Notice of Allowability	Application No.	Applicant(s)	
	10/525,006	SAWA ET AL.	
	Examiner	Art Unit	
	LAYLA SOROUSH	1627	

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

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to *the response to arguments submitted on September 6, 2011*.

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

3. ☒ The allowed claim(s) is/are *41,43-51,53-56,58-60 and 64-68*.

4. ☒ 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 the:
      1. ☒ Certified copies of the priority documents have been received.
      2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
      3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

5. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.

6. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
      1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
   (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

   Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

7. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☐ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
3. ☐ Information Disclosure Statements (PTO/SB/08), Paper No./Mail Date _____
4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5. ☐ Notice of Informal Patent Application
6. ☐ Interview Summary (PTO-413), Paper No./Mail Date _____ .
7. ☒ Examiner's Amendment/Comment
8. ☒ Examiner's Statement of Reasons for Allowance
9. ☐ Other _____.

SENJU EXHIBIT 2005
METRICS v. SENJU
IPR2014-01043

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Warren Cheek on December 16, 2011. This application has been amended as follows:

In claim 41, lines 3-4 after a hydrate thereof, **insert** – wherein the hydrate is at least one selected from a 1/2 hydrate, 1 hydrate, and 3/2 hydrate -- .

In claim 64, line 2-3 after a hydrate thereof, **insert** – wherein the hydrate is at least one selected from a 1/2 hydrate, 1 hydrate, and 3/2 hydrate -- .

Reasons for Allowance

The following is an examiner's statement of reasons for allowance:

The composition as claimed are found to be patentable over the prior art because the prior art does not teach or fairly suggest an aqueous liquid preparation consisting essentially of the following two components, wherein the first component is 2-amino-3-(4- bromobenzoyl)phenylacetic acid or a pharmacologically acceptable salt thereof, and the second component is tyloxapol wherein said liquid preparation is formulated for ophthalmic administration, and wherein when a quaternary ammonium compound is included in said liquid preparation, the quaternary ammonium compound is benzalkonium chloride.

The transitional phrase “consisting essentially of” limits the scope of a claim to the specified materials or steps “and those that do not materially affect the basic and novel characteristic(s)” of the claimed invention. In re Herz, 537 F.2d 549, 551-52, 190 USPQ 461, 463 (CCPA 1976) (emphasis in original).

The closest prior arts of record, namely Yanni et al. and Desai et al. Yanni et al. teaches a composition comprising an active agent see specifically Preparation XV (3-benzoylphenylacetic acid derivatives, salts are known) in 0.01-0.5%, polysorbate 80 in 0.01%, benzalkonium chloride, disodium EDTA, monobasic sodium phosphate, dibasic sodium phosphate, sodium chloride, pH adjustment with NaOH and/or HCl, water. Desai et al. teach an ophthalmic composition comprising bromfenac (2-amino-3-(4-bromobenzoyl)phenylacetic acid) and its ophthalmically acceptable salts, esters, amides or prodrugs thereof (column 3, lines 13-29, claims 4 and 7) and polysorbates such as tweens and tyloxapol and further comprising boric acid buffer (column 2, lines 18-44).

Applicants have found that tyloxapol is not equivalent to polysorbate 80 when combined with bromfenac. The present inventors have discovered that tyloxapol has an unexpected property in stabilizing an aqueous solution ofbromfenac in comparison with polysorbate 80. Please see the description of Experimental Example 1 and Table 1 on pages 14-16 of the specification. In the Experimental Example, the stability of an aqueous solution ofbromfenac was measured by storing the bromfenac solution with polysorbate 80 (see Comparison Example 1) and, separately, with tyloxapol (see A-02), under conditions of pH 7.0 at 60℃ for 4 weeks. The remaining rate % of bromfenac was measured after the test. As shown in Table 1, only 51.3% ofbromfenac remained in the

aqueous solution when stored with polysorbate 80. In contrast, 73.8% of bromfenac remained in the aqueous solution when stored with tyloxapol. Thus the present inventors have found that tyloxapol has an unexpected stabilizing effect on an aqueous solution ofbromfenac in comparison to polysorbate 80. Therefore the present inventors have found that tyloxapol and polysorbate 80 are not equivalent compounds. Such unequivalency, and such remarkable effects, could not have been obvious to one skilled in the art from the cited references. For the foregoing reasons, it is respectfully submitted that the teachings of the cited references do not suggest the claimed bromfenac preparation as amended, nor the unexpected properties of the preparation. Additionally, Desai et al. teach that the problems with benzalkonium chloride and other quaternary ammonium compounds can be avoided by using certain polymeric quaternary ammonium compounds in combination with boric acid. Hence, an essential component of the Desai composition is a polymeric quaternary ammonium compound. However, the instant claims as amended require that, when the claimed liquid preparation includes a quaternary ammonium compound, the quaternary ammonium compound is limited to benzalkonium chloride. Thus the polymeric quaternary ammonium compounds disclosed in Desai et al. are excluded from the amended claims.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled “Comments on Statement of Reasons for Allowance.”

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Layla Soroush whose telephone number is (571)272-5008. The examiner can normally be reached on 8:30a.m.-5:00p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan can be reached on (571)272-0629. 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.

/SREENI PADMANABHAN/

Supervisory Patent Examiner, Art Unit 1627

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.
10/525,006	03/28/2005	Shirou Sawa	2005_0232A	1756

513 7590 11/15/2011

WENDEROTH, LIND & PONACK, L.L.P.
1030 15th Street, N.W.,
Suite 400 East
Washington, DC 20005-1503

EXAMINER	
SOROUSH, LAYLA	
ART UNIT	PAPER NUMBER
1627	

NOTIFICATION DATE	DELIVERY MODE
11/15/2011	ELECTRONIC

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

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

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

ddalecki@wenderoth.com
eoa@wenderoth.com

Applicant-Initiated Interview Summary	Application No.	Applicant(s)	
	10/525,006	SAWA ET AL.	
	Examiner	Art Unit	
	LAYLA SOROUSH	1627	

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

(1) *LAYLA SOROUSH*. (3) *Warren Cheek*.

(2) *Sreeni Padmanabhan*. (4)_____.

Date of Interview: *01 September 2011*.

Type: ☐ Telephonic ☐ Video Conference
☒ Personal [copy given to: ☐ applicant ☐ applicant's representative]

Exhibit shown or demonstration conducted: ☐ Yes ☐ No.
If Yes, brief description: _____.

Issues Discussed ☐101 ☐112 ☐102 ☒103 ☐Others
(For each of the checked box(es) above, please describe below the issue and detailed description of the discussion)

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

Identification of prior art discussed: *Yanni*.

Substance of Interview
(For each issue discussed, provide a detailed description and indicate if agreement was reached. Some topics may include: identification or clarification of a reference or a portion thereof, claim interpretation, proposed amendments, arguments of any applied references etc...)

Applicant argues - not necessarily is the claimed compound useful in the example
Applicant will consider amending claims to Bromfenac and tyloxapol
Applicant will deleter the method claims.

Applicant recordation instructions: 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

Examiner recordation instructions: Examiners must summarize the substance of any interview of record. A complete and proper recordation of the substance of an interview should include the items listed in MPEP 713.04 for complete and proper recordation including the identification of the general thrust of each argument or issue discussed, a general indication of any other pertinent matters discussed regarding patentability and the general results or outcome of the interview, to include an indication as to whether or not agreement was reached on the issues raised.

☐ Attachment

/Layla Soroush/ Examiner, Art Unit 1627	

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.

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/525,006	03/28/2005	Shirou Sawa	2005_0232A	1756

513 7590 11/15/2011

WENDEROTH, LIND & PONACK, L.L.P.
1030 15th Street, N.W.,
Suite 400 East
Washington, DC 20005-1503

EXAMINER	
SOROUSH, LAYLA	
ART UNIT	PAPER NUMBER
1627	

NOTIFICATION DATE	DELIVERY MODE
11/15/2011	ELECTRONIC

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

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

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

ddalecki@wenderoth.com
eoa@wenderoth.com

Office Action Summary	Application No.	Applicant(s)	
	10/525,006	SAWA ET AL.	
	Examiner	Art Unit	
	LAYLA SOROUSH	1627	

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

Period for Reply

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

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

Status

1)☒ Responsive to communication(s) filed on *06 September 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) *41,43-51,53-56,58-60 and 64-68* is/are pending in the application.

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

6)☐ Claim(s) _____ is/are allowed.

7)☒ Claim(s) *41,43-51,53-56,58-60 and 64-68* 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

The response filed September 6, 2011 presents remarks and arguments submitted to the office action mailed May 6, 2011 is acknowledged.

Applicant's arguments over the 35 U.S.C. 103 (a) rejection of claims 41, 43-48, 50-51, 53-55, and 58-59 over as being unpatentable over Yanni et al. (5475034) in view of Guy et al.(5540930) is not persuasive. Therefore, the rejection of record is herewith maintained.

Applicant's arguments over the 35 U.S.C. 103 (a) rejection of claims 49, 56, 60, and 64-68 over as being unpatentable over P Yanni et al. (5475034) and Guy et al. (5540930), as applied to claims 41-48, 50-51, 53-55, and 58-59, and further in view of Gamache et al. (WO 01/15677) is not persuasive. Therefore, the rejection of record is herewith maintained.

The ODP rejection is maintained for the reasons of record.

The following rejections are made:

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 41, 43-48, 50-51, 53-55, and 58-59 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yanni et al. (5475034) in view of Guy et al.(5540930).

Yanni et al. teaches a composition comprising an active agent see specifically Preparation XV (3-benzoylphenylacetic acid derivatives, salts are known) in 0.01-0.5%, polysorbate 80 in 0.01%, benzalkonium chloride, disodium EDTA, monobasic sodium phosphate, dibasic sodium phosphate, sodium chloride, pH adjustment with NaOH and/or HCl, water.

The reference fails to teach the specific elected second agent tyloxapol.

Guy et al. teaches non-ionic surfactant surface active agent include polysorbate 80 and tyloxapol in 0.05-1%.

It would have been obvious to one of ordinary skill in the art at the time of the invention to interchange polysorbate 80 and tyloxapol. The motivation comes from the teaching of Guy et al. that both compounds are non-ionic surfactant surface active agents. Hence, a skilled artisan would have had reasonable expectation of successfully producing a composition with similar efficacy and results.

Claims 49, 56, 60, and 64-68 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yanni et al. (5475034) and Guy et al. (5540930), as applied to claims 41-48, 50-51, 53-55, and 58-59, and further in view of Gamache et al. (WO 01/15677).

Yanni et al. and Guy et al. are as applied above.

Yanni et al. and Guy et al. do not teach the specific buffer boric acid and/or sodium borate/sodium tetraborate; thickners, polyvinylpyrrolidone; stabilizer is sodium sulfite.

Gamache et al. teaches anti-inflammatory agents include bromfenac and Moxifloxacin, viscosity building agents include, for example, polyvinyl alcohol, polyvinyl pyrrolidone, methyl cellulose, hydroxypropyl methylcellulose, hydroxyethyl cellulose, carboxymethyl cellulose, hydroxypropyl cellulose or other agents known to those skilled in the art. An appropriate buffer system (e. g., sodium phosphate, sodium acetate or sodium borate) may be added to prevent pH drift under storage conditions. Exemplified is an otic/nasal suspension: Ingredient 1B/1D agonist 0.1-1.0% w/v, Moxifloxacin 0.3% w/v, Benzalkonium Chloride 0.01% w/v, Edetate Disodium, USP 0.01% w/v, Sodium Chloride, USP 0.3% w/v, Sodium Sulfate, USP 1.2% w/v, Tyloxapol, USP 0.05% w/v, Hydroxyethylcellulose 0.25% w/v, Sulfuric Acid and/or Sodium Hydroxide, NF q. s., and purified water q. s. to 100%.

