n/a	D0306
MOBS	6.9–8.3	n/a	7.60	n/a	M3295	n/a	n/a
TAPSO	7.0–8.2	n/a	7.60	7.39	T9269	T5566	T0432
Trizma	7.0–9.0	8.20	8.06	7.72	T1503	T6066	T6791
HEPPSO	7.1–8.5	n/a	7.80	6.66	H3137	n/a	n/a
POPSO	7.2–8.5	n/a	7.80	7.63	P3405	n/a	P7088
TEA	7.3–8.3	n/a	7.80	n/a	T1377	n/a	n/a
EPPS	7.3–8.7	n/a	8.00	n/a	E9502	E0276	E1894
Tricine	7.4–8.8	8.16	8.05	7.80	T0377	T5816	T9784
Gly-Gly	7.5–8.9	n/a	8.20	n/a	G1002	G3915	G7278
Bicine	7.6–9.0	8.35	8.26	8.04	B3876	n/a	B8660
HEPBS	7.6–9.0	n/a	8.30	n/a	H6903	n/a	n/a
TAPS	7.7-9.1	8.49	8.40	8.18	T5130	T5316	T9659
AMPD	7.8–9.7	n/a	8.80	n/a	A9754	n/a	A9074
TABS	8.2–9.6	n/a	8.90	n/a	T1302	n/a	n/a
AMPSO	8.3–9.7	n/a	9.00	9.10	A6659	n/a	A7585
CHES	8.6–10.0	9.55	9.49	9.36	C2885	n/a	C8210
CAPSO	8.9–10.3	n/a	9.60	9.43	C2278	n/a	C8085
AMP	9.0–10.5	n/a	9.70	n/a	A9879	n/a	A9199
CAPS	9.7–11.1	10.56	10.40	10.02	C2632	n/a	C6070
CABS	10.0–11.4	n/a	10.70	n/a	C5580	n/a	n/a

Trizma Buffer Table – pH vs. Temperature

pH at Temperature			g/L for 0.05 M Solution	
5 °C	25 °C	37 °C	Trizma HCL	Trizma Base
7.76	7.20	6.91	7.02	0.67
7.89	7.30	7.02	6.85	0.80
7.97	7.40	7.12	6.61	0.97
8.07	7.50	7.22	6.35	1.18
8.18	7.60	7.30	6.06	1.39
8.26	7.70	7.40	5.72	1.66

8.37	7.80	7.52	5.32	1.97
8.48	7.90	7.62	4.88	2.30
8.58	8.00	7.71	4.44	2.65
8.68	8.10	7.80	4.02	2.97
8.78	8.20	7.91	3.54	3.34
8.88	8.30	8.01	3.07	3.70
8.98	8.40	8.10	2.64	4.03
9.09	8.50	8.22	2.21	4.36
9.18	8.60	8.31	1.83	4.65
9.28	8.70	8.42	1.50	4.90
9.36	8.80	8.51	1.23	5.13
9.47	8.90	8.62	0.96	5.32
9.56	9.00	8.70	0.76	5.47

Phosphate Buffer Table – 0.2M solution

Potassium Phosphate Monobasic Anhydrous g/L	Sodium Phosphate Dibasic Heptahydrate g/L	23 °C pH	Potassium Phosphate Monobasic Anhydrous g/L	Sodium Phosphate Dibasic Heptahydrate g/L	23 °C pH
22.4	3.49	5.7	10.80	29.51	6.9
22.08	4.29	5.8	9.36	32.73	7.0
21.60	5.37	5.9	7.92	35.95	7.1
21.05	6.60	6.0	6.72	38.63	7.2
20.40	8.05	6.1	5.52	41.31	7.3
19.56	9.93	6.2	4.56	43.46	7.4
18.60	12.07	6.3	3.84	45.07	7.5
17.64	14.22	6.4	3.12	46.68	7.6
16.44	16.90	6.5	2.52	48.55	7.7
15.00	20.12	6.6	2.04	49.09	7.8
13.56	23.34	6.7	1.68	49.89	7.9
12.24	26.29	6.8	1.27	50.81	8.0

Citric Acid – Na_2HPO_4 Buffer Solutions, pH approx. 2.6–7.6[1]

Citric acid monohydrate, $C_6H_8O_7 \cdot H_2O$, M. wt. 210.14; 0.1M-solution contains 21.01 g/l, Na_2HPO_4, M. wt. 141.98; 0.2M-solution contains 28.40 g/l, or $Na_2HPO_4 \cdot 2H_2O$, M. wt. 178.05; 0.2M-solution contains 35.61 g/l.

x ml 0.1M-citric acid and y ml 0.2M-Na_2HPO_4 mixed.

pH	x ml 0.1M-citric acid	y ml 0.2-Na_2HPO_4
2.6	89.10	10.90
2.8	84.15	15.85
3.0	79.45	20.55
3.2	75.30	24.70
3.4	71.50	28.50
3.6	67.80	32.20
3.8	64.50	35.50
4.0	61.45	38.55
4.2	58.60	41.40
4.4	55.90	44.10
4.6	53.25	46.75
4.8	50.70	49.30
5.0	48.50	51.50
5.2	46.40	53.60
5.4	44.25	55.75
5.6	42.00	58.00
5.8	39.55	60.45
6.0	36.85	63.15
6.2	33.90	66.10
6.4	30.75	69.25
6.6	27.25	72.75
6.8	22.75	77.25
7.0	17.65	82.35
7.2	13.05	86.95
7.4	9.15	90.85
7.6	6.35	93.65

Citric Acid – Sodium Citrate Buffer Solutions, pH 3.0–6.2[1]

Citric acid monohydrate, $C_6H_8O_7 \cdot H_2O$, M. wt. 210.14; 0.1M-solution contains 21.01 g/l. Trisodium citrate dihydrate, $C_6H_5O_7Na_3 \cdot 2H_2O$, M. wt. 294.12; 0.1M-solution contains 29.41 g/l.

x ml 0.1M-citric acid and y ml 0.1M-trisodium citrate mixed.

pH	x ml 0.1 M-citric acid	y ml 0.1M-trisodium citrate
3.0	82.0	18.0
3.2	77.5	22.5
3.4	73.0	27.0
3.6	68.5	31.5
3.8	63.5	36.5
4.0	59.0	41.0
4.2	54.0	46.0
4.4	49.5	50.5
4.6	44.5	55.5
4.8	40.0	60.0
5.0	35.0	65.0
5.2	30.5	69.5
5.4	25.5	74.5
5.6	21.0	79.0
5.8	16.0	84.0
6.0	11.5	88.5
6.2	8.0	92.0

Sodium Acetate – Acetic Acid Buffer Solutions, pH 3.7–5.6[1]

Sodium acetate trihydrate, $CH_3COONa \cdot 3H_2O$, M. wt. 136.09; 0.2M-solution contains 27.22 g/l.

x ml 0.2M-NaOAc and y ml 0.2M-HOAc mixed.

