



(51) International Patent Classification:
A01N 43/42 (2006.01) *A61K 31/44* (2006.01)

(21) International Application Number:
PCT/US2009/030662

(22) International Filing Date:
9 January 2009 (09.01.2009)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
61/020,139 9 January 2008 (09.01.2008) US
61/043,037 7 April 2008 (07.04.2008) US
61/060,758 11 June 2008 (11.06.2008) US

(71) Applicant (for all designated States except US):
CHARLESTON LABORATORIES, INC. [US/US];
548 Clearview Drive, Charleston, SC 29412 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **BOSSE, Paul** [US/US]; 548 Clearview Drive, Charleston, SC 29412 (US). **AMELING, John** [US/US]; 151 W. 7th Street, Apt. # 503, Cincinnati, OH 45202 (US). **SCHACHTEL, Bernard** [US/US]; 109 Quayside Drive, Jupiter, FL 33477 (US). **TAKIGIKU, Ray** [US/US]; 3952 Timberwoods Ct., Loveland, OH 45140 (US).

(74) Agent: **AKHAVAN, Ray**; Wilson Sonsini Goodrich & Rosati, 650 Page Mill Road, Palo Alto, CA 94304-1050 (US).

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME,

[Continued on next page]

(54) Title: PHARMACEUTICAL COMPOSITIONS

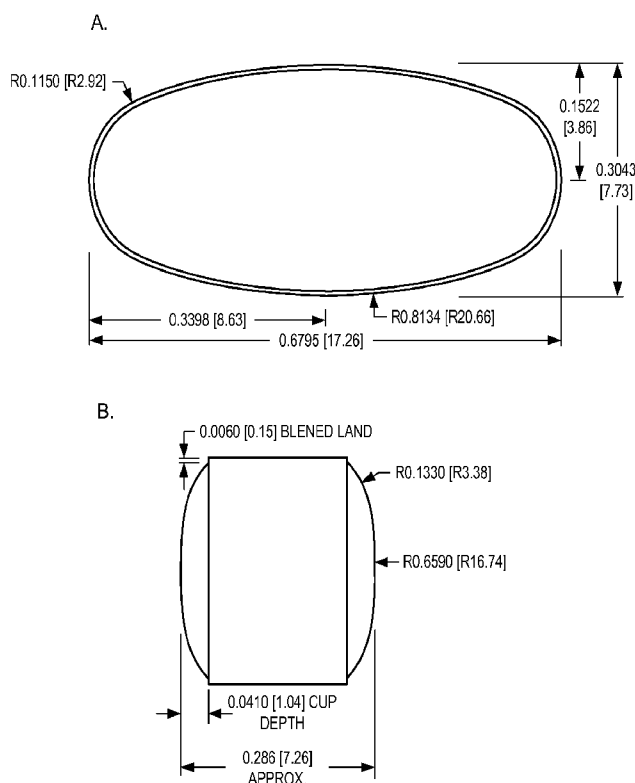


FIG. 2

(57) Abstract: Methods and compositions are provided which comprise effective amounts of analgesic to treat a subject, including reducing or eliminating an adverse effect associated with the analgesic.



MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

MC, MK, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

— with international search report (Art. 21(3))

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV,

(88) Date of publication of the international search report:

14 January 2010

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 09/30662

A. CLASSIFICATION OF SUBJECT MATTER

IPC(8) - A01N 43/42; A61K 31/44 (2009.01)

USPC - 514/282

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)

USPC- 514/282

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
USPC- 424/468; 424/471; 514/255.04 (see keywords below)

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

WEST: DB=PGPB,USPT,USOC,EPAB,JPAB: Google Scholar/patents: opioid stimulant caffeine antiemetic oxycam controlled release immediate release tablet layer

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 2005/0074493 A1 (MEHTA et al.) 07 April 2005 (07.04.2005) para [0020], [0022], [0024], [0033]-[0035], [0039], [0044], [0053], [0063]-[0065]	1-23
Y	US 2006/0204578 A1 (VERGEZ et al.) 14 September 2006 (14.09.2006) para [0002], [0042]-[0043], [0057], [0153]-[0154]	1-23
Y	US 2005/0272810 A1 (DAVIS et al.) 08 December 2005 (08.12.2005) para [0006], [0055], [0061], [0072], [0146]	6, 11, 14-15, 20, 22

☐ Further documents are listed in the continuation of Box C.