It would have been obvious to one of ordinary skill in the art at the time of the invention to use the specific buffer boric acid and/or sodium borate/sodium tetraborate; thickners, polyvinylpyrrolidone; stabilizer is sodium sulfite. The motivation comes from the teaching of Gamache et al. that the anti-inflammatory agents, viscosity building agents, and buffer systems are interchangeable. Hence, a skilled artisan would have had reasonable expectation of successfully producing a composition with similar efficacy and results.

Double Patenting

Claims 41-51, 53-56, 58-60 and 64-68 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-43 of copending Application No. 11/755662.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the copending application contains claims drawn to method of treating pain and/or inflammation associated with an ocular condition, by administering the aqueous solutions of the instant claims. It would have been obvious to one of ordinary skill in the art at the time of the invention to use the formulations of the instant claims in the methods of the copending application, since the claims recite that the formulations are eye drops, and the instant abstract also teaches some of the conditions treated of the copending application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Response to Arguments

Applicant's main argument is that "Bromfenac is mentioned in Yanni in Table 1, merely as a reference compound for comparison purposes with the novel amide and ester derivatives of Yanni. It can be seen from the description of the anti-inflammatory tests described in columns 13 and 14 that bromfenac was tested merely in a 0.1% solution of the compound, and not in a pharmaceutical composition." Examiner states Yanni clearly discloses a single topical dose of 0.1% drug solution/suspension comprising Bromfenac. The Examiners

contention is that the reference does not specify the specific components of the comparative formulation (or in fact, the novel formulations) of the tests. However, the Example of the ophthalmic composition disclosing 0.01-0.5% of an active agent in a formulation renders obvious the use of the comparative example- Bromfenac, in such a formulation.

The arguments are not persuasive and the rejection is made **FINAL**.

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 mailing date of this final action.

Conclusion

No claims allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Layla Soroush whose telephone number is

(571)272-5008. The examiner can normally be reached on Monday through Friday from 8:30 a.m. to 5:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan, can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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/SREENI PADMANABHAN/

Supervisory Patent Examiner, Art Unit 1627

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of	:	Attorney Docket No. 2005_0232A
Shirou SAWA et al.	:	Confirmation No. 1756
Serial No. 10/525,006	:	Group Art Unit 1627
Filed March 28, 2005	:	Examiner Layla Soroush
AQUEOUS LIQUID PREPARATION CONTAINING 2-AMINO-3-(4-BROMOBENZOYL)PHENYLACETIC ACID	:	**Mail Stop: Amendment**

AMENDMENT

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

Sir:

Responsive to the Official Action dated May 6, 2011, the time for responding thereto being extended for one month in accordance with a petition for extension submitted concurrently herewith, please amend the above-identified application as follows:

The Commissioner is authorized to charge any deficiency or to credit any overpayment associated with this communication to Deposit Account No. 23-0975, with the EXCEPTION of deficiencies in fees for multiple dependent claims in new applications.

REMARKS

Favorable reconsideration is respectfully solicited in view of the foregoing amendments and following remarks.

Applicants wish to thank the Examiner Soroush and SPE Padmanabhan for their courtesy and assistance provided to the Applicants' representative during the personal interview held on September 1, 2011.

The claims have been amended as proposed by the Applicants and as suggested by the Examiners. Specifically, the second component has been limited to tyloxapol to expedite allowance. Such limitation is made without prejudice to the filing of a divisional application. Claim 41 has been amended to remove the "limited to" phrase, and method claims 61-62 are cancelled without prejudice.

Turning to the rejections, claims 41-48, 50-51, 53-55 and 58-59 are rejected under 35 USC 103 as unpatentable over Yanni in view of Guy. Such rejection is respectfully traversed as applied to the amended claims.

As discussed during the interview, the rejection appears to take the position that Yanni discloses in Preparation XV a composition of bromfenac with polysorbate 80. However Preparation XV does not disclose bromfenac, the acid, but an amide derivative thereof.

Moreover, Yanni teaches that bromfenac acids have problems such as difficulty in formulating stable solutions, and provoking ocular irritation. See column 1, line 60 to column 2, line 3. The object of Yanni is to make amide and ester derivatives of bromfenac which the inventors found to have better stability while having similar anti-inflammatory activity. See for example column 2, lines 23-43.

Bromfenac is mentioned in Yanni in Table 1, merely as a reference compound for comparison purposes with the novel amide and ester derivatives of Yanni. It can be seen from the description of the anti-inflammatory tests described in columns 13 and 14 that bromfenac was tested merely in a 0.1% solution of the compound, and not in a pharmaceutical composition.

The pharmaceutical compositions disclosed in the Tables of columns 16 and 17 of Yanni are directed to compositions of an "Active Agent" with polysorbate 80 and other components. The "Active Agent" is defined on lines 50-51 of column 16 to mean "one or more compounds of Formula I". The compounds of Formula I are described from the bottom of column 2 to 3. From

the definition of "Y" in the compounds, it is apparent that these compounds are limited to the amide or ester of bromfenac and do not encompass the bromfenac acid itself.

In summary, neither Preparation XV nor the remainder of Yanni disclose a composition of bromfenac as claimed, or its salt or hydrate, together with polysorbate 80 as contended in the rejection.

Moreover, Yanni teach away from using bromfenac as claimed, due to problems with obtaining stable solutions and provoking ocular irritation. See column 1 line 60 to column 2 line 3.

Therefore Yanni do not teach or suggest a composition of bromfenac with polysorbate 80.

Guy is cited for teaching the equivalency of polysorbate 80 and tyloxapol.

However Guy is directed to solving the problem of agglomeration of water insoluble steroid compounds such as loteprednol etabonate. See for example column 2, lines 45-65. On the other hand, bromfenac is a nonsteroidal compound.

Therefore one skilled in the art would not have been motivated to combine the teachings of Yanni directed to nonsteroidal compositions with Guy directed to steroidal compositions.

According to the USTPO guidelines, "[i]t is improper to combine references where the references teach away from their combination." See MPEP § 2145, citing *In re Grasselli*, 713 F.2d 731, 743 (Fed. Cir. 1983); see also *McGinley v. Franklin Sports, Inc.*, 262 F.3d 1339, 1354 (Fed.Cir. 2001) ("It is well-established that references which "teach away cannot serve to create a prima facie case of obviousness.") (citations omitted).

Moreover, the present inventors have found that tyloxapol is not equivalent to polysorbate 80 when combined with bromfenac.

The present inventors have discovered that tyloxapol has an unexpected property in stabilizing an aqueous solution of bromfenac in comparison with polysorbate 80. Please see the description of Experimental Example 1 and Table 1 on pages 14-16 of the specification.

In the Experimental Example, the stability of an aqueous solution of bromfenac was measured by storing the bromfenac solution with polysorbate 80 (see Comparison Example 1) and, separately, with tyloxapol (see A-02), under conditions of pH 7.0 at 60°C for 4 weeks. The remaining rate % of bromfenac was measured after the test.

As shown in Table 1, only 51.3% of bromfenac remained in the aqueous solution when stored with polysorbate 80. In contrast, 73.8% of bromfenac remained in the aqueous solution when stored with tyloxapol.

Thus the present inventors have found that tyloxapol has an unexpected stabilizing effect on an aqueous solution of bromfenac in comparison to polysorbate 80. Therefore the present inventors have found that tyloxapol and polysorbate 80 are not equivalent compounds. Such unequivalency, and such remarkable effects, could not have been obvious to one skilled in the art from the cited references.

For the foregoing reasons, it is respectfully submitted that the teachings of the cited references do not suggest the claimed bromfenac preparation as amended, nor the unexpected properties of the preparation.

Claims 49, 56, 60 and 64-68 are rejected under 103 as unpatentable over Yanni, Guy and Gamache.

The rejection of these claims is believed to be overcome in view of the foregoing amendments and remarks.

Lastly, claims 41-51, 53-56, 58-60 and 64-68 are provisionally rejected on the ground of non-statutory obviousness-type double patenting as being unpatentable over claims 1-43 of copending application Serial No. 11/755,662.

It is believed that all other grounds of rejection have been overcome in view of the instant response. Accordingly, it is respectfully submitted that this provisional ground of rejection should be withdrawn and the application passed on to allowance.

In summary, it is believed that each ground of rejection set forth in the Official Action has been overcome, and that the application is now in condition for allowance. Accordingly such allowance is solicited.

Respectfully submitted,

Shirou SAWA et al.

By /Warren M. Cheek/

Digitally signed by /Warren M. Cheek/
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September 6, 2011

Amendments to the Claims

1-40. (Cancelled)

41. (Currently amended) An aqueous liquid preparation consisting essentially of the following two components, wherein the first component is 2-amino-3-(4-bromobenzoyl)phenylacetic acid or a pharmacologically acceptable salt thereof or a hydrate thereof, and the second component is tyloxapol ~~an alkyl aryl polyether alcohol type polymer or a polyethylene glycol fatty acid ester~~, wherein said liquid preparation is formulated for ophthalmic administration, and wherein when a quaternary ammonium compound is included in said liquid preparation, the quaternary ammonium compound is ~~limited to~~ benzalkonium chloride.

42. (Cancelled)

43. (Previously presented) The aqueous liquid preparation according to claim 41, wherein the first component is a 2-amino-3-(4-bromobenzoyl)phenylacetic acid sodium salt.

44. (Previously presented) The aqueous liquid preparation according to claim 41, wherein the second component is tyloxapol and the pharmacologically acceptable salt of 2-amino-3-(4-bromobenzoyl)phenylacetic acid is a sodium salt , wherein the concentration of the tyloxapol is from about 0.01 w/v % to about 0.5 w/v %; and

wherein the first component is a 2-amino-3-(4-bromobenzoyl)phenylacetic acid sodium salt, wherein the concentration of the 2-amino-3-(4-bromobenzoyl)phenylacetic acid sodium salt is from about 0.01 to about 0.5 w/v %.

45. (Previously presented) The aqueous liquid preparation according to claim 44, wherein the concentration of the tyloxapol is from about 0.01 w/v % to about 0.3 w/v % and the concentration of the 2-amino-3-(4-bromobenzoyl)phenylacetic acid sodium salt is from about 0.05 to about 0.2 w/v %.

46. (Previously presented) The aqueous liquid preparation according to claim 45, wherein the concentration of the 2-amino-3-(4-bromobenzoyl)phenylacetic acid sodium salt is about 0.1 w/v %.

47. (Previously presented) The aqueous liquid preparation according to claim 45, wherein the concentration of the tyloxapol is about 0.02 w/v %.

48. (Previously presented) The aqueous liquid preparation according to claim 41, wherein the formulation further includes one or more additives selected from the group consisting of a preservative, buffer, thickener, stabilizer, chelating agent, and pH controlling agent.

49. (Previously presented) The aqueous liquid preparation according to claim 48, wherein said preservative is benzalkonium chloride; wherein said buffer is boric acid and/or sodium borate; wherein said thickener is polyvinylpyrrolidone; wherein said stabilizer is sodium sulfite; wherein said chelating agent is sodium edetate; and wherein said pH controlling agent is sodium hydroxide.

50. (Previously presented) The aqueous liquid preparation according to claim 49, wherein the pH is from about 7 to about 9.

51. (Previously presented) The aqueous liquid preparation according to claim 49, wherein the pH is from about 7.5 to about 8.5.

52. (Cancelled)

53. (Previously presented) The aqueous liquid preparation according to claim 45, wherein the concentration of the 2-amino-3-(4-bromobenzoyl)phenylacetic acid sodium salt is about 0.2 w/v %.