pH, 18 °C	x ml 0.2M-NaOAc	y ml 0.2M-HOAc
3.7	10.0	90.0
3.8	12.0	88.0
4.0	18.0	82.0
4.2	26.5	73.5
4.4	37.0	63.0
4.6	49.0	51.0
4.8	59.0	41.0
5.0	70.0	30.0
5.2	79.0	21.0
5.4	86.0	14.0
5.6	91.0	9.0

Na_2HPO_4 – NaH_2PO_4 Buffer Solutions, pH 5.8–8.0 at 25 °C[1]

$Na_2HPO_4 \cdot 2H_2O$, M. wt. 178.05; 0.2M-solution contains 35.61 g/l. $Na_2HPO_4 \cdot 12H_2O$, M. wt. 358.22; 0.2M-solution contains 71.64 g/l. $NaH_2PO_4 \cdot H_2O$, M. wt. 138.01; 0.2M-solution contains 27.6 g/l. $NaH_2PO_4 \cdot 2H_2O$, M. wt. 156.03; 0.2M-solution contains 31.21 g/l.

x ml 0.2M-Na_2HPO_4, y ml 0.2M-NaH_2PO_4; diluted to 100 ml with H_2O.

pH, 25 °C	x ml 0.2M-Na_2HPO_4	y ml 0.2M-NaH_2PO_2
5.8	4.0	46.0
6.0	6.15	43.85
6.2	9.25	40.75
6.4	13.25	36.75
6.6	18.75	31.25
6.8	24.5	25.5
7.0	30.5	19.5
7.2	36.0	14.0
7.4	40.5	9.5
7.6	43.5	6.5
7.8	45.75	4.25
8.0	47.35	2.65

Imidazole (glyoxaline) – HCl buffer solutions, pH 6.2–7.8 at 25 °C[1]

Imidazole, $C_3H_4N_2$, M. wt. 68.08.

25 ml 0.2M-Imidazole (13.62 g/l), x ml 0.2M-HCl, diluted to 100 ml with H_2O.

pH, 25 °C	x ml 0.2M-HCl
6.2	21.45
6.4	19.9
6.6	17.75
6.8	15.2
7.0	12.15
7.2	9.3
7.4	6.8
7.6	4.65
7.8	3.0

Sodium Carbonate – Sodium Bicarbonate Buffer Solutions, pH 9.2–10.8[1]

$Na_2CO_3 \cdot 10H_2O$, M. wt. 286.2; 0.1M-solution contains 28.62 g/l. $NaHCO_3$, M. wt. 84.0; 0.1M-solution contains 8.40 g/l.

x ml 0.1M-Na_2CO_3 and y ml 0.1M-Na_2HCO_3 mixed.

pH		x ml 0.1M-Na_2CO_3	y ml 0.1M-$NaHCO_3$
20 °C	37 °C		
9.2	8.8	10	90
9.4	9.1	20	80
9.5	9.4	30	70
9.8	9.5	40	60
9.9	9.7	50	50
10.1	9.9	60	40
10.3	10.1	70	30
10.5	10.3	80	20
10.8	10.6	90	10

Helpful Formulas

Percentage by weight (w/v)

(% buffer desired / 100) x final buffer volume (ml) = g of starting material needed.

Molar Solutions

desired molarity x formula weight x solution final volume (L) = grams needed

Henderson-Hasselbach Equation

$$pH = pKa + \log\frac{[A^-]}{[HA]}$$

Reference

1. Dawson, R. M. C.; Elliot, D. C.; Elliot, W. H.; Jones, K. M. *Data for Biochemical Research;* 3rd ed., Oxford Science Publ., 1986.

back to top

PTO/SB/32 (07-09)
Approved for use through 01/31/2013. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

REQUEST FOR ORAL HEARING BEFORE THE PATENT TRIAL AND APPEAL BOARD

Docket Number (Optional): BAN 102

I hereby certify that this correspondence is being facsimile transmitted to the USPTO, EFS-Web transmitted to the USPTO, or deposited with the United States Postal Service as first class mail with sufficient postage in an envelope addressed to "Commissioner for Patents, P. O. Box 1450, Alexandria VA 22313-1450" [37 CFR 1.8(a)] on December 12, 2012

Signature /Cindy Phillips/

Typed or printed name Cindy Phillips

In re Application of: Nachiappan Chidambaram

Application Number: 11/367,238 | Filed: 03/03/2006

For: Solvent System for Enhancing the Solubility of Pharmaceutical Agents

Art Unit: 1618 | Examiner: Jake Minh Vu

Applicant hereby requests an oral hearing before the Patent Trial and Appeal Board in the appeal of the above-identified application.

The fee for this Request for Oral Hearing is (37 CFR 41.20(b)(3)) $ 1,260.00

- ☐ Applicant claims small entity status. See 37 CFR 1.27. Therefore, the fee shown above is reduced by half, and the resulting fee is: $ _____
- ☐ A check in the amount of the fee is enclosed.
- ☐ Payment by credit card. Form PTO-2038 is attached.
- ☐ The Director has already been authorized to charge fees in this application to a Deposit Account. I have enclosed a duplicate copy of this sheet.
- ☐ The Director is hereby authorized to charge any fees which may be required, or credit any overpayment to Deposit Account No. _____.
- ■ Payment made via EFS-Web.
- ☐ A petition for an extension of time under 37 CFR 1.136(b) (PTO/SB/23) is enclosed. For extensions of time in reexamination proceedings, see 37 CFR 1.550.

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.

I am the

- ☐ applicant.
- ■ attorney or agent of record. Registration number 57,633
- ☐ attorney or agent acting under 37 CFR 1.34. Registration number if acting under 37 CFR 1.34. _____

Signature

Michael J. Terapane, Ph.D., J.D.
Typed or printed name

December 12, 2012
Date

404-879-2155
Telephone number

NOTE: This form must be signed in accordance with 37 CFR 1.33. See 37 CFR 1.4 for signature requirements and certifications. Submit multiple forms if more than one signature is required, see below*.

☐ *Total of _____ forms are submitted.

Electronic Patent Application Fee Transmittal

Application Number:	11367238
Filing Date:	03-Mar-2006
Title of Invention:	Solvent system for enhancing the solubility of pharmaceutical agents
First Named Inventor/Applicant Name:	Nachiappan Chidambaram
Filer:	Michael John Terapane/Cindy Phillips
Attorney Docket Number:	BAN 102

Filed as Large Entity

Utility under 35 USC 111(a) Filing Fees

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Basic Filing:				
Pages:				
Claims:				
Miscellaneous-Filing:				
Petition:				
Patent-Appeals-and-Interference:				
Request for oral hearing	1403	1	1260	1260
Post-Allowance-and-Post-Issuance:				
Extension-of-Time:				

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Miscellaneous:				
		Total in USD ($)		**1260**