* 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 application or patent 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

14 May 2009 (14.05.2009)

Date of mailing of the international search report

22 MAY 2009

Name and mailing address of the ISA/US

Mail Stop PCT, Attn: ISA/US, Commissioner for Patents

P.O. Box 1450, Alexandria, Virginia 22313-1450

Facsimile No. 571-273-3201

Authorized officer:

Lee W. Young

PCT Helpdesk: 571-272-4300

PCT OSP: 571-272-7774

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 09/30662

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:
see extra sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of additional fees.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
1-23

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
- ☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 09/30662

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I: claims 1-23, drawn to compositions comprising (1) an effective amount of: (a) an opioid analgesic; (b) a stimulant; (c) an antiemetic; and (2) a pharmaceutically acceptable carrier or vehicle, etc.

Group II: claims 24-36, compositions comprising (1) an effective amount (a) oxycodone/morphine or a pharmaceutically acceptable salt thereof, (b) promethazine or a pharmaceutically acceptable salt thereof, (c) modafinil or a pharmaceutically acceptable salt thereof, and (d) naltrexone or a pharmaceutically acceptable salt thereof; and (2) a pharmaceutically acceptable carrier or vehicle, etc.

Group III: claims 37-45, drawn to compositions comprising (1) an effective amount of: (a) an opioid analgesic agent, (b) a non-opioid analgesic agent, and (c) a barbiturate agent; and (2) a pharmaceutically acceptable carrier or vehicle, etc.

Group IV: claims 46-49, drawn to compositions comprising (1) an effective amount of (a) butalbital or a pharmaceutically acceptable salt thereof, (b) acetaminophen and (c) promethazine or a pharmaceutically acceptable salt thereof; and (2) a pharmaceutically acceptable carrier or vehicle, etc.

Group V: claims 50-54 and 56, drawn to compositions comprising (1) an effective amount of (a) an opioid analgesic agent; (b) an antiemetic agent and (c) a beta blocker, serotonin receptor agonist, vasoconstrictor, anti-platelet agent, anti-convulsant, triptan, ergot, or calcitonin gene-related peptide receptor antagonist; and (2) a pharmaceutically acceptable carrier or vehicle, etc.

Group VI: claims 55 and 57-61, drawn to comprising (1) an effective amount of (a) an opioid analgesic agent and (b) sumatriptan or a pharmaceutically acceptable salt thereof; and (2) a pharmaceutically acceptable carrier or vehicle, etc.

Group VII: claims 62-71, drawn to compositions comprising (1) an effective amount of (a) an opioid analgesic agent, (b) a Cox-2 inhibitor agent, an antidepressant agent, an anti-convulsant agent, an anti-cholinergic agent, an NMDA receptor antagonist agent, an anesthetic agent or an uTadrenoreceptor agonist agent, (c) an opioid antagonist agent, (d) an agent that reduces or eliminates an adverse effect of the opioid agent; and (2) a pharmaceutically acceptable carrier or vehicle, etc.

Group VIII: claims 72-80, drawn to compositions comprising (1) an effective amount of (a) an opioid analgesic agent, (b) a non-opioid analgesic agent, (c) cyclazacine or levallorphan; (d) an agent that reduces or eliminates an adverse effect of the opioid analgesic agent; and (2) a pharmaceutically acceptable carrier.

Group IX: claims 81-84, composition comprising (1) an effective amount of (a) an opioid analgesic agent, (b) a non-opioid analgesic agent, (c) an opioid antagonist agent, (d) aprepitant, perphenazine, acetylcholine monoethanolamine, azasetron, benzquinamide, bietanautine, bromopride, clebopride, diphenidol, methallatal, metopimazine, oxypemdy, pipamazine, sulpiride, thiethylperazine, thioproperazine, or a pharmaceutically acceptable salt thereof; and (2) a pharmaceutically acceptable carrier or vehicle, etc.