54. (Previously presented) The aqueous liquid preparation according to claim 45, wherein the concentration of the tyloxapol is about 0.3 w/v %.

55. (Previously presented) The aqueous liquid preparation according to claim 54, wherein the formulation further includes one or more additives selected from the group consisting of a preservative, buffer, thickener, stabilizer, chelating agent, and pH controlling agent.

56. (Previously presented) The aqueous liquid preparation according to claim 55, wherein said preservative is benzalkonium chloride; wherein said buffer is boric acid and/or sodium borate; wherein said thickener is polyvinylpyrrolidone; wherein said stabilizer is sodium sulfite; wherein said chelating agent is sodium edetate; and wherein said pH controlling agent is sodium hydroxide.

57. (Cancelled)

58. (Previously presented) The aqueous liquid preparation according to claim 53, wherein the concentration of the tyloxapol is about 0.02 w/v %.

59. (Previously presented) The aqueous liquid preparation according to claim 58, wherein the formulation further includes one or more additives selected from the group consisting of a preservative, buffer, thickener, stabilizer, chelating agent, and pH controlling agent.

60. (Previously presented) The aqueous liquid preparation according to claim 59, wherein said preservative is benzalkonium chloride; wherein said buffer is boric acid and/or sodium borate; wherein said thickener is polyvinylpyrrolidone; wherein said chelating agent is sodium edetate; and wherein said pH controlling agent is sodium hydroxide.

61-63. (Cancelled)

64. (Previously presented) An aqueous liquid preparation consisting essentially of:
(a) 2-amino-3-(4- bromobenzoyl)phenylacetic acid or a pharmacologically acceptable salt thereof or a hydrate thereof,
(b) tyloxapol,
(c) boric acid,
(d) sodium tetraborate,
(e) EDTA sodium salt,
(f) benzalkonium chloride,
(g) polyvinylpyrrolidone, and
(h) sodium sulfite, ~~and~~
wherein said liquid preparation is formulated for ophthalmic administration, and
wherein benzalkonium chloride is the only quaternary ammonium compound which is included in said liquid preparation.

65. (Previously presented) The aqueous liquid preparation of claim 64, wherein (a) is a 2-amino-3-(4-bromobenzoyl)phenylacetic acid sodium salt.

66. (Previously presented) The aqueous liquid preparation of claim 65, wherein the concentration of the 2-amino-3-(4-bromobenzoyl)phenylacetic acid sodium salt is from about 0.01 to about 0.5 w/v % and the concentration of the tyloxapol is about 0.02 w/v %.

67. (Previously presented) The aqueous liquid preparation of claim 66, wherein the concentration of the 2-amino-3-(4-bromobenzoyl)phenylacetic acid sodium salt is about 0.01 w/v %.

68. (Previously presented) The aqueous liquid preparation of claim 66, wherein the concentration of the 2-amino-3-(4-bromobenzoyl)phenylacetic acid sodium salt is about 0.1 w/v %.

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/525,006	03/28/2005	Shirou Sawa	2005_0232A	1756

513 7590 05/06/2011

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EXAMINER	
SOROUSH, LAYLA	
ART UNIT	PAPER NUMBER
1627	

NOTIFICATION DATE	DELIVERY MODE
05/06/2011	ELECTRONIC

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

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

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/525,006	SAWA ET AL.	
	Examiner	Art Unit	
	LAYLA SOROUSH	1627	

-- 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 *25 October 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) *41-51,53-56,58-62 and 64-68* is/are pending in the application.

4a) Of the above claim(s) *61 and 62* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *41-51,53-56,58-60 and 64-68* 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

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 October 25, 2010 has been entered.

The original restriction election is carried over from the response to the office action mailed on July 24, 2007.

The following rejections are made:

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 41-48, 50-51, 53-55, and 58-59 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yanni et al. (5475034) in view of Guy et al.(5540930).

Yanni et al. teaches a composition comprising an active agent see specifically Preparation XV (3-benzoylphenylacetic acid derivatives, salts are known) in 0.01-0.5%, polysorbate 80 in 0.01%, benzalkonium chloride, disodium EDTA, monobasic sodium

phosphate, dibasic sodium phosphate, sodium chloride, pH adjustment with NaOH and/or HCl, water.

The reference fails to teach the specific elected second agent tyloxapol.

Guy et al. teaches non-ionic surfactant surface active agent include polysorbate 80 and tyloxapol in 0.05-1%.

It would have been obvious to one of ordinary skill in the art at the time of the invention to interchange polysorbate 80 and tyloxapol. The motivation comes from the teaching of Guy et al. that both compounds are non-ionic surfactant surface active agents. Hence, a skilled artisan would have had reasonable expectation of successfully producing a composition with similar efficacy and results.

Claims 49, 56, 60, and 64-68 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yanni et al. (5475034) and Guy et al. (5540930), as applied to claims 41-48, 50-51, 53-55, and 58-59, and further in view of Gamache et al. (WO 01/15677).

Yanni et al. and Guy et al. are as applied above.

Yanni et al. and Guy et al. do not teach the specific buffer boric acid and/or sodium borate/sodium tetraborate; thickners, polyvinylpyrrolidone; stabilizer is sodium sulfite.

Gamache et al. teaches anti-inflammatory agents include bromfenac and Moxifloxacin, viscosity building agents include, for example, polyvinyl alcohol, polyvinyl pyrrolidone, methyl cellulose, hydroxypropyl methylcellulose, hydroxyethyl cellulose, carboxymethyl cellulose, hydroxypropyl cellulose or other agents known to those skilled

in the art. An appropriate buffer system (e. g., sodium phosphate, sodium acetate or sodium borate) may be added to prevent pH drift under storage conditions. Exemplified is an otic/nasal suspension: Ingredient 1B/1D agonist 0.1-1.0% w/v, Moxifloxacin 0.3% w/v, Benzalkonium Chloride 0.01% w/v, Edetate Disodium, USP 0.01% w/v, Sodium Chloride, USP 0.3% w/v, Sodium Sulfate, USP 1.2% w/v, Tyloxapol, USP 0.05% w/v, Hydroxyethylcellulose 0.25% w/v, Sulfuric Acid and/or Sodium Hydroxide, NF q. s., and purified water q. s. to 100%.

It would have been obvious to one of ordinary skill in the art at the time of the invention to use the specific buffer boric acid and/or sodium borate/sodium tetraborate; thickners, polyvinylpyrrolidone; stabilizer is sodium sulfite. The motivation comes from the teaching of Gamache et al. that the anti-inflammatory agents, viscosity building agents, and buffer systems are interchangeable. Hence, a skilled artisan would have had reasonable expectation of successfully producing a composition with similar efficacy and results.

Double Patenting

Claims 41-51, 53-56, 58-60 and 64-68 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-43 of copending Application No. 11/755662.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the copending application contains claims drawn to method of treating pain and/or inflammation associated with an ocular condition, by administering the aqueous solutions of the instant claims. It would have been obvious to one of

ordinary skill in the art at the time of the invention to use the formulations of the instant claims in the methods of the copending application, since the claims recite that the formulations are eye drops, and the instant abstract also teaches some of the conditions treated of the copending application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Response to Arguments

Applicant's arguments filed October 25, 2010 have been fully considered. The response to the arguments is as discussed below:

Applicant's arguments with respect to claims 41-51, 53-56, and 58-60, and 64-68 have been considered but are moot in view of the new ground(s) of rejection. More specifically, the Applicant states the Polyquad component is required in the Desai et al. reference while the amended claims herein are drawn to a composition wherein when a quaternary ammonium compound is included in said liquid preparation, the quaternary ammonium compound is limited to benzalkonium chloride. The newly modified rejections above address the amendments made to the claims.

Conclusion

No claims allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Layla Soroush whose telephone number is (571)272-

5008. The examiner can normally be reached on Monday through Friday from 8:30 a.m. to 5:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan, can be reached on (571) 272-0629. 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).

/SREENI PADMANABHAN/

Supervisory Patent Examiner, Art Unit 1627

Notice of References Cited	Application/Control No. 10/525,006	Applicant(s)/Patent Under Reexamination SAWA ET AL.	
	Examiner LAYLA SOROUSH	Art Unit 1627	Page 1 of 1

U.S. PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Name	Classification
*	A	US-5,475,034	12-1995	Yanni et al.	514/619
*	B	US-5,540,930	07-1996	Guy et al.	424/427
	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	WO 0115677 A2	03-2001	World Intellect	GAMACHE D A et al.	
	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.

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/525,006	03/28/2005	Shirou Sawa	2005_0232A	1756

513 7590 01/20/2011

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EXAMINER	
JAGOE, DONNA A	
ART UNIT	PAPER NUMBER
1619	

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01/20/2011	ELECTRONIC

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

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

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

ddalecki@wenderoth.com
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Interview Summary	Application No.	Applicant(s)	
	10/525,006	SAWA ET AL.	
	Examiner	Art Unit	
	Donna Jagoe	1619	

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

(1) *Donna Jagoe*. (3)_____.

(2) *Warren Cheek*. (4)_____.

Date of Interview: *14 January 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: *The claims in general*.

Identification of prior art discussed: *Desai et al. of record*.

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: *See Continuation Sheet*.

(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.

/Donna Jagoe/ Examiner, Art Unit 1619	/Robert A. Wax/ Supervisory Patent Examiner, Art Unit 1615

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.

Continuation of Substance of Interview including description of the general nature of what was agreed to if an agreement was reached, or any other comments: Applicants' representative pointed out changes to the independent claims to limit the quaternary ammonium compound to benzalkonium chloride. This amendment would specifically exclude polymeric quaternary ammonium compounds, necessary for the composition of Desai et al. Desai et al. teaches away from benzalkonium chloride with ophthamic compositions of drugs with acidic groups such as NSAIDs because they lose their ability to function because they form complexes with the charged drug compounds (column 1, lines 27-34)..

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of	:	Attorney Docket No. 2005_0232A
Shirou SAWA et al.	:	Confirmation No. 1756
Serial No. 10/525,006	:	Group Art Unit 1614
Filed March 28, 2005	:	Examiner Donna A. Jagoe
AQUEOUS LIQUID PREPARATION CONTAINING 2-AMINO-3-(4-BROMOBENZOYL)PHENYLACETIC ACID	:	**Mail Stop: RCE**

PRELIMINARY AMENDMENT

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

Sir:

The present Amendment is filed concurrently with an RCE, and is responsive to the Official Action dated June 24, 2010.

Please amend the above-identified application as follows:

The Commissioner is authorized to charge any deficiency or to credit any overpayment associated with this communication to Deposit Account No. 23-0975, with the EXCEPTION of deficiencies in fees for multiple dependent claims in new applications.

Amendments to the Claims

1-40. (Cancelled)

41. (Currently amended) An aqueous liquid preparation consisting essentially of the following two components, wherein the first component is 2-amino-3-(4-bromobenzoyl)phenylacetic acid or a pharmacologically acceptable salt thereof or a hydrate thereof, and the second component is an alkyl aryl polyether alcohol type polymer or a polyethylene glycol fatty acid ester, wherein said liquid preparation is formulated for ophthalmic administration, and wherein when a quaternary ammonium compound is included in said liquid preparation, the quaternary ammonium compound is limited to benzalkonium chloride.

42. (Previously presented) The aqueous liquid preparation according to claim 41, wherein the second component is tyloxapol.

43. (Previously presented) The aqueous liquid preparation according to claim 41, wherein the first component is a 2-amino-3-(4-bromobenzoyl)phenylacetic acid sodium salt.