Electronic Acknowledgement Receipt

EFS ID:	14446527
Application Number:	11367238
International Application Number:	
Confirmation Number:	5524
Title of Invention:	Solvent system for enhancing the solubility of pharmaceutical agents
First Named Inventor/Applicant Name:	Nachiappan Chidambaram
Customer Number:	23579
Filer:	Michael John Terapane/Cindy Phillips
Filer Authorized By:	Michael John Terapane
Attorney Docket Number:	BAN 102
Receipt Date:	12-DEC-2012
Filing Date:	03-MAR-2006
Time Stamp:	15:16:35
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	Credit Card
Payment was successfully received in RAM	$1260
RAM confirmation Number	1927
Deposit Account	
Authorized User	

File Listing:

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

1		BAN_102_Reply_Brief_1212.pdf	1315017 8090578bd916625e5ce308212e8f3c5065c4efbb	yes	24

Multipart Description/PDF files in .zip description		
Document Description	**Start**	**End**
Reply Brief Filed	1	13
Non Patent Literature	14	24

Warnings:

Information:

2	Request for Oral Hearing	BAN_102_Request_Oral_Hearing_1212.pdf	83771 f9896bd1d5ee0dd9a0546cf83fbca2c7934180f9	no	1

Warnings:

Information:

3	Fee Worksheet (SB06)	fee-info.pdf	30146 cf0d7b51543eb4b8fb10ef39ccd088648791142b	no	2

Warnings:

Information:

Total Files Size (in bytes):	1428934

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

New Applications Under 35 U.S.C. 111

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

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

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

New International Application Filed with the USPTO as a Receiving Office

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

UNITED STATES PATENT AND TRADEMARK OFFICE

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

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
11/367,238	03/03/2006	Nachiappan Chidambaram	BAN 102	5524

23579 7590 12/19/2012

Pabst Patent Group LLP
1545 PEACHTREE STREET NE
SUITE 320
ATLANTA, GA 30309

EXAMINER	
VU, JAKE MINH	
ART UNIT	**PAPER NUMBER**
1618	
MAIL DATE	**DELIVERY MODE**
12/19/2012	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

PABST PATENT GROUP LLP
1545 PEACHTREE STREET NE
SUITE 320
ATLANTA, GA 30309

Appeal No: 2013-002545
Application: 11/367,238
Appellant: Nachiappan Chidambaram et al.

Patent Trial and Appeal Board Docketing Notice

Application 11/367,238 was received from the Technology Center at the Board on December 17, 2012 and has been assigned Appeal No: 2013-002545.

In all future communications regarding this appeal, please include both the application number and the appeal number.

The mailing address for the Board is:

PATENT TRIAL and APPEAL BOARD
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 referencing the appeal number listed above.

By order of the Patent Trial and Appeal Board.

UNITED STATES PATENT AND TRADEMARK OFFICE

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

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
11/367,238	03/03/2006	Nachiappan Chidambaram	BAN 102	5524

23579 7590 08/25/2015

Pabst Patent Group LLP
1545 PEACHTREE STREET NE
SUITE 320
ATLANTA, GA 30309

EXAMINER	
VU, JAKE MINH	

ART UNIT	PAPER NUMBER
1618	

MAIL DATE	DELIVERY MODE
08/25/2015	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.

The United States Patent and Trademark Office
PATENT TRIAL AND APPEAL BOARD

PABST PATENT GROUP LLP
1545 PEACHTREE STREET NE
SUITE 320
ATLANTA, GA 30309

Appeal No:	2013-002,545
Appellant:	Nachiappan Chidambaram, Aqeel Fatmi et al.
Application No:	11/367,238
Hearing Room:	D
Hearing Docket:	A
Hearing Date:	Tuesday, October 06, 2015
Hearing Time:	09:00 AM
Location:	Madison Building - East Wing 600 Dulany Street, 9th Floor Alexandria, Virginia 22313-1450

NOTICE OF HEARING
RESPONSE REQUIRED WITHIN 21 DAYS

Your attention is directed to 37 CFR § 41.47. The above identified appeal will be heard by the Patent Trial and Appeal Board on the date indicated. Hearings will commence at the time set, and as soon as the argument in one appeal is concluded, the succeeding appeal will be taken up. **The time allowed for argument is 20 minutes** unless additional time is requested and approved before the argument commences. **If the application involved in this appeal has been published, the hearing will be open to the public.**

CONFIRMATION OF ATTENDANCE OR WAIVER OF THE HEARING IS REQUIRED WITHIN **21 DAYS** OF THE MAILING DATE OF THIS NOTICE. Failure to respond may subject Appellant(s) to waiver of the oral hearing. If Appellant is no longer interested in having an oral hearing, Appellant must still file a waiver of oral hearing with the Board. This allows the panel to promptly act on the appeal without waiting for the oral hearing date.

Confirmation or waiver of the hearing should be indicated by completing the form below and returning it to the Board. This form may be filed with the Board by any one of the following three alternative methods:

1. Via the USPTO Electronic Filing System (EFS) at http://www.uspto.gov/patents/process/file/efs/
2. ***PREFERRED***: Facsimile transmitted to: The USPTO Central fax number (official copy): **(571) 273-8300** ***and*** the PTAB Hearing fax number (courtesy copy): **(571) 273-9797.**
3. By mail at the PTAB mailing address: Patent Trial and Appeal Board
   United States Patent and Trademark Office
   P.O. BOX 1450
   Alexandria, Virginia 22313-1450

In all communications relating to this appeal, please identify the appeal by its number.

CHECK ONE:

( ) IN-PERSON HEARING - ATTENDANCE CONFIRMED *(EFS-Web selection: Confirmation of Hearing by Appellant)*

( ) TELEPHONIC HEARING - ATTENDANCE CONFIRMED *(EFS-Web selection: Confirmation of Hearing by Appellant)*

( ) VIDEO HEARING - ATTENDANCE CONFIRMED *(EFS-Web selection: Confirmation of Hearing by Appellant)*

( ) HEARING ATTENDANCE WAIVED *(EFS-Web selection: Waiver of Hearing by Appellant)*

To aid the oral hearings staff in scheduling hearing rooms, please indicate the total number of participating and observing attendees if more than three are expected: _____

To aid the judges in determining whether any conflicts exist that may require a recusal, please list in the 'Comments' section the names of any additional person(s) who will be participating in the oral hearing. (Upon arrival, all persons presenting arguments must sign in at the Usher's desk.)

Comments/Special Requests:

_____

_____

_____ _____

Typed or Printed Name of Attorney/Agent/Appellant Registration No.

_____ _____

Signature of Attorney/Agent/Appellant Date

The 'Hearings' tab of the PTAB webpage http://www.uspto.gov/ip/boards/bpai/index.jsp provides additional information about oral hearings.

Please direct other inquiries to the PTAB Hearings Clerk at 571-272-9797.

UNITED STATES PATENT AND TRADEMARK OFFICE

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
11/367,238	03/03/2006	Nachiappan Chidambaram	BAN 102	5524

23579 7590 08/25/2015

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ART UNIT	PAPER NUMBER
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PATENT TRIAL AND APPEAL BOARD

PABST PATENT GROUP LLP
1545 PEACHTREE STREET NE
SUITE 320
ATLANTA, GA 30309

Appeal No:	2013-002,545
Appellant:	Nachiappan Chidambaram, Aqeel Fatmi et al.
Application No:	11/367,238
Hearing Room:	D
Hearing Docket:	A
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   P.O. BOX 1450
   Alexandria, Virginia 22313-1450

In all communications relating to this appeal, please identify the appeal by its number.