Group X: claims 85-93, drawn to bi-layer tablets comprising: (1) a controlled-release layer comprising from about 6.5 mg to about 8.5 mg of hydrocodone or a pharmaceutically acceptable salt thereof; and (2) an immediate-release layer comprising from about 11 mg to about 14 mg of promethazine or a pharmaceutically salt thereof, etc.

Group XI: claims 94-100, drawn to bi-layer tablets comprising (1) an effective amount of (a) an opioid analgesic and (b) an antiemetic; and (2) a pharmaceutically acceptable carrier or vehicle, etc.

Group XII: claims 101-105, drawn to bi-layer tablets comprising: (1) a controlled-release layer comprising (a) from about 6.5 mg to about 8.5 mg of hydrocodone or a pharmaceutically acceptable salt thereof, (b) from about 135 mg to about 170 mg of silicified microcrystalline cellulose, (c) from about 17 mg to about 23 mg of hydroxy methyl propyl cellulose, (d) from about 1 mg to about 4 mg of magnesium stearate, and (e) from about 1mg to about 4 mg of stearic acid; and (2) an immediate release layer comprising (a) from about 11 mg to about 14 mg of promethazine or a pharmaceutically acceptable salt thereof, (b) from about 100 mg to about 140 mg of silicified microcrystalline cellulose, (c) from about 12 mg to about 18 mg of croscarmellose sodium and (d) from about 0.8 mg to about 1.5 mg of magnesium stearate, etc.

Group XIII: claims 106-110, drawn to composition comprising (1) an effective amount of (a) hydrocodone or a pharmaceutically acceptable salt thereof or oxycodone or a pharmaceutically acceptable salt thereof; (b) acetaminophen or a pharmaceutically acceptable salt thereof, (c) promethazine or a pharmaceutically acceptable salt thereof and (d) about 0.75 mg of naltrexone or a pharmaceutically acceptable salt thereof; and (2) a pharmaceutically acceptable carrier or vehicle, etc.

Group XIV: claims 111-115, drawn to compositions consisting of (1) an effective amount of (a) oxycodone or a pharmaceutically acceptable salt thereof, (b) promethazine or a pharmaceutically acceptable salt thereof and (c) naltrexone or a pharmaceutically acceptable salt thereof; and (2) a pharmaceutically acceptable carrier or vehicle, etc.

Group XV: claims 116-120, compositions consisting of (1) an effective amount of (a) promethazine or a pharmaceutically acceptable salt thereof, (b) propoxyphene or a pharmaceutically acceptable salt thereof, (c) naproxen or a pharmaceutically acceptable salt thereof; and (2) a pharmaceutically acceptable carrier or vehicle, etc.

Group XVI: claims 121-126, drawn to methods for treating or preventing pain, comprising administering to a subject in need thereof an effective amount of (a) an opioid analgesic agent, (b) an antiemetic agent or an antihistamine, and (c) a stimulant agent, etc.

Group XVII: claims 127-131, drawn to methods for treating or preventing photophobia comprising administering to a subject in need thereof an effective amount of (a) an opioid analgesic agent; and (b) an antiemetic agent, etc.

-----continued on next page-----

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 09/30662

Groups XVIII-XXIII-claims 132, 133, 134, 135, 136, and 137-138, respectively, drawn to various methods as described in each claim.

The claims of the various groups as defined above do not share any special technical feature that is an advance over the prior art. Combination compositions, and related methods of use, comprising the various disparate components are well known in the art. See US 20050079137 A1 to Blondino et al. (14 April 2005), abstract, for example. In addition, the various groups do not share any unknown special feature or component over the prior art. The various components are all well known in the art.

Thus, the inventions listed as Groups I-XXIII do not relate to a single general inventive concept under PCT Rule 13.1 because under PCT Rule 13.2 they lack the same or corresponding special technical feature. According to PCT Rule 13.2, unity of invention exists only when the same or corresponding technical feature is shared by all claimed inventions.

In this case the first named invention that will be searched without additional fees is Group I represented by claims 1-23.