44. (Previously presented) The aqueous liquid preparation according to claim 41, wherein the second component is tyloxapol and the pharmacologically acceptable salt of 2-amino-3-(4-bromobenzoyl)phenylacetic acid is a sodium salt , wherein the concentration of the tyloxapol is from about 0.01 w/v % to about 0.5 w/v %; and

wherein the first component is a 2-amino-3-(4-bromobenzoyl)phenylacetic acid sodium salt, wherein the concentration of the 2-amino-3-(4-bromobenzoyl)phenylacetic acid sodium salt is from about 0.01 to about 0.5 w/v %.

45. (Previously presented) The aqueous liquid preparation according to claim 44, wherein the concentration of the tyloxapol is from about 0.01 w/v % to about 0.3 w/v % and the concentration of the 2-amino-3-(4-bromobenzoyl)phenylacetic acid sodium salt is from about 0.05 to about 0.2 w/v %.

46. (Previously presented) The aqueous liquid preparation according to claim 45, wherein the concentration of the 2-amino-3-(4-bromobenzoyl)phenylacetic acid sodium salt is about 0.1 w/v %.

47. (Previously presented) The aqueous liquid preparation according to claim 45, wherein the concentration of the tyloxapol is about 0.02 w/v %.

48. (Previously presented) The aqueous liquid preparation according to claim 41, wherein the formulation further includes one or more additives selected from the group consisting of a preservative, buffer, thickener, stabilizer, chelating agent, and pH controlling agent.

49. (Previously presented) The aqueous liquid preparation according to claim 48, wherein said preservative is benzalkonium chloride; wherein said buffer is boric acid and/or sodium borate; wherein said thickener is polyvinylpyrrolidone; wherein said stabilizer is sodium sulfite; wherein said chelating agent is sodium edetate; and wherein said pH controlling agent is sodium hydroxide.

50. (Previously presented) The aqueous liquid preparation according to claim 49, wherein the pH is from about 7 to about 9.

51. (Previously presented) The aqueous liquid preparation according to claim 49, wherein the pH is from about 7.5 to about 8.5.

52. (Cancelled)

53. (Previously presented) The aqueous liquid preparation according to claim 45, wherein the concentration of the 2-amino-3-(4-bromobenzoyl)phenylacetic acid sodium salt is about 0.2 w/v %.

54. (Previously presented) The aqueous liquid preparation according to claim 45, wherein the concentration of the tyloxapol is about 0.3 w/v %.

55. (Previously presented) The aqueous liquid preparation according to claim 54, wherein the formulation further includes one or more additives selected from the group consisting of a preservative, buffer, thickener, stabilizer, chelating agent, and pH controlling agent.

56. (Previously presented) The aqueous liquid preparation according to claim 55, wherein said preservative is benzalkonium chloride; wherein said buffer is boric acid and/or sodium borate; wherein said thickener is polyvinylpyrrolidone; wherein said stabilizer is sodium sulfite; wherein said chelating agent is sodium edetate; and wherein said pH controlling agent is sodium hydroxide.

57. (Cancelled)

58. (Previously presented) The aqueous liquid preparation according to claim 53, wherein the concentration of the tyloxapol is about 0.02 w/v %.

59. (Previously presented) The aqueous liquid preparation according to claim 58, wherein the formulation further includes one or more additives selected from the group consisting of a preservative, buffer, thickener, stabilizer, chelating agent, and pH controlling agent.

60. (Previously presented) The aqueous liquid preparation according to claim 59, wherein said preservative is benzalkonium chloride; wherein said buffer is boric acid and/or sodium borate; wherein said thickener is polyvinylpyrrolidone; wherein said chelating agent is sodium edetate; and wherein said pH controlling agent is sodium hydroxide.

61. (Withdrawn-Currently amended) A method for stabilizing 2-amino-3-(4-bromobenzoyl)phenylacetic acid or a pharmacologically acceptable salt thereof or a hydrate

thereof in an aqueous liquid preparation, which comprises incorporating tyloxapol or polyethylene glycol monostearate into an aqueous liquid preparation containing 2-amino-3-(4-bromobenzoyl)phenylacetic acid or a pharmacologically acceptable salt thereof or a hydrate thereof, to obtain an aqueous liquid preparation consisting essentially of the following two components, the first component being 2-amino-3-(4-bromobenzoyl)phenylacetic acid or a pharmacologically acceptable salt thereof or a hydrate thereof, and the second component being tyloxapol or polyethylene glycol monostearate, wherein said liquid preparation is formulated for ophthalmic administration, and wherein when a quaternary ammonium compound is included in said liquid preparation, the quaternary ammonium compound is limited to benzalkonium chloride.

62. (Withdrawn-Currently amended) A method for inhibiting decrease in preservative effect of a preservative in an aqueous liquid preparation of 2-amino-3-(4-bromobenzoyl)phenylacetic acid or a pharmacologically acceptable salt thereof or a hydrate thereof, which comprises incorporating tyloxapol or polyethylene glycol monostearate into an aqueous liquid preparation containing 2-amino-3-(4-bromobenzoyl)phenylacetic acid or a pharmacologically acceptable salt thereof or a hydrate thereof and a preservative, to obtain an aqueous liquid preparation consisting essentially of the following two components, the first component being 2-amino-3-(4-bromobenzoyl)phenylacetic acid or a pharmacologically acceptable salt thereof or a hydrate thereof, and the second component being tyloxapol or polyethylene glycol monostearate, together with a preservative, wherein said liquid preparation is formulated for ophthalmic administration, and wherein when a quaternary ammonium compound is included in said liquid preparation, the quaternary ammonium compound is limited to benzalkonium chloride.

63. (Cancelled)

64. (Currently amended) An aqueous liquid preparation consisting essentially of:
(a) 2-amino-3-(4- bromobenzoyl)phenylacetic acid or a pharmacologically acceptable salt thereof or a hydrate thereof,
(b) tyloxapol,

(c) boric acid,
(d) sodium tetraborate,
(e) EDTA sodium salt,
(f) benzalkonium chloride,
(g) polyvinylpyrrolidone, and
(h) sodium sulfite, ~~and~~
wherein said liquid preparation is formulated for ophthalmic administration, and
wherein benzalkonium chloride is the only quaternary ammonium compound which is included in said liquid preparation.

65. (Previously presented) The aqueous liquid preparation of claim 64, wherein (a) is a 2-amino-3-(4-bromobenzoyl)phenylacetic acid sodium salt.

66. (Previously presented) The aqueous liquid preparation of claim 65, wherein the concentration of the 2-amino-3-(4-bromobenzoyl)phenylacetic acid sodium salt is from about 0.01 to about 0.5 w/v % and the concentration of the tyloxapol is about 0.02 w/v %.

67. (Previously presented) The aqueous liquid preparation of claim 66, wherein the concentration of the 2-amino-3-(4-bromobenzoyl)phenylacetic acid sodium salt is about 0.01 w/v %.

68. (Previously presented) The aqueous liquid preparation of claim 66, wherein the concentration of the 2-amino-3-(4-bromobenzoyl)phenylacetic acid sodium salt is about 0.1 w/v %.

REMARKS

Favorable reconsideration is respectfully solicited in view of the following remarks.

A personal interview with the Examiner is respectfully requested prior to issuance of a first Office Action in this RCE application.

Claims 41, 61 and 62 have been amended to require that "when a quaternary ammonium compound is included in said liquid preparation, the quaternary ammonium compound is limited to benzalkonium chloride". Support for this limitation is found, for example, in the paragraph bridging pages 3-4 of the specification; and on lines 3-7 on page 12 of the specification. Claim 64, which requires benzalkonium chloride, has similarly been amended to require that "benzalkonium chloride is the only quaternary ammonium compound which is included in said liquid preparation".

Turning to the last Official Action, claims 41-42 are newly rejected as anticipated under 35 U.S.C. 102 by U.S. Patent No. 5,603,929 to Desai et al. This ground of rejection is deemed to be untenable as applied to the claims after the foregoing amendments for the following reasons.

Desai et al. teach at column 1, lines 27-34 that:

> Benzalkonium chloride is a widely used preservative in ophthalmic solutions. However, benzalkonium chloride and other quaternary ammonium compounds are generally considered to be incompatible with ophthalmic compositions of drugs with acidic groups, such as nonsteroidal anti-inflammatory drugs ("NSAIDS"). These preservative [sic] lose their ability to function as they form complexes with the charged drug compounds.

As recognized by the Examiner, bromfenac used in the claimed preparation is an acidic "NSAID" drug.

Desai et al. further note at column 2, lines 1-5 that:

> The use of POLYQUAD® and other polymeric quaternary ammonium compounds as a disinfectant and preservative in

> contact lens care and artificial tear solutions is known. See, for example, U.S. Pat. Nos. 5,037,647; 4,525,346; and 4,407,791.

Desai et al. summarize the intended purpose of their invention at column 2, lines 18-30 as follows:

> It has now been discovered that the use of a combination of a polymeric quaternary ammonium compound such as POLYQUAD® and boric acid in ophthalmic compositions of acidic drugs provides a storage-stable composition which has surprisingly good preservative efficacy. This preservative combination of a polymeric quaternary ammonium compound and boric acid is useful in ophthalmic compositions of acidic drugs such as prostaglandins, antifungals, antibactedals [sic], and diagnostic agents. This preservative combination is especially useful in ophthalmic solutions of drugs containing either a carboxyl group such as non-steroidal anti-inflammatory drugs (NSAIDS) or a sulfonamide group such as antibacterial drugs.

Desai et al. further mention at column 3, lines 30-38 that:

> The compositions of the present invention may additionally include other ophthalmically acceptable components such as …. other preservatives (e.g. benzalkonium chloride) … tyloxapol…

Thus, Desai et al. teach away from using a quaternary ammonium compound such as benzalkonium chloride as a preservative with acidic NSAID drugs like bromfenac. Desai et al. teach that the problems with benzalkonium chloride and other quaternary ammonium compounds can be avoided by using certain polymeric quaternary ammonium compounds in combination with boric acid.

Hence, an essential component of the Desai composition is a polymeric quaternary ammonium compound.

However, the instant claims as amended require that, when the claimed liquid preparation includes a quaternary ammonium compound, the quaternary ammonium compound is limited to benzalkonium chloride.

Thus the polymeric quaternary ammonium compounds disclosed in Desai et al. are excluded from the amended claims.

Therefore the amended claims 41-42 are not anticipated by Desai et al.

Claims 43-51, 53-56, 58-60 and 64-68 are newly rejected as obvious under 35 U.S.C. 103 over Desai et al. in view of U.S. Patent No. 5,475,034 to Yanni et al. and U.S. Patent No. 5,998,465 to Hellberg et al. This ground of rejection is deemed to be untenable as applied to the claims after the foregoing amendments for the following reasons.

As discussed above, each independent claim 41, 61 and 62 has been amended to require that "when a quaternary ammonium compound is included in said liquid preparation, the quaternary ammonium compound is limited to benzalkonium chloride". In addition, independent claim 64, which requires benzalkonium chloride, has similarly been amended to require that "benzalkonium chloride is the only quaternary ammonium compound which is included in said liquid preparation".

Thus, the instant claims as amended require that, when the claimed liquid preparation includes a quaternary ammonium compound, the quaternary ammonium compound is limited to benzalkonium chloride.

On the other hand, Desai et al. teach away from using a quaternary ammonium compound such as benzalkonium chloride as a preservative with acidic NSAID drugs like bromfenac. Desai et al. teach that the problems with benzalkonium chloride and other quaternary ammonium compounds can be avoided by using certain polymeric quaternary ammonium compounds in combination with boric acid.

Hence, an essential component of the Desai composition is a polymeric quaternary ammonium compound. However the polymeric quaternary ammonium compounds disclosed in Desai et al. are excluded from the amended claims.