CHECK ONE:

(X) IN-PERSON HEARING - ATTENDANCE CONFIRMED *(EFS-Web selection: Confirmation of Hearing by Appellant)*

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( ) VIDEO HEARING - ATTENDANCE CONFIRMED *(EFS-Web selection: Confirmation of Hearing by Appellant)*

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Comments/Special Requests:

Patrea L. Pabst	31,284
Typed or Printed Name of Attorney/Agent/Appellant	Registration No.
	September 14, 2015
Signature of Attorney/Agent/Appellant	Date

The 'Hearings' tab of the PTAB webpage http://www.uspto.gov/ip/boards/bpai/index.jsp provides additional information about oral hearings.

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FAX COVER SHEET

TO	Central Fax
COMPANY	USPTO
FAXNUMBER	15712738300
FROM	Kathleen Taylor-Saurer
DATE	2015-09-14 14:56:33 GMT
RE	U.S.S.N.11/367,238 - Response to Notice of Hearing (confirming attendance)

COVER MESSAGE

Dear Sir/Madam:

Attached is our response to Notice of Hearing confirming our attendance at the appellate hearing on Tuesday, October 6, 2015, beginning at 9:00 a.m.

Thank you and best, Kathleen Taylor-Saurer (for Patrea L. Pabst)

The United States Patent and Trademark Office
PATENT TRIAL AND APPEAL BOARD

PABST PATENT GROUP LLP
1545 PEACHTREE STREET NE
SUITE 320
ATLANTA, GA 30309

Appeal No:	2013-002,545
Appellant:	Nachiappan Chidambaram, Aqeel Fatmi et al.
Application No:	11/367,238
Hearing Room:	D
Hearing Docket:	A
Hearing Date:	Tuesday, October 06, 2015
Hearing Time:	09:00 AM
Location:	Madison Building - East Wing 600 Dulany Street, 9th Floor Alexandria, Virginia 22313-1450

NOTICE OF HEARING
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   United States Patent and Trademark Office
   P.O. BOX 1450
   Alexandria, Virginia 22313-1450

In all communications relating to this appeal, please identify the appeal by its number.

CHECK ONE:

(X) IN-PERSON HEARING - ATTENDANCE CONFIRMED *(EFS-Web selection: Confirmation of Hearing by Appellant)*

( ) TELEPHONIC HEARING - ATTENDANCE CONFIRMED *(EFS-Web selection: Confirmation of Hearing by Appellant)*

( ) VIDEO HEARING - ATTENDANCE CONFIRMED *(EFS-Web selection: Confirmation of Hearing by Appellant)*

( ) HEARING ATTENDANCE WAIVED *(EFS-Web selection: Waiver of Hearing by Appellant)*

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To aid the judges in determining whether any conflicts exist that may require a recusal, please list in the 'Comments' section the names of any additional person(s) who will be participating in the oral hearing. (Upon arrival, all persons presenting arguments must sign in at the Usher's desk.)

Comments/Special Requests:

Carlos A. Zuniga, Ph.D., of the Pabst Patent Group, will be a speaker at the in-person hearing. Attached is a copy of ~~his curriculum vitae.~~

Patrea L. Pabst	31,284
Typed or Printed Name of Attorney/Agent/Appellant	Registration No.
	09/25/2015
Signature of Attorney/Agent/Appellant	Date

The 'Hearings' tab of the PTAB webpage http://www.uspto.gov/ip/boards/bpai/index.jsp provides additional information about oral hearings.

Please direct other inquiries to the PTAB Hearings Clerk at 571-272-9797.

Carlos A. Zuniga, Ph.D.

1925 Monroe Dr NE 1628
Atlanta GA, 30324
(404) 769-8682, czunig01@gmail.com

Education

2011 – 2014	***Massachusetts Institute of Technology*** - Cambridge, MA, Dept. of Chemistry Research Advisor: Prof. Timothy M. Swager *Postdoctoral Fellow*
2006 – 2011	***Georgia Institute of Technology*** - Atlanta, GA, School of Chemistry and Biochemistry Research Advisor: Prof. Seth R. Marder *Ph.D., Organic/Polymer Chemistry*
2005	***Florida International University*** - Miami, FL, School of Chemistry and Biochemistry Research Advisor: Prof. Yong Cai *B. Sc., Chemistry* (Magna Cum Laude)

Research and Professional Experience

2011 – 2014	***Massachusetts Institute of Technology*** – Cambridge, MA Postdoctoral Research Fellow Research Advisor: Prof. Timothy M. Swager Focus: Synthesis and applications of graphene-based materials for environmental sensing and energy storage applications
2007 – 2011	***Georgia Institute of Technology*** – Atlanta, GA Graduate Research Assistant Research Advisor: Prof. Seth R. Marder Thesis Focus: Development of high triplet energy solution-processable polymer hosts for phosphorescent OLEDs
2006	***Applied Research Center (ARC)*** – Miami, FL Research Chemist Research Supervisor: Dr. Georgio Tachiev
2005 – 2006	***Southeast Environmental Research Center and Environmental Bioinorganic Analytical Chemistry Group (EBACG)*** – Miami, FL Research Assistant Research Supervisor: Prof. Yong Cai
2005	***Dow Corning Coporation*** – Midland, MI Research Intern - Photonics Solutions Group Research Supervisor: Mr. Jonathan Hannington

2003 – 2005	***Florida International University*** – Miami, FL Undergraduate Research and Teaching Assistant (General Chemistry and Organic Chemistry I & II) Research Advisor: Prof. Yong Cai

Technical Expertise/Skills

- Organic chemistry, synthesis, polymers, materials chemistry, organic electronics, graphene/graphene oxide chemistry, nanomaterials, gas sensors, energy storage, NMR, UV-vis., fluorescence, GPC, FT-IR, GC-MS, electrochemistry, surface chemistry, thin films, ball milling, TGA, DSC, BET, DLS, zeta potential, SEM, TEM, and XPS

Honors/Fellowships

2012 – Present	Henry and Camille Dreyfus Environmental Chemistry Postdoctoral Fellow
2008	National Science Foundation Graduate Fellowship: Honorable Mention
2008	Carl J. Storm Travel Fellow
2007 – 2008	Cherry Emerson Graduate Fellow
2006 – 2011	Roberto C. Goizueta Graduate Fellow
2006- 2007	Polymer GAANN Fellow
2005	Outstanding Graduating Senior in Chemistry from the College of Arts and Sciences - Florida International University
2005	Outstanding Graduating Senior - American Chemical Society – South Florida Chapter
2000 – 2005	Florida Medallion Scholar

Publications and Patents

- Eight publications in peer-reviewed journals

FAX COVER SHEET

TO	USPTO
COMPANY	Central Fax
FAXNUMBER	15712738300
FROM	Kathleen Taylor-Saurer
DATE	2015-09-25 14:48:42 GMT
RE	U.S.S.N.11/367,238 - Supplemental Response to Notice of Hearing

COVER MESSAGE

Please see attached Supplemental Response to Notice of Hearing commenting on presence of Carlos A. Zuniga, Ph.D., who will speak at hearing, together with his curriculum vitae.