There is no motivation or suggestion in the cited prior art to modify the Desai composition to replace the polymeric quaternary ammonium compound taught in Desai et al. with benzalkonium chloride. The intended purpose of the invention disclosed in Desai et al., as mentioned above, is to provide a storage-stable ophthalmic composition for acidic NSAID drugs,

like bromfenac, having good preservative efficacy. This preservative combination is a polymeric quaternary ammonium compound and boric acid.

The USPTO has made clear that "[i]f [the] proposed modification would render the prior art invention being modified unsatisfactory for its intended purpose, then there is no suggestion or motivation to make the proposed modification." See MPEP section 2143.01 V, citing *In re Gordon*, 733 F.2d 900 (Fed. Cir. 1984). Additionally, section 2143.01 VI of the MPEP plainly states: "The proposed modification cannot change the principle of operation of a reference. If the proposed modification or combination of the prior art would change the principle of operation of the prior art invention being modified, then the teachings of the references are not sufficient to render the claims *prima facie* obvious." See also *In re Ratti*, 270 F.2d 810, 123 USPQ 349 (CCPA 1959).

Here, a substitution of the Desai polymeric quaternary ammonium compound with benzalkonium chloride would render the Desai et al. invention unsatisfactory for its intended purpose.

Applicant therefore respectfully submits a prima facie case of obviousness cannot be based on the combination of Desai et al. with Yanni et al. and Hellberg et al.

In addition to the argument that the proposed modification changes the principle operation and intended purpose of Desai et al., Applicant reiterates that Desai et al. explicitly teach away from the use of a quaternary ammonium compound, such as benzalkonium chloride, as the only quaternary ammonium compound in an ophthalmic solution for an acidic NSAID drug such as bromfenac.

According to the USTPO guidelines, "[i]t is improper to combine references where the references teach away from their combination." See MPEP § 2145, citing *In re Grasselli*, 713 F.2d 731, 743 (Fed. Cir. 1983); see also *McGinley v. Franklin Sports, Inc.*, 262 F.3d 1339, 1354 (Fed.Cir. 2001) ("It is well-established that references which "teach away cannot serve to create a prima facie case of obviousness.") (citations omitted).

For the reasons detailed above, Applicant respectfully requests withdrawal of the rejection of all claims under 35 USC 103 as being unpatentable over Desai et al., Yanni et al. and Hellberg et al.

Lastly, claims 41-51, 53-56, 58-60 and 64-68 are provisionally rejected on the ground of non-statutory obviousness-type double patenting as being unpatentable over claims 1-43 of copending application Serial No. 11/755,662.

It is believed that all other grounds of rejection have been overcome in view of the instant response. Accordingly, it is respectfully submitted that this provisional ground of rejection should be withdrawn and the application passed on to allowance.

In summary, it is believed that each ground of rejection set forth in the Official Action has been overcome, and that the application is now in condition for allowance. Accordingly such allowance is solicited.

Rejoinder and allowance of the withdrawn method claims is also solicited.

Respectfully submitted,

Shirou SAWA et al.

/Warren M. Cheek/

Digitally signed by /Warren M. Cheek/
DN: cn=/Warren M. Cheek/, o, ou, email=wcheek@wenderoth.com, c=US
Date: 2010.10.25 14:57:48 -04'00'

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October 25, 2010

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/525,006	03/28/2005	Shirou Sawa	2005_0232A	1756

513 7590 06/24/2010

WENDEROTH, LIND & PONACK, L.L.P.
1030 15th Street, N.W.,
Suite 400 East
Washington, DC 20005-1503

EXAMINER	
JAGOE, DONNA A	

ART UNIT	PAPER NUMBER
1619	

NOTIFICATION DATE	DELIVERY MODE
06/24/2010	ELECTRONIC

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

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

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

ddalecki@wenderoth.com
eoa@wenderoth.com

Office Action Summary	Application No.	Applicant(s)	
	10/525,006	SAWA ET AL.	
	Examiner	Art Unit	
	Donna Jagoe	1619	

-- 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 *24 March 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) *41-51,53-56,58-62 and 64-68* is/are pending in the application.

4a) Of the above claim(s) *61 and 62* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *41-51,53-56,58-60 and 64-68* 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 *4/8/10*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 41-51, 53-56, 58-62 and 64-68 are pending in this application. Claims 61 and 62 are withdrawn. Claims 41-51, 53-56, 58-60 and 64-68 are rejected.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on April 8, 2010 has been considered by the examiner. See attached 1449.

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 41 and 42 are rejected under 35 U.S.C. 102(b) as being anticipated by Desai et al. U.S. Patent No. 5,603,929.

Desai et al. teach an ophthalmic composition comprising bromfenac (2-amino-3-(4-bromobenzoyl)phenylacetic acid) and its ophthalmically acceptable salts, esters, amides or prodrugs thereof (column 3, lines 13-29, claims 4 and 7) and polysorbates such as tweens and tyloxapol and further comprising boric acid buffer (column 2, lines 18-44).

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.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

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

Claims 43-51, 53-56, 58-60 and 64-68 are rejected under 35 U.S.C. 103(a) as being unpatentable over Desai et al U.S. Patent No. 5,603,929 as applied to claims 41 and 42 above, and further in view of Yanni et al. U.S. Patent No. 5,475,034 and Hellberg et al. U.S. Patent No. 5,998,465.

Desai et al. teach an ophthalmic composition comprising bromfenac (2-amino-3-(4-bromobenzoyl)phenylacetic acid) and its ophthalmically acceptable salts, esters, amides or prodrugs thereof (column 3, lines 13-29, claims 4 and 7) and polysorbates such as tweens and tyloxapol and further comprising boric acid buffer (column 2, lines 18-44). It does not teach the concentration of about 0.01% to about 0.5% w/v. Yanni et al. teach 2-amino-3-4-bromobenzoylphenylacetamide (compound 15, column 9) and teach topically administrable ophthalmic compositions such as solutions, gels or ointment in concentrations of from about 0.01 to about 0.5% preferably (column 15, lines 1-55). Yanni et al. teach tyloxapol but it does not recite the specific amount. Hellberg et al. teach tyloxapol in an ophthalmic solution comprising NSAIA moieties include bromfenac (col. 3, line 57; claim 5); examples 2 and 3 (col. 11) in an amount of 0.01 to 0.05 % w/v (see examples 2 and 3, column 11). Addressing instant claims 48, 49, 55, 56, 59 and 60 drawn to the addition of one or more additives selected from a preservative, buffer, thickener, stabilizer, chelating agent and pH controlling agent, Desai et al. teach preservatives such as boric acid (column 2, lines 18-22), and benzalkonium chloride (column 3, lines 30-35), viscosity modifying agents (thickeners) such as polyvinyl pyrrolidone (column 3, lines 46-57), chelating agents (column 3, line 43) and pH controlling agent such as sodium hydroxide (see formulation example 1,

column 4). The pH is adjusted to 7.4 (see example 1, column 4) which is encompassed by instant claim 50 drawn to a pH of from about 7 to 9. Addressing instant claim 51, drawn to a pH from about 7.5 to about 8.5, Desai teach a pH of about 7.4 as noted supra. A prima facie case of obviousness exists where the claimed ranges and prior art ranges do not overlap but are close enough that one skilled in the art would have expected them to have the same properties. *Titanium Metals Corp. of America v. Banner*, 778 F.2d 775, 227 USPQ 773 (Fed. Cir. 1985). Addressing instant claim 64, Desai et al. teach an ophthalmic composition comprising bromfenac (2-amino-3-(4-bromobenzoyl)phenylacetic acid) and its ophthalmically acceptable salts, esters, amides or prodrugs thereof (column 3, lines 13-29, claims 4 and 7) and tyloxapol and further comprising boric acid buffer (a.k.a. sodium tetraborate) (column 2, lines 18-44), Benzalkonium chloride (column 3, line 34), polyvinyl pyrrolidone (column 3, line 52). It does not teach EDTA sodium salt and sodium sulfite, however, Yanni et al. teach ophthalmic solutions comprising 2-amino-3-4-bromobenzoylphenylacetamide (compound 15, column 9) and further teach incorporation of sulfites such as sodium (column 2, lines 12-14) and EDTA sodium salt (disodium EDTA) (see column 16, line 57 and column 17, line 5). It would have been obvious to employ said sodium sulfite and EDTA sodium salt in an ophthalmic formulation motivated by the teaching of Yanni et al. who disclose disodium EDTA and sodium sulfite in ophthalmic formulations of bromfenac for the purpose of stabilizing the solution (column 2, lines 2-14).

Double Patenting

Claims 41-51, 53-56, 58-60 and 64-68 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-43 of copending Application No. 11/755662.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the copending application contains claims drawn to method of treating pain and/or inflammation associated with an ocular condition, by administering the aqueous solutions of the instant claims. It would have been obvious to one of ordinary skill in the art at the time of the invention to use the formulations of the instant claims in the methods of the copending application, since the claims recite that the formulations are eye drops, and the instant abstract also teaches some of the conditions treated of the copending application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

No claims are allowed.

Response to Arguments

Applicant's arguments with respect to claims 41-51, 53-56, 58-60 and 64-68 have been considered but are moot in view of the new ground(s) of rejection. Applicant asserts that the Hellberg reference teaches bifunctional ester compounds having both anti-inflammatory and anti-oxidant activity. The rejection has been withdrawn, however

Hellberg et al. is relied on supra for its teaching of the amount of tyloxapol incorporated into the ophthalmic solution. The double patenting rejection is maintained and hereby repeated.

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.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Donna Jagoe whose telephone number is (571) 272-0576. The examiner can normally be reached on Monday through Friday from 8:00 A.M. - 4:30 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne (Bonnie) Eyler can be reached on (571) 272-0871. 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.

/YVONNE L. EYLER/
Supervisory Patent Examiner, Art Unit 1619

Donna Jagoe /D. J./
Examiner
Art Unit 1619

June 15, 2010

Notice of References Cited	Application/Control No. 10/525,006	Applicant(s)/Patent Under Reexamination SAWA ET AL.	
	Examiner Donna Jagoe	Art Unit 1619	Page 1 of 1

U.S. PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Name	Classification
*	A	US-5,603,929	02-1997	Desai et al.	424/78.04
*	B	US-5,475,034	12-1995	Yanni et al.	514/619
	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.

Sheet 1 of 1	INFORMATION DISCLOSURE STATEMENT	
FORM PTO/SB/08 A&B (*modified*) U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE LIST OF REFERENCES CITED BY APPLICANT(S) (*Use several sheets if necessary*) Date Submitted to PTO: April 8, 2010	ATTY DOCKET NO. 2005_0232A	SERIAL NO. 10/525,006
	APPLICANT Shirou SAWA et al.	
	FILING DATE March 28, 2005	GROUP 1614

OPAP IAP17 APR 08 2010 PATENT & TRADEMARK OFFICE

U.S. PATENT DOCUMENTS

*EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE
/D.J./	AA	6,395,746	5/2002	Cagle et al.			
	AB						
	AC						
	AD						
	AE						
	AF						
	AG						
	AH						
	AI						

FOREIGN PATENT DOCUMENTS

		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION YES	TRANSLATION NO
	BA							
	BB							
	BC							
	BD							
	BE							

OTHER DOCUMENT(S) *(Including Author, Title, Date, Pertinent Pages, Etc.)*

/D.J./	CA	http://medical-dictionary.thefreedictionary.com/prophylactic accessed 12/15/2009.
	CB	
	CC	
	CD	

EXAMINER	/Donna Jagoe/ (06/14/2010)	DATE CONSIDERED

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

Sheet 1 of 1	INFORMATION DISCLOSURE STATEMENT	
FORM PTO/SB/08 A&B (*modified*) U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE LIST OF REFERENCES CITED BY APPLICANT(S) (*Use several sheets if necessary*) Date Submitted to PTO: April 8, 2010	ATTY DOCKET NO. 2005_0232A	SERIAL NO. 10/525,006
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OPAP IAP17 APR 08 2010 PATENT & TRADEMARK OFFICE

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	AA	6,395,746	5/2002	Cagle et al.			
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	AD						
	AE						
	AF						
	AG						
	AH						
	AI						

FOREIGN PATENT DOCUMENTS

		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION YES	TRANSLATION NO
	BA							
	BB							
	BC							
	BD							
	BE							

OTHER DOCUMENT(S) *(Including Author, Title, Date, Pertinent Pages, Etc.)*

	CA	http://medical-dictionary.thefreedictionary.com/prophylactic accessed 12/15/2009.
	CB	
	CC	
	CD	

EXAMINER	DATE CONSIDERED

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

OPAP IAP17 APR 08 2010 PATENT & TRADEMARK OFFICE

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of	:	Attorney Docket No. 2005_0232A
Shirou SAWA et al.	:	**Confirmation No. 1756**
Serial No. 10/525,006	:	Group Art Unit 1614
Filed March 28, 2005	:	Examiner Donna A. Jagoe
AQUEOUS LIQUID PREPARATION CONTAINING 2-AMINO-3-(4-BROMOBENZOYL)PHENYLACETIC ACID	:	**Mail Stop: AMENDMENT**

PATENT OFFICE FEE TRANSMITTAL FORM

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

Sir:

Attached hereto is a Credit Card Payment Form authorizing payment in the amount of $180.00 to cover Patent Office fees relating to filing the following attached papers:

Information Disclosure Statement	$180.00

Respectfully submitted,

Shirou SAWA et al.

By _____
Warren M. Cheek
Registration No. 33,367
Attorney for Applicants

WMC/dlk
Washington, D.C. 2005-1503
Telephone (202) 721-8200
Facsimile (202) 721-8250
April 8, 2010

The USPTO is hereby authorized to charge any fees under 37 C.F.R. §§ 1.16, 1.17, and 1.492, which may be required by this paper to Deposit Account No. 23-0975.

OPAP
APR 08 2010
PATENT & TRADEMARK OFFICE

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of	:	Attorney Docket No. 2005_0232A
Shirou SAWA et al.	:	**Confirmation No. 1756**
Serial No. 10/525,006	:	Group Art Unit 1614
Filed March 28, 2005	:	Examiner Donna A. Jagoe
AQUEOUS LIQUID PREPARATION CONTAINING 2-AMINO-3-(4-BROMOBENZOYL)PHENYLACETIC ACID	:	**Mail Stop: AMENDMENT**

INFORMATION DISCLOSURE STATEMENT

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

Sir:

Pursuant to the provisions of 37 CFR 1.56, 1.97 and 1.98, Applicants request consideration of the reference listed on attached Form PTO/SB/08 and any additional information identified below in paragraph 3. A legible copy of each reference listed on the Form PTO/SB/08 is enclosed, except a copy is not provided for:

[X] each U.S. Patent and U.S. Patent application publication;

[] each reference previously cited in prior parent application Serial No._____.

1a. [] This Information Disclosure Statement is submitted:

within three months of the filing date (or of entry into the National Stage) of the above-entitled application, **or**

before the mailing of a first Office Action on the merits or the mailing of a first Office Action after the filing of an RCE,

and thus no certification and/or fee is required.

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The USPTO is hereby authorized to charge any fees under 37 C.F.R. §§ 1.16, 1.17, and 1.492, which may be required by this paper to Deposit Account No. 23-0975.

1b. [X] This Information Disclosure Statement is submitted

after the events of above paragraph 1a and prior to the mailing date of a final Office Action or a Notice of Allowance or an action which otherwise closes prosecution in the application, and thus:

(1) [] the certification of paragraph 2 below is provided, or

(2) [X] the fee of $180.00 specified in 37 CFR 1.17(p) is enclosed.

1c. [] This Information Disclosure Statement is submitted:

after the mailing date of a final Office Action or Notice of Allowance or action which otherwise closes prosecution in the application, and prior to payment of the issue fee, and thus:

the certification of paragraph 2 below is provided, and

the fee of $180.00 specified in 37 CFR 1.17(p) is enclosed.

2. It is hereby certified

a. [] that each item of information contained in this Information Disclosure Statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of the Statement, or

b. [] that no item of information contained in the Information Disclosure Statement was cited in a communication from a foreign patent office in a counterpart foreign application and, to the knowledge of the person signing the certification after making reasonable inquiry, was known to any individual designated in §1.56(c) more than three months prior to the filing of the Statement.

3. [X] Consideration of the following list of additional information (including any copending or abandoned U.S. application, prior uses and/or sales, etc.) is requested.

Copending application Serial No. 11/755,662 which is a CIP of the instant application.

4. For each non-English language reference listed on the attached Form PTO/SB/08, reference is made to:

a. [] a full or partial English language translation submitted herewith,

b. [] a foreign patent office search report (in the English language) submitted herewith,

c. [] the concise explanation contained in the specification of the present application at page ,

d. [] the concise explanation set forth in the attached English language abstract,

e. [] the concise explanation set forth below or on a separate sheet attached to the reference:

5. [] A foreign patent office search report citing one or more of the references is enclosed.

6. [] Statement Under 37 CFR 1.704(d)

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

Respectfully submitted,

Shirou SAWA et al.

By _____

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April 8, 2010

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of	:	Attorney Docket No. 2005_0232A
Shirou SAWA et al.	:	Confirmation No. 1756
Serial No. 10/525,006	:	Group Art Unit 1614
Filed March 28, 2005	:	Examiner Donna A. Jagoe
AQUEOUS LIQUID PREPARATION CONTAINING 2-AMINO-3-(4-BROMOBENZOYL)PHENYLACETIC ACID	:	**Mail Stop: Amendment**

AMENDMENT

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

Sir:

Responsive to the Official Action dated December 24, 2009, please amend the above-identified application as follows:

The Commissioner is authorized to charge any deficiency or to credit any overpayment associated with this communication to Deposit Account No. 23-0975, with the EXCEPTION of deficiencies in fees for multiple dependent claims in new applications.

PAGE 2/19 * RCVD AT 3/24/2010 4:34:20 PM [Eastern Daylight Time] * SVR:USPTO-EFXRF-6/30 * DNIS:2738300 * CSID:202 721 8250 * DURATION (mm-ss):03-32

Amendments to the Claims

1-40. (Cancelled)

41. (Currently amended) An aqueous liquid preparation consisting essentially of ~~at least~~ the following two components, wherein the first component ~~comprising~~ is 2-amino-3-(4-bromobenzoyl)phenylacetic acid or a pharmacologically acceptable salt thereof or a hydrate thereof, and the second component ~~comprising~~ is an alkyl aryl polyether alcohol type polymer or a polyethylene glycol fatty acid ester, wherein said liquid preparation is formulated for ophthalmic administration.

42. (Currently amended) The aqueous liquid preparation according to claim 41, wherein the ~~alkyl aryl polyether alcohol type polymer~~ second component is tyloxapol;

~~wherein the concentration of the tyloxapol is selected from a range of about 0.01 w/v % to about 0.5 w/v %; and~~

~~wherein the concentration of the 2-amino-3-(4-bromobenzoyl)phenylacetic acid or a pharmacologically acceptable salt thereof or a hydrate thereof is selected from a range of about 0.01 to about 0.5 w/v %.~~

43. (Currently amended) The aqueous liquid preparation according to claim ~~42~~41, wherein the first component is ~~pharmacologically acceptable salt of~~ a 2-amino-3-(4-bromobenzoyl)phenylacetic acid ~~is a~~ sodium salt.

44. (Currently amended) The aqueous liquid preparation according to claim ~~43~~41, wherein the second component is tyloxapol and the pharmacologically acceptable salt of 2-amino-3-(4-bromobenzoyl)phenylacetic acid is a sodium salt , wherein the concentration of the tyloxapol is from about 0.01 w/v % to about 0.5 w/v %; and

wherein the first component is a 2-amino-3-(4-bromobenzoyl)phenylacetic acid sodium salt, wherein the concentration of the 2-amino-3-(4-bromobenzoyl)phenylacetic acid sodium salt is from about 0.01 to about 0.5 w/v %

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~~2-amino-3-(4-bromobenzoyl)phenylacetic acid sodium salt is selected from a range of about 0.05 to about 0.2 w/v %.~~

45. (Currently amended) The aqueous liquid preparation according to claim 44, wherein the concentration of the tyloxapol is ~~selected~~ from ~~a range of~~ about 0.01 w/v % to about 0.3 w/v % and the concentration of the 2-amino-3-(4-bromobenzoyl)phenylacetic acid sodium salt is from about 0.05 to about 0.2 w/v %.

46. (Previously presented) The aqueous liquid preparation according to claim 45, wherein the concentration of the 2-amino-3-(4-bromobenzoyl)phenylacetic acid sodium salt is about 0.1 w/v %.

47. (Currently amended) The aqueous liquid preparation according to claim ~~46~~45, wherein the concentration of the tyloxapol is about 0.02 w/v %.

48. (Currently amended) The aqueous liquid preparation according to claim ~~47~~41, wherein the formulation further includes one or more additives selected from the group consisting of a preservative, buffer, thickener, stabilizer, chelating agent, and pH controlling agent.

49. (Previously presented) The aqueous liquid preparation according to claim 48, wherein said preservative is benzalkonium chloride; wherein said buffer is boric acid and/or sodium borate; wherein said thickener is polyvinylpyrrolidone; wherein said stabilizer is sodium sulfite; wherein said chelating agent is sodium edetate; and wherein said pH controlling agent is sodium hydroxide.

50. (Previously presented) The aqueous liquid preparation according to claim 49, wherein the pH is from about 7 to about 9.

51. (Currently amended) The aqueous liquid preparation according to claim ~~50~~49, wherein the pH is from about 7.5 to about 8.5.

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52. (Cancelled)

53. (Previously presented) The aqueous liquid preparation according to claim 45, wherein the concentration of the 2-amino-3-(4-bromobenzoyl)phenylacetic acid sodium salt is about 0.2 w/v %.

54. (Currently amended) The aqueous liquid preparation according to claim ~~53~~45, wherein the concentration of the tyloxapol is about 0.3 w/v %.

55. (Previously presented) The aqueous liquid preparation according to claim 54, wherein the formulation further includes one or more additives selected from the group consisting of a preservative, buffer, thickener, stabilizer, chelating agent, and pH controlling agent.

56. (Previously presented) The aqueous liquid preparation according to claim 55, wherein said preservative is benzalkonium chloride; wherein said buffer is boric acid and/or sodium borate; wherein said thickener is polyvinylpyrrolidone; wherein said stabilizer is sodium sulfite; wherein said chelating agent is sodium edetate; and wherein said pH controlling agent is sodium hydroxide.

57. (Cancelled)

58. (Previously presented) The aqueous liquid preparation according to claim 53, wherein the concentration of the tyloxapol is about 0.02 w/v %.

59. (Previously presented) The aqueous liquid preparation according to claim 58, wherein the formulation further includes one or more additives selected from the group consisting of a preservative, buffer, thickener, stabilizer, chelating agent, and pH controlling agent.

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60. (Previously presented) The aqueous liquid preparation according to claim 59, wherein said preservative is benzalkonium chloride; wherein said buffer is boric acid and/or sodium borate; wherein said thickener is polyvinylpyrrolidone; wherein said chelating agent is sodium edetate; and wherein said pH controlling agent is sodium hydroxide.