Thank you and best.

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
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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
11/367,238	03/03/2006	Nachiappan Chidambaram	BAN 102	5524

23579 7590 10/27/2015

Pabst Patent Group LLP
1545 PEACHTREE STREET NE
SUITE 320
ATLANTA, GA 30309

EXAMINER	
VU, JAKE MINH	

ART UNIT	PAPER NUMBER
1618	

MAIL DATE	DELIVERY MODE
10/27/2015	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

BEFORE THE PATENT TRIAL AND APPEAL BOARD

Ex parte NACHIAPPAN CHIDAMBARAM and AQEEL FATMI

Appeal 2013-002545
Application 11/367,238
Technology Center 1600

Before DEMETRA J. MILLS, ERIC B. GRIMES and
ROBERT A. POLLOCK, *Administrative Patent Judges*.

MILLS, *Administrative Patent Judge*.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134. The Examiner has rejected the claims for anticipation and obviousness. We have jurisdiction under 35 U.S.C. § 6(b).

STATEMENT OF CASE

The following claims are representative.

1. A pharmaceutical composition comprising

(a) a salt of one or more either acidic or basic pharmaceutically active agents; and

(b) a deionizing agent in an amount from about 0.2 to about 1.0 mole equivalents per mole of the pharmaceutically active agent(s), which at least partially neutralizes the pharmaceutically active agent(s); and

(c) polyethylene glycol;

wherein when the salt is a salt of a weak acid and a strong base, the deionizing agent is a hydrogen ion species and when the salt is a salt of a weak base and a strong acid, the deionizing agent is a hydroxide ion species.

19. A softgel capsule comprising a fill material, wherein the fill material comprises

(a) a salt of one or more either acidic or basic pharmaceutically active agents; and

(b) a deionizing agent in an amount from about 0.2 to about 1.0 mole equivalents per mole of the pharmaceutically active agent(s), which at least partially neutralizes the pharmaceutically active agent(s); and

(c) polyethylene glycol;

wherein, when the salt is a salt of a weak acid and a strong base, the deionizing agent is a hydrogen ion species and when the salt is a salt of a weak base and a strong acid, the deionizing agent is a hydroxide ion species.

32. The composition of claim 1, wherein the pharmaceutically active agent is naproxen sodium and the deionizing agent is a hydrogen ion species.

33. The composition of claim 19, wherein the pharmaceutically active agent is naproxen sodium and the deionizing agent is a hydrogen ion species.

34. The composition of claim 32, wherein the hydrogen ion species is selected from the group consisting of hydrochloric acid, hydrobromic acid, hydroiodic acid, sulfuric acid, fumaric cid, maleic acid, tartaric acid, methane-, ethane-, and benzene sulfonates, citric acid, malic acid, acetic acid, proprionic acid, pyruvic acid, butanoic acid, and lactic acid.

35. The composition of claim 33, wherein the hydrogen ion species is selected from the group consisting of hydrochloric acid, hydrobromic acid, hydroiodic sulfonates, citric acid, malic acid, acetic acid, proprionic acid, pyruvic acid, butanoic acid, and lactic acid.

40. A pharmaceutical composition prepared by a method comprising

(a) mixing a salt of one or more acidic or basic pharmaceutically active agents;

(b) a deionizing agent in an amount from about 0.2 to about 1.0 mole

equivalents per mole of the salt of the pharmaceutically active agent(s), which at least partially neutralizes the salt of pharmaceutically active agent(s); and

(c) polyethylene glycol;

wherein when the salt is a salt of a weak acid and a strong base, the deionizing agent is a hydrogen ion species, and when the salt is the salt of a weak base and a strong acid, the deionizing agent is a hydroxide ion species, and wherein the pharmaceutically active agent(s) are not amphoteric.

41. A softgel capsule prepared by a method comprising

(a) producing a fill material by mixing

(i) a salt of one or more acidic or basic pharmaceutically active agents;

(ii) a deionizing agent in an amount from about 0.2 to about 1.0 mole

equivalents per mole of the pharmaceutically active agent(s) to cause partial deionization of the salt of the pharmaceutically active agent(s); and

(iii) polyethylene glycol;

(b) encapsulating the mixture in a softgel capsule;

wherein when the salt is a salt of a weak acid and a strong base, the deionizing agent is a hydrogen ion species, and when the salt is the salt of a weak base and a strong acid, the deionizing agent is a hydroxide ion species.

Cited References

Yu	US 5,360,615	Nov. 1, 1994
Sawyer	US 6,383,515 B2	May 7, 2002
Cupps	US 5,541,210	Jul. 30, 1996
McEntee	US 5,885,608	Mar. 23, 1999

Grounds of Rejection

1. Claims 1-2, 6-13, 19-20, 24-31, and 40-41 are rejected under 35 U.S.C. § 102(b) as being anticipated by Yu.
2. Claims 1-2, 6-13, 19-20, and 24-35 are rejected under 35 U.S.C. § 102(b) as being anticipated by Sawyer.
3. Claims 1-2, 6, 8-13,19-20, 24, 26-35, and 38-41 rejected under 35 U.S.C. § 102(b) as being anticipated by Cupps.
4. Claims 1-2, 6-13, 19-20, and 24-41 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Sawyer in view of McEntee.

FINDINGS OF FACT

The Examiner's findings of fact are set forth in the Answer at pages 5-10.

PRINCIPLES OF LAW

In making our determination, we apply the preponderance of the evidence standard. *See, e.g., Ethicon, Inc. v. Quigg*, 849 F.2d 1422, 1427 (Fed. Cir. 1988) (explaining the general evidentiary standard for proceedings before the Office). The Board "determines the scope of claims in patent applications not solely on the basis of the claim language, but upon giving claims their broadest reasonable construction 'in light of the specification as it would be interpreted by one of ordinary skill in the art.'" *Phillips v. AWH Corp.,* 415 F.3d 1303, 1316 (Fed. Cir. 2005) (quoting *In re Am. Acad. of Sci. Tech. Ctr.*, 367 F.3d 1359, 1364 (Fed. Cir. 2004).

In order for a prior art reference to serve as an anticipatory reference, it must disclose every limitation of the claimed invention, either explicitly or inherently. See *In re Schreiber*, 128 F.3d 1473 (Fed. Cir. 1997).

"In rejecting claims under 35 U.S.C. § 103, the examiner bears the initial burden of presenting a *prima facie* case of obviousness. Only if that burden is met, does the burden of coming forward with evidence or argument shift to the applicant." *In re Rijckaert*, 9 F.3d 1531, 1532 (Fed. Cir. 1993) (citations omitted). In order to determine whether a prima facie case of obviousness has been established, we consider the factors set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 17 (1966): (1) the scope and content of the prior art; (2) the differences between the prior art and the claims at issue; (3) the level of ordinary skill in the relevant art; and (4) objective evidence of nonobviousness, if present.

ISSUE

The issue is: Does the cited prior art support the Examiner's finding that the claimed subject matter is anticipated?

Anticipation Yu

Claims 1-2, 6-13, 19-20, 24-31, and 40-41 are rejected under 35 U.S.C. §102(b) as being anticipated by Yu.

ANALYSIS

We agree with the Examiner's fact finding, statement of the rejection and responses to Appellants' arguments as set forth in the Answer. We find that the Examiner has provided evidence to support a prima facie case of anticipation. We provide the following additional comment to argument set forth in the Answer.

The Examiner relies on Yu, Example 8, reproduced below, to reject claim 1.

EXAMPLE VIII

Formulation for a Highly Concentrated Solution of Diclofenac Sodium

The following formulation produces a highly concentrated (20% by weight) solution of diclofenac sodium suitable as a softgel fill and having a water content of 8.0% w/w.

Diclofenac Sodium	100.0 mg	
Polyethylene Glycol 600	357.7 mg	
Hydrochloric Acid (36.5% w/w solution)	6.5 mg	(0.2 mole equivalent)
Water	35.8 mg	
Total	500.0 mg	

Yu, col. 1, ll. 19-20 discloses that the Yu solvent system is suitable for encapsulation in soft, elastic, gelatin capsules. The Examiner finds that an amphoteric drug is "an acidic or basic depending on the pH environment.

Appellant's claims recite 'either acidic or basic', wherein an amphoteric drug can be literally either acidic or basic." Ans. 10.

Appellants contend that diclofenac in Yu Example 8 is an amphoteric pharmaceutical substance and therefore excluded by pending claim 1 which requires "a salt of one or more either acidic or basic pharmaceutically active agents." (App. Br. 12.) Appellants cite to Figure 1 of Palomo, et al., *J Pharm Biomed. Anal.,* 21: 83-94 (1999), arguing that, "it is known in the art that strong acids, such as hydrochloric acid, catalyze the cyclization of diclofenac sodium to an indolinone derivative." (App. Br 13.)

We are not persuaded by Appellants' arguments. Under the doctrine of claim differentiation, we conclude that when Appellants desired to specifically exclude amphoteric pharmaceutical compounds from the scope of the claims it was done with an exclusionary clause (claim 40). Thus, we agree with the Examiner that amphoteric pharmaceutical compounds, that may be either acidic or basic depending upon their environment, such as diclofenac are within the scope of claim 1.

We are further not persuaded by Appellants' argument that strong acids, such as the hydrochloric acid used in Yu, catalyze the cyclization of diclofenac sodium to an indolinone derivative. (App. Br. 13.) Palomo, page 93, actually concludes that, "[c]ontrary to the literature…., diclofenac sodium did not undergo intramolecular cyclization in acidic conditions." (See also applicability to separately argued claim 41, which is essentially the same as claim 1 except the pharmaceutical composition is recited to be in a softgel capsule.) Moreover, whereas Appellants argue that cyclization is pH dependent, the claims recite no pH requirements. The rejection of claim 1 and its dependent claims is affirmed.

Claim 40

Appellants present separate argument for claim 40 on page 14 of the Appeal Brief. Because amphoteric pharmaceutical compounds are specifically excluded from the scope of claim 40, we reverse the anticipation rejection of claim 40 over Yu.

Thus we find that the weight of the evidence fails to overcome the anticipation rejection of 1-2, 6-13, 19-20, 24-31, and 41 over Yu which is affirmed, except the rejection of claim 40 is reversed.

Anticipation Sawyer

Claims 1-2, 6-13, 19-20, and 24-35 are rejected under 35 U.S.C. § 102(b) as being anticipated by Sawyer. The Examiner finds that Sawyer, Example 17, reproduced below, anticipates the claimed invention.

TABLE 17

Formulation of Example 17

Ingredient	Amount	Weight Percent (%)
Naproxen sodium	3.6033 g	21.67
Polyethylene Glycol 300	10.0332 g	72.46
Potassium hydroxide	6.66 mg	0.05
Sodium propionate	0.8153 g	5.88

Appellants contend that, "the Examiner has provided no evidence to demonstrate that propionic acid is present in an amount between 0.2 to 1.0 mole equivalents of the active agent(s), as required by the claims." (App. Br. 15.) Appellants provide attorney argument in the form of acid/base equilibrium concentrations, and further indicating that the impact of other species present in solution on the equilibrium between propionate and propionic acid is ignored. (App. Br. 15.) We are not persuaded by the

acid/base equilibrium concentrations set forth in the Appeal Brief and Reply Brief. "Unsupported attorney argument, presented for the first time on appeal, is an inadequate substitute for record evidence. *See Gemtron Corp. v. Saint-Gobain Corp.*, 572 F.3d 1371, 1380 … (Fed. Cir. 2009) (emphasizing that 'unsworn attorney argument … is not evidence')." *Becton, Dickinson and Co. v. Tyco Healthcare Group LP*, 616 F.3d 1249, 1260 (Fed. Cir. 2010). The credibility of Appellants' calculations is further called into question by an admission by Appellant's counsel at oral hearing that counsel did not fully understand the "math and chemistry" of the acid base calculations.[1] The Examiner further finds error in Appellants' equilibrium calculations, including Appellants' failure to include the effect of sodium hydroxide on the equilibrium calculation. (Ans. 4.)

Claims 32-35

Appellants provide separate argument for claims 32-35, contending that

> When one includes the contribution of potassium hydroxide, the pH of the composition is significantly more basic which drives the equilibrium further to the left and results in even less propionic acid in solution. The excess potassium hydroxide in solution will also serve to prevent the neutralization of the active agent by any propionic acid present. Sawyer does not disclose or suggest, explicitly or inherently, the elements of claims 32 and 33. Accordingly, claims 32 and 33 are novel over Sawyer.

---

[1] Transcript of Oral Hearing dated October 6, 2015 at page 2 ("This is Dr. Carlos Zuniga. He is here to answer questions on math and chemistry because I can't do it.") and page 16 ("The calculations are difficult, like I said I can't do them . . .").

(App. Br. 18.) Each of claims 32-35 encompass an embodiment wherein the hydrogen ion species is propionic acid, which is disclosed in Sawyer Example 17. (Ans. 6.)

For reasons similar to the rejection of claim 1 over Sawyer, we do not accept Appellants' attorney argument regarding acid/base equilibrium concentrations set forth in the Appeal Brief and Reply Brief. The rejections of claims 32-35 are affirmed for the reasons herein and of record.

Anticipation Cupps

Claims 1-2, 6, 8-13, 19-20, 24, 26-35, and 38-41 are rejected under 35 U.S.C. §102(b) as being anticipated by Cupps. The Examiner relies on Example R of Cupps, reproduced below.