61. (Withdrawn-Currently amended) A method for stabilizing 2-amino-3-(4-bromobenzoyl)phenylacetic acid or a pharmacologically acceptable salt thereof or a hydrate thereof in an aqueous liquid preparation, which comprises incorporating tyloxapol or polyethylene glycol monostearate into an aqueous liquid preparation containing 2-amino-3-(4-bromobenzoyl)phenylacetic acid or a pharmacologically acceptable salt thereof or a hydrate thereof, to obtain an aqueous liquid preparation consisting essentially of ~~at least~~ the following two components, the first component ~~comprising~~ being 2-amino-3-(4-bromobenzoyl)phenylacetic acid or a pharmacologically acceptable salt thereof or a hydrate thereof, and the second component ~~comprising~~ being tyloxapol or polyethylene glycol monostearate, wherein said liquid preparation is formulated for ophthalmic administration.

62. (Withdrawn-Currently amended) A method for inhibiting decrease in preservative effect of a preservative in an aqueous liquid preparation of 2-amino-3-(4-bromobenzoyl)phenylacetic acid or a pharmacologically acceptable salt thereof or a hydrate thereof, which comprises incorporating tyloxapol or polyethylene glycol monostearate into an aqueous liquid preparation containing 2-amino-3-(4-bromobenzoyl)phenylacetic acid or a pharmacologically acceptable salt thereof or a hydrate thereof and a preservative, to obtain an aqueous liquid preparation consisting essentially of ~~at least~~ the following two components, the first component ~~comprising~~ being 2-amino-3-(4-bromobenzoyl)phenylacetic acid or a pharmacologically acceptable salt thereof or a hydrate thereof, and the second component ~~comprising being~~ tyloxapol or polyethylene glycol monostearate, together with a preservative, wherein said liquid preparation is formulated for ophthalmic administration.

63. (Cancelled)

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64. (New) An aqueous liquid preparation consisting essentially of:

(a) 2-amino-3-(4- bromobenzoyl)phenylacetic acid or a pharmacologically acceptable salt thereof or a hydrate thereof,

(b) tyloxapol,

(c) boric acid,

(d) sodium tetraborate,

(e) EDTA sodium salt,

(f) benzalkonium chloride,

(g) polyvinylpyrrolidone, and

(h) sodium sulfite, and wherein said liquid preparation is formulated for ophthalmic administration.

65. (New) The aqueous liquid preparation of claim 64, wherein (a) is a 2-amino-3-(4-bromobenzoyl)phenylacetic acid sodium salt.

66. (New) The aqueous liquid preparation of claim 65, wherein the concentration of the 2-amino-3-(4-bromobenzoyl)phenylacetic acid sodium salt is from about 0.01 to about 0.5 w/v % and the concentration of the tyloxapol is about 0.02 w/v %.

67. (New) The aqueous liquid preparation of claim 66, wherein the concentration of the 2-amino-3-(4-bromobenzoyl)phenylacetic acid sodium salt is about 0.01 w/v %.

68. (New) The aqueous liquid preparation of claim 66, wherein the concentration of the 2-amino-3-(4-bromobenzoyl)phenylacetic acid sodium salt is about 0.1 w/v %.

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REMARKS

Favorable reconsideration is respectfully solicited in view of the following remarks.

Initially, Applicant wishes to express its sincere thanks for the courtesy and cooperation provided to its representatives by Examiner Donna Jagoe during the personal interview held on February 16, 2010. The following is a summary of the items discussed during the interview.

Claims 19-40 have been cancelled without prejudice to the filing of a divisional application thereto.

Claims 41, 61 and 62 have been amended to make minor corrections as discussed during the interview.

Claims 42-45, 47-48, 51 and 54 have been amended in minor respects to reorganize the claimed subject matter and change the dependencies.

Claim 63 is cancelled without prejudice.

New claims 64-68 are added for additional patent protection and are supported in the specification at page 8, lines 19-26; page 12, lines 8-28, Table 1 on page 15; and Table 2 on page 17 of the specification. Note that sodium tetraborate is also known as borax, and EDTA sodium salt is also known as sodium edetate, which latter components are recited in Table 2.

Applicant acknowledges with thanks the Examiner's indication that the 103 rejection of claims 41 et al. are likely to be withdrawn in view of the arguments presented at the interview, which arguments are essentially reiterated hereinbelow.

Turning to the Official Action, claims 19-29, 31-34 and 36-38 are rejected under 35 U.S.C. 103 as obvious over Gamache et al. (WO 01/15677) in view of ISTA or Nolan et al.

This ground of rejection is deemed to be overcome by the cancellation of all rejected claims.

Claims 19-29, 31-34, 36-38, 41-51, 53-56, 58-60 and 63 are rejected under 35 USC 103 as being unpatentable over Hellberg et al. and Nolan et al. This ground of rejection is respectfully traversed as applied to the pending claims for the reasons explained during the interview.

The Examiner asserts that it would have been obvious to substitute the bifunctional ester compounds of Hellberg et al. having anti-inflammatory and anti-oxidant activity with bromfenac as disclosed in Nolan et al. because of "the art recognized equivalent activity of bromfenac as an

PAGE 8/19 * RCVD AT 3/24/2010 4:34:20 PM [Eastern Daylight Time] * SVR:USPTO-EFXRF-6/30 * DNIS:2738300 * CSID:202 721 8250 * DURATION (mm-ss):03-32

anti-inflammatory agent in topical usage." See Official Action date December 24, 2009 at page 4. Applicant respectfully disagrees that bromfenac is equivalent to the Hellberg bifunctional ester compounds having both anti-inflammatory and anti-oxidant activity.

The intended purpose of the invention disclosed in Hellberg et al. is to provide "[c]ompounds having anti-inflammatory ***and*** antioxidant activity." See Hellberg et al., Abstract (emphasis added); see also Hellberg at column 2, lines 13-18 ("***The present invention provides*** new compounds having potent anti-inflammatory ***and*** anti-oxidant activity.") (emphasis added). Indeed, Hellberg et al. explicitly state that the principle of operation of the anti-inflammatory and antixodixant compounds is to provide a two-pronged therapeutic approach not previously available in the art:

> The compounds of the present invention are capable of protecting against cellular damage by a wide range of insults. Since the compounds provide this protection by decreasing free radical or oxidative damage, reducing cyclooxygenase or lipoxygenase mediated inflammation, and improving site delivery, this therapy represents an improved two-pronged approach to cytoprotection.

See Hellberg et al. at Column 2, lines 57-63. Therefore, the intended purpose of the invention disclosed in Hellberg et al. is to provide compounds with not only anti-inflammatory activity, but also anti-oxidant activity for improved therapeutic functionality:

> The compounds also include an anti-oxidant component. As oxidative stress has been implicated in inflammatory responses, the presence of an anti-oxidant will further help treat the target tissue.

See Hellberg et al. at Column 2, lines 38-40.

Moreover, the compounds of Hellberg et al. are intended to offer advantages not provided by the mere administration of individual agents such as bromfenac. Such intended advantages include a uniform delivery of an active molecule, simplifying issues of drug metabolism, toxicity and delivery, as well as 5-lipooxygenase inhibitory activity not present in the individual agents.

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> The use of a single agent having both activities over a combination of two different agents provides uniform delivery of an active molecule, thereby simplifying issues of drug metabolism, toxicity and delivery.

See Hellberg et al. at Column 2, lines 7-10.

> Additionally, the compounds of the present invention exhibit 5-lipoxygenase inhibitory activity not present in the individual compounds.

See Hellberg et al. at Column 2, lines 16-18.

> The compounds of the present invention also exhibit properties present only in the combined molecule, ***not in the individual components***. One such property is the inhibitory efficacy against 5-lipoxygenase, an enzyme known to be involved in inflammation.

See Hellberg et al. at Column 2, lines 41-44 (emphasis added).

An additional intended advantage of the Hellberg bifunctional ester compounds is disclosed at Col. 2, lines 46 to 56:

> Another advantage of the present invention is that the anti-inflammatory moiety and the anit-oxidant moiety are linked through an ester bond. Since the carboxylic acid moiety of the NSAIA has been converted to an ester, the resultant molecule is neutrally charged, thus increasing lipohilicity and drug delivery.

Thus, the Hellberg bifunctional ester compounds are intended to increase lipophilicity and drug delivery relative to bromfenac alone.

The USPTO has made clear that "[i]f [the] proposed modification would render the prior art invention being modified unsatisfactory for its intended purpose, then there is no suggestion or motivation to make the proposed modification." See MPEP section 2143.01 V, citing *In re Gordon*, 733 F.2d 900 (Fed. Cir. 1984). Additionally, section 2143.01 VI of the MPEP plainly states: "The proposed modification cannot change the principle of operation of a reference. If the proposed modification or combination of the prior art would change the principle of

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operation of the prior art invention being modified, then the teachings of the references are not sufficient to render the claims *prima facie* obvious." See also *In re Ratti*, 270 F.2d 810, 123 USPQ 349 (CCPA 1959).

Here, the proposed substitution of the Hellberg bifunctional anti-inflammatory, anti-oxidant ester compounds with bromfenac would render the Hellberg et al. invention unsatisfactory for its intended purpose of providing "compounds having potent anti-inflammatory and anti-oxidant activity" with increased "lipophilicity and drug delivery" and "5-lipoxygenase inhibitory activity not present in the individual compounds." Applicant respectfully submits that this proposed modification would radically change the principle of operation of Hellberg et al. from "an improved two-pronged approach to cytoprotection" to a mere one-pronged approach based on anti-inflammatory action alone.

Therefore, because bromfenac is not equivalent to the Hellberg bifunctional ester compounds and because the proposed substitution would render the Hellberg et al. invention unsatisfactory for its intended purpose and radically change the principle of operation of Hellberg et al., Applicant respectfully submits a prima facie case of obviousness cannot be based on the combination of Hellberg et al. and Nolan et al.

In addition to the argument that the proposed modification changes the principle operation and intended purpose of Hellberg et al., Applicant submits that Hellberg et al. explicitly teach away from the use of a compound, such as bromfenac, having only anti-inflammatory activity. Hellberg et al. explicitly exclude the use of a single action non-steroidal anti-inflammatory agents such as bromfenac:

> Non-steroidal anti-inflammatory agents (NSAIA) have been used for the treatment of inflammatory disorders. The following references may be referred to for further background concerning this use of NSAIAs:
>
> Ophthalmoscope, volume 8, page 257 (1910);
>
> FASEB Journal, volume 1, page 89 (1987); and
>
> Inflammation and Mechanisms and Actions of Traditional Drugs, vol. I Anti-inflammatory and Anti-rheumatic drugs. Boca Raton, Fla., CRC Press, (1985).
>
> However, ***there are some problems associated with NSAIA treatment including delivery to the appropriate site of action and side effects*** (Goodman and Gilman's The Pharmacological

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> Basis of Therapeutics, pages 638-669, Pergman Press, NY (1990)).

See Hellberg et al. at Column 1, lines 28-37 (emphasis added).

See also U.S. Patent No. 5,886,030, a copy of which is enclosed, which states:

> Stinging and burning sensations, as well as general discomfort, are often associated with the topical ophthalmic application of certain types of ophthalmic agents. It is believed that such ocular discomfort is due to the presence of certain functional groups in these agents. Examples of such agents which product ocular discomfort include, but are not limited to, β-blockers such as betaxolol; prostaglandins and prostaglandin derivatives; muscarinics such as pilocarpine; a-adrenergics such as epinephrine, clonidine and apraclonidine; cholinergics such as carbochol; and nonsteroidal anti-inflammatory drugs ("NSAIDS") such as diclofenac and suprofen.

See U.S. Patent No. 5,886,030 at Column 1, lines 21-32.