EXAMPLE R

For the relief of minor aches, pains, headache, muscular aches, sore throat pain, and fever associated with a cold or flu. Relieves nasal congestion, cough due to minor throat and bronchial irritations, runny nose, and sneezing associated with the common cold. Adults 12 and over take one fluid ounce every six hours.

	mg/fl oz
naproxen sodium anhydrous, USP	220 mg
doxylamine succinate, USP	12.5

-continued

	mg/fl oz
dextromethorphan hydrobromide, USP	30
Subject Compound 1	6
Dow XYS-40010.00 resin	3
high fructose corn syrup	16000
polyethylene glycol, NF	3000
propylene glycol, USP	3000
alcohol, USP	2500
sodium citrate dihydrate, USP	150
citric acid, anhydrous, USP	50
saccharin sodium, USP	20
flavor	3.5
purified water, USP	3800
total	28795 mg

Appellants argue that, "Example R describes a formulation containing approximately ***0.075 mole equivalents*** of citric acid per mole of naproxen sodium. In contrast, the claims require the deionizing agent to be present in an amount ***between 0.2 and 1.0 mole equivalents*** per mole of active agent." (Br. 21.)

The Examiner does not dispute that Cupps' composition contains about 0.075 mole equivalents of citric acid per mole of naproxen sodium, but responds to Appellants' argument finding that, "Appellant's claims recite '<u>about</u> 0.2 and <u>about</u> 1.0 mole equivalent', wherein 0.075 mole is about 0.1 mole, which is about 0.2 mole. Furthermore, the citrate [sic] in trisodium citrate dihydrate would increase the amount of citric acid." (Ans. 17.)

We find that Appellants have the better argument here. The Examiner has not set forth any evidentiary basis for assuming that "0.075 mole is about 0.1 mole, which is about 0.2 mole." (id.)

The anticipation rejection of claims 1-2, 6, 8-13, 19-20, 24, 26-35, and 38-41 over Cupps is reversed.

Obviousness Sawyer and McEntee

4. Claims 1-2, 6-13, 19-20, and 24-41 are rejected under 35 U.S.C. §103(a) as being unpatentable over Sawyer in view of McEntee.

The Examiner acknowledges that Sawyer does not teach using an organic acid, such as lactic acid in a solvent system for enhancing pharmaceutical agent solubility, particularly in a soft gel capsule. (Ans. 8.) The Examiner finds that McEntee teaches that organic acids, such as citric acid and lactic acid are well known pharmaceutical and supplement additives in the prior art (see col. 10, line 17-19). (*id.*) McEntee is relied on particularly for rejection of claims 34-37 and 39, which recite lactic acid as the hydrogen ion species.

Appellants contend that McEntee does not overcome the deficiencies of Sawyer. (Br. 24.) Having found no deficiencies in Sawyer (for the reasons above) we also affirm the obviousness rejection over Sawyer in view of McEntee.

CONCLUSION OF LAW

The cited references support the Examiner's anticipation rejections over Yu (except claim 40) and Sawyer, and obviousness rejection over Sawyer in view of McEntee, which are affirmed. The anticipation rejection over Cupps is reversed. The anticipation rejection of claim 40 over Yu is reversed. Every claim is rejected over at least one of the cited references, thus the rejection of the claims is affirmed.

AFFIRMED

tc

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
11/367,238	03/03/2006	Nachiappan Chidambaram	BAN 102	5524

23579 7590 01/29/2016

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EXAMINER	
VU, JAKE MINH	

ART UNIT	PAPER NUMBER
1618	

MAIL DATE	DELIVERY MODE
01/29/2016	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.

Notice of Abandonment	Application No.	Applicant(s)
	11/367,238	CHIDAMBARAM ET AL.
	Examiner	Art Unit
	JAKE VU	1618

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

This application is abandoned in view of:

1. ☐ Applicant's failure to timely file a proper reply to the Office letter mailed on _____.
   (a) ☐ A reply was received on _____ (with a Certificate of Mailing or Transmission dated _____), which is after the expiration of the period for reply (including a total extension of time of _____ month(s)) which expired on _____.
   (b) ☐ A proposed reply was received on _____, but it does not constitute a proper reply under 37 CFR 1.113 to the final rejection.
   (A proper reply under 37 CFR 1.113 to a final rejection consists only of: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) if this is utility or plant application, a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. Note that RCEs are not permitted in design applications.)
   (c) ☐ A reply was received on _____ but it does not constitute a proper reply, or a bona fide attempt at a proper reply, to the non-final rejection. See 37 CFR 1.85(a) and 1.111. (See explanation in box 7 below).
   (d) ☐ No reply has been received.

2. ☐ Applicant's failure to timely pay the required issue fee and publication fee, if applicable, within the statutory period of three months from the mailing date of the Notice of Allowance (PTOL-85).
   (a) ☐ The issue fee and publication fee, if applicable, was received on _____ (with a Certificate of Mailing or Transmission dated _____), which is after the expiration of the statutory period for payment of the issue fee (and publication fee) set in the Notice of Allowance (PTOL-85).
   (b) ☐ The submitted fee of $_____ is insufficient. A balance of $_____ is due.
   The issue fee required by 37 CFR 1.18 is $_____. The publication fee, if required by 37 CFR 1.18(d), is $_____.
   (c) ☐ The issue fee and publication fee, if applicable, has not been received.

3. ☐ Applicant's failure to timely file corrected drawings as required by, and within the three-month period set in, the Notice of Allowability (PTO-37).
   (a) ☐ Proposed corrected drawings were received on _____ (with a Certificate of Mailing or Transmission dated _____), which is after the expiration of the period for reply.
   (b) ☐ No corrected drawings have been received.

4. ☐ The letter of express abandonment which is signed by the attorney or agent of record or other party authorized under 37 CFR 1.33(b). See 37 CFR 1.138(b).

5. ☐ The letter of express abandonment which is signed by an attorney or agent (acting in a representative capacity under 37 CFR 1.34) upon the filing of a continuing application.

6. ☒ The decision by the Board of Patent Appeals and Interference rendered on *27 October 2015* and because the period for seeking court review of the decision has expired and there are no allowed claims.

7. ☐ The reason(s) below:

/JAKE VU/
Primary Examiner, Art Unit 1618

Petitions to revive under 37 CFR 1.137, or requests to withdraw the holding of abandonment under 37 CFR 1.181, should be promptly filed to minimize any negative effects on patent term.

PTO/AIA/80 (07-12)
Approved for use through 11/30/2014. OMB 0651-0035
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POWER OF ATTORNEY TO PROSECUTE APPLICATIONS BEFORE THE USPTO

I hereby revoke all previous powers of attorney given in the application identified in the attached statement under 37 CFR 3.73(c).

I hereby appoint:

■ Practitioners associated with Customer Number: 129259

OR

☐ Practitioner(s) named below (if more than ten patent practitioners are to be named, then a customer number must be used):

Name	Registration Number	Name	Registration Number

As attorney(s) or agent(s) to represent the undersigned before the United States Patent and Trademark Office (USPTO) in connection with any and all patent applications assigned only to the undersigned according to the USPTO assignment records or assignments documents attached to this form in accordance with 37 CFR 3.73(c).

Please change the correspondence address for the application identified in the attached statement under 37 CFR 3.73(c) to:

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☐	Firm or Individual Name			
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	City		State	Zip
	Country			
	Telephone		Email	

Assignee Name and Address: BANNER LIFE SCIENCES, LLC
4125 Premier Drive
High Point, NC 27265

A copy of this form, together with a statement under 37 CFR 3.73(c) (Form PTO/AIA/96 or equivalent) is required to be Filed in each application in which this form is used. The statement under 37 CFR 3.73(c) may be completed by one of The practitioners appointed in this form, and must identify the application in which this Power of Attorney is to be filed.

SIGNATURE of Assignee of Record

The individual whose signature and title is supplied below is authorized to act on behalf of the assignee

Signature	Claudia A. Garcia	Date	March 9, 2016
Name	Claudia A. Garcia	Telephone	336 812 7033
Title	Assistant Secretary, BANNER LIFE SCIENCES LLC		

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

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PTO/**AIA**/96 (08-12)
Approved for use through 01/31/2013. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

STATEMENT UNDER 37 CFR 3.73(c)

Applicant/Patent Owner: Banner Life Sciences, LLC

Application No./Patent No.: 11/367,238 Filed/Issue Date: March 3, 2006

Titled: Solvent System for Enhancing the Solubility of Pharmaceutical Agents

Banner Life Sciences, LLC, a Corporation

(Name of Assignee) (Type of Assignee, e.g., corporation, partnership, university, government agency, etc.)

states that, for the patent application/patent identified above, it is (choose **one** of options 1, 2, 3 or 4 below):

1. ☑ The assignee of the entire right, title, and interest.

2. ☐ An assignee of less than the entire right, title, and interest (check applicable box):

   ☐ The extent (by percentage) of its ownership interest is _____%. Additional Statement(s) by the owners holding the balance of the interest must be submitted to account for 100% of the ownership interest.

   ☐ There are unspecified percentages of ownership. The other parties, including inventors, who together own the entire right, title and interest are:

   Additional Statement(s) by the owner(s) holding the balance of the interest must be submitted to account for the entire right, title, and interest.

3. ☐ The assignee of an undivided interest in the entirety (a complete assignment from one of the joint inventors was made). The other parties, including inventors, who together own the entire right, title, and interest are:

   Additional Statement(s) by the owner(s) holding the balance of the interest must be submitted to account for the entire right, title, and interest.

4. ☐ The recipient, via a court proceeding or the like (*e.g.*, bankruptcy, probate), of an undivided interest in the entirety (a complete transfer of ownership interest was made). The certified document(s) showing the transfer is attached.

The interest identified in option 1, 2 or 3 above (not option 4) is evidenced by either (choose **one** of options A or B below):

A. ☐ An assignment from the inventor(s) of the patent application/patent identified above. The assignment was recorded in the United States Patent and Trademark Office at Reel _____, Frame _____, or for which a copy thereof is attached.

B. ☑ A chain of title from the inventor(s), of the patent application/patent identified above, to the current assignee as follows:

1. From: S. Karunakar, N. Chidambaram, A. Fatmi To: Banner Pharmacaps, Inc.

   The document was recorded in the United States Patent and Trademark Office at
   Reel 017602, Frame 0314, or for which a copy thereof is attached.

2. From: Banner Pharmacaps, Inc. To: Banner Life Sciences LLC

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STATEMENT UNDER 37 CFR 3.73(c)

3. From: _____ To: _____

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☐ Additional documents in the chain of title are listed on a supplemental sheet(s).

☑ As required by 37 CFR 3.73(c)(1)(i), the documentary evidence of the chain of title from the original owner to the assignee was, or concurrently is being, submitted for recordation pursuant to 37 CFR 3.11.

[NOTE: A separate copy (i.e., a true copy of the original assignment document(s)) must be submitted to Assignment Division in accordance with 37 CFR Part 3, to record the assignment in the records of the USPTO. See MPEP 302.08]

The undersigned (whose title is supplied below) is authorized to act on behalf of the assignee.

/Bernard A. Brown II/	April 6, 2016
Signature	Date
Bernard A. Brown II	60,543
Printed or Typed Name	Title or Registration Number

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7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (*i.e.*, GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.
8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspection or an issued patent.
9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

Electronic Acknowledgement Receipt

EFS ID:	25415824
Application Number:	11367238
International Application Number:	
Confirmation Number:	5524
Title of Invention:	Solvent system for enhancing the solubility of pharmaceutical agents
First Named Inventor/Applicant Name:	Nachiappan Chidambaram
Customer Number:	23579
Filer:	Bernard Andrew Brown II/Michele Capozzi
Filer Authorized By:	Bernard Andrew Brown II
Attorney Docket Number:	BAN 102
Receipt Date:	06-APR-2016
Filing Date:	03-MAR-2006
Time Stamp:	15:33:36
Application Type:	Utility under 35 USC 111(a)

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File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Power of Attorney	banner-POA-2016.pdf	89971 61e0d2cebf98416b43f9b4cd6000a1558d0044f4	no	1

Warnings:	
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2	Assignee showing of ownership per 37 CFR 3.73	373C_Statement_for_11-36723 8.pdf	78995 15d6c4a694d13a292bc912e1462136f7752 3cb20	no	3

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New Applications Under 35 U.S.C. 111

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

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

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

New International Application Filed with the USPTO as a Receiving Office

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

UNITED STATES PATENT AND TRADEMARK OFFICE

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

APPLICATION NUMBER	FILING OR 371(C) DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO./TITLE
11/367,238	03/03/2006	Nachiappan Chidambaram	

CONFIRMATION NO. 5524

POA ACCEPTANCE LETTER

129259
BGL/Banner Life Sciences
c/o CPA Global
P.O. Box 52050
Minneapolis, MN 55402

OC000000082052356

Date Mailed: 04/08/2016

NOTICE OF ACCEPTANCE OF POWER OF ATTORNEY

This is in response to the Power of Attorney filed 04/06/2016.

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

Questions about the contents of this notice and the requirements it sets forth should be directed to the Office of Data Management, Application Assistance Unit, at **(571) 272-4000** or **(571) 272-4200** or **1-888-786-0101**.

/dtvernon/

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Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NUMBER	FILING OR 371(C) DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO./TITLE
11/367,238	03/03/2006	Nachiappan Chidambaram	BAN 102

CONFIRMATION NO. 5524

POWER OF ATTORNEY NOTICE

23579
Pabst Patent Group LLP
1545 PEACHTREE STREET NE
SUITE 320
ATLANTA, GA 30309

OC000000082052354

Date Mailed: 04/08/2016

NOTICE REGARDING CHANGE OF POWER OF ATTORNEY

This is in response to the Power of Attorney filed 04/06/2016.

- The Power of Attorney to you in this application has been revoked by the assignee who has intervened as provided by 37 CFR 3.71. Future correspondence will be mailed to the new address of record(37 CFR 1.33).

Questions about the contents of this notice and the requirements it sets forth should be directed to the Office of Data Management, Application Assistance Unit, at **(571) 272-4000** or **(571) 272-4200** or **1-888-786-0101**.

/dtvernon/