According to the USTPO guidelines, "[i]t is improper to combine references where the references teach away from their combination." See MPEP § 2145, citing *In re Grasselli*, 713 F.2d 731, 743 (Fed. Cir. 1983); see also *McGinley v. Franklin Sports, Inc.*, 262 F.3d 1339, 1354 (Fed.Cir. 2001) ("It is well-established that references which "teach away cannot serve to create a prima facie case of obviousness.") (citations omitted).

Here, Hellberg et al. exclude the use of a single NSAIA's by disclosing that such compounds are associated with "problems" such as "side effects" and "delivery to the appropriate site of action." In light of this teaching away from the use of a non-steroidal anti-inflammatory agent (NSAIA), one skilled in the art would not substitute bromfenac, a known NSAIA, for the anti-inflammatory and anti-oxidant compounds disclosed in Hellberg et al. Therefore, because Hellberg et al. teach away from the use of bromfenac, Applicant respectfully submits a prima facie case of obviousness cannot be based on the combination of Hellberg et al. and Nolan et al.

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In addition, one skilled in the art would not have been motivated along the lines of the claimed invention by Hellberg et al. The claimed invention uses the second component as a cosolvent to assist in stabilizing the bromfenac. The second component of the claimed invention is an alkyl aryl polyether alcohol type polymer or a polyethylene glycol fatty acid ester, preferably tyloxapol.

Hellberg et al., however, fail to list tyloxapol as a cosolvent. See column 9, lines 1-5. Instead, Hellberg et al. use tyloxapol for an entirely different purpose. Whereas bromfenac is relatively soluble, the bifunctional ester compounds of Hellberg et al. are relatively lipophilic and insoluble. According to Example 3 bridging columns 11-12, the tyloxapol is apparently used as a milling diluent to grind the relatively insoluble bifunctional ester compound of Hellberg et al. to improve the solubility of the more lipophilic Hellberg ester compounds. In addition, the tyloxapol apparently helps to prevent the ground bifunctional ester compounds from aggregating into larger particles. Therefore the only apparent reason that tyloxapol is used in the compositions of Examples 2 and 3 of Hellberg et al. is as a grinding and anti-aggregation agent for the relatively lipophilic insoluble bifunctional ester compounds of Hellberg et al. Hence one skilled in the art, reading Hellberg et al., would not have been motivated to use tyloxapol in combination with bromfenac, because bromfenac does not suffer from the problems of lipophilicity and insolubility relative to the bifunctional ester compounds of Hellberg et al.

For the reasons detailed above, Applicant respectfully requests withdrawal of the rejection of claims 19-38, 41-60 and 63 under 35 USC 103 as being unpatentable over Hellberg et al. and Nolan et al.

Lastly, claims 19-38 are provisionally rejected on the ground of non-statutory obviousness-type double patenting as being unpatentable over claims 1-43 of copending application Serial No. 11/755,662.

It is believed that all other grounds of rejection have been overcome in view of the instant response. Accordingly, it is respectfully submitted that this provisional ground of rejection should be withdrawn and the application passed on to allowance.

In summary, it is believed that each ground of rejection set forth in the Official Action has been overcome, and that the application is now in condition for allowance. Accordingly such allowance is solicited.

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Rejoinder and allowance of the withdrawn method claims is also solicited.

Respectfully submitted,

Shirou SAWA et al.

By _____
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March 24, 2010

PAGE 14/19 * RCVD AT 3/24/2010 4:34:20 PM [Eastern Daylight Time] * SVR:USPTO-EFXRF-6/30 * DNIS:2738300 * CSID:202 721 8250 * DURATION (mm-ss):03-32

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/525,006	03/28/2005	Shirou Sawa	2005_0232A	1756

513 7590 03/02/2010

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EXAMINER	
JAGOE, DONNA A	

ART UNIT	PAPER NUMBER
1619	

NOTIFICATION DATE	DELIVERY MODE
03/02/2010	ELECTRONIC

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

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

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

ddalecki@wenderoth.com
eoa@wenderoth.com

Interview Summary	Application No.	Applicant(s)	
	10/525,006	SAWA ET AL.	
	Examiner	Art Unit	
	Donna Jagoe	1619	

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

(1) *Donna Jagoe*.

(2) *Jim Currie*.

(3)*Ken Jenkins and Warren Cheek*.

(4)*Martin Voet*.

Date of Interview: *16 February 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: *the claims in general*.

Identification of prior art discussed: *Hellberg et al. 5,998,465*.

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: *Applicant pointed out the difference between the prior art and the instant claims. There was a discussion regarding the Hellberg ester compounds drawn tyloxapol used for ball milling, not as a cosolvent* .

(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.

/Donna Jagoe/ Examiner, Art Unit 1619	/YVONNE L. EYLER/ Supervisory Patent Examiner, Art Unit 1619

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.
10/525,006	03/28/2005	Shirou Sawa	2005_0232A	1756

513 7590 12/24/2009

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EXAMINER	
JAGOE, DONNA A	
ART UNIT	PAPER NUMBER
1619	

MAIL DATE	DELIVERY MODE
12/24/2009	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)	
	10/525,006	SAWA ET AL.	
	Examiner	Art Unit	
	Donna Jagoe	1619	

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

Period for Reply

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

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

Status

1)☒ Responsive to communication(s) filed on *05 October 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) *19-29,31-34,36-51,53-56 and 58-63* is/are pending in the application.

4a) Of the above claim(s) *39,40,61 and 62* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *19-29,31-34,36-38,41-51,53-56,58-60 and 63* 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

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 October 5, 2009 has been entered.

Claims 19-29, 31-34, 36-51, 53-56 and 58-63 are pending in this application.

Claims 39, 40, 61 and 62 are withdrawn from further consideration.

Claims 19-29, 31-34, 36-38, 41-51, 53-56, 58-60 and 63 are rejected.

Priority

Receipt is acknowledged of the Japanese priority application and certified translation submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 19-29, 31-34, 36-38, 41-51, 53-56, 58-60 and 63 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hellberg et al. (US 5,998,465; 1999) and Nolan, et al. ("The topical anti-inflammatory and analgesic properties of bromfenac in rodents; Agents and Actions; 1988 Aug; 25(1-2):77-85; cited with previous Interview Summary).

Hellberg teaches pharmaceutical compositions of anti-inflammatory compounds (abstract); the compounds include a non-steroidal anti-inflammatory moiety (NSAIA) and an antioxidant moiety linked through an ester bond formed by the carboxylic acid moiety of the NSAIA (col. 2, lines 20-24); NSAIA moieties include bromfenac (col. 3, line 57; claim 5); examples 2 and 3 (col. 11) teach topical ophthalmic formulations useful for treating inflammation, both of these formulations include tyloxapol at 0.01-0.05 w/v %, HPMC (thickener), benzalkonium chloride (preservative), edetate disodium (chelating agent) (col. 11, Examples 2-3); the pH is adjusted to 7.4 (about 7.5; col. 11, line 64); topical formulations administered by drops (eye drops; col. 10, lines 15-18). Hellberg does not teach bromfenac (only the ester of bromfenac). Nolan teaches bromfenac (the sodium salt, sesquihydrate form) was effective as a topical analgesic at concentrations of 0.1-0.32 % in mice and more potent than the other drugs tested (abstract). It would have been obvious for one of ordinary skill in the art at the time of the invention to substitute bromfenac, taught by Nolan for the compounds of Hellberg in the example formulation giving formulations of the instant claims and to select concentrations of bromfenac sodium, sesquihydrate of 0.1, about 0.2 and about 0.32 %, in the invention of Gamache, since these values have demonstrated efficacy for topical use. It would

also have been obvious to adjust the concentration of tyloxapol, to optimize the formulations for the effect would on the solubility and stability of the aqueous preparations, which would have resulted in the effective tyloxapol concentrations of about 0.02 and 0.3 w/v%, recited in claims 25 and 32. The motivation to substitute bromfenac in the Hellberg formulations would have bee the art-recognized equivalent activity of bromfenac as an anti-inflammatory agent in topical usage. The motivation to adjust concentrations would have been the routine optimization of these topical ophthalmic formulations for anti-inflammatory use in the eye.

Claims 19-29, 31-34 and 36-38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gamache, et al. (WO 01/15677 A2; 03/2001; previously cited) and ISTA Pharmaceuticals ("New Drug Applications: Xibrom", http://www.drugs.com/nda/xibrom_040525.html, accessed online 9/19/2007; previously cited) or Nolan, et al. ("The topical anti-inflammatory and analgesic properties of bromfenac in rodents; Agents and Actions; 1988 Aug; 25(1-2):77-85; provided with Interview Summary).

Gamache teaches compositions for otic and intranasal use (p.6, lines 5-6) that contain a combination of a 5-HT agonist and an anti-inflammatory agent (p. 6, lines 1-4; p. 12 lines 9-10) or alternatively sequential or concurrent dosing of separate compositions that contain the 5-HT antagonist in one composition and the anti-inflammatory agent in a second composition (p. 12, lines 9-11); specifically claimed is the anti-inflammatory specie bromfenac (2-amino-3-(4-bromobenzoyl)phenylacetic

acid). Typical concentrations of anti-inflammatory agents, such as bromfenac, are taught in the range 0.01-1.0 % (w/v) (overlapping with 0.01-0.5; p. 13, lines 6-8); aqueous formulations are preferred (p. 10, lines 11-14); tyloxapol is taught in a concentration of 0.05 % (w/v) (p. 16, line 30). It is noted that instant claim 21 and further dependent claims limit the options for the salt of bromfenac to the sodium salt, and that the specific concentrations recited in dependent claims apply to the sodium salt; the other options (bromfenac or a hydrate of bromfenac) are still viable choices that are part of instant claim 21 claims depending therefrom (which depend on and include the options of claim 20). Gamache teaches bromfenac in the concentration range of claim 20 (which is also an option of claims 21-24 and 31). The salt form of bromfenac in solution will be the same when the acid is dissolved in a solution followed by adjustment to the desired pH with NaOH/HCl (Gamache, p. 15, line 33) as when the sodium salt is dissolved in solution adjusted to the same pH; in this case Gamache also teaches the sodium salt limitation of instant claim 21, albeit not the sodium salt concentration limitation of instant claim 22 and further dependent claims, since the claim is drawn to an aqueous liquid preparation, irrespective of how it is prepared. However, the concentration range of 0.01-1.0% overlaps and encompasses the claimed concentration range of the sodium salt of bromfenac instantly claimed.

The ISTA Pharmaceuticals news release demonstrates that products containing 0.1 % bromfenac sodium acquired US marketing rights for Xibrom in May 2002 (were known by others in this country before applicant's priority date, a 35 USC 102(a) date). Nolan teaches bromfenac (the sodium salt, sesquihydrate form) was effective as a

topical analgesic at concentrations of 0.1-0.32 % in mice and more potent than the other drugs tested (abstract). It would have been obvious for one of ordinary skill in the art at the time of the invention to select concentrations of bromfenac sodium, sesquihydrate of 0.1, about 0.2 and about 0.32 %, in the invention of Gamache, since these values have demonstrated efficacy for topical use. It would have been obvious to adjust the concentration of tyloxapol, to see what the effect would be on the solubility and stability of the aqueous preparations, which would have resulted in the effective concentrations of the instant claims. It would also have been obvious to adjust the pH to values in the 7.5 to 8.5 range, with the potential of dissolving and/or stabilizing more of the acidic drug, bromfenac, in a more aqueous soluble ionic form. The motivation would have been to prepare pharmaceutical products with optimal drug dosage and stability.

Double Patenting

Claims 19-29, 31-34, 36-38, 41-51, 53-56, 58-60 and 63 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-43 of copending Application No. 11/755662.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the copending application contains claims drawn to method of treating pain and/or inflammation associated with an ocular condition, by administering the aqueous solutions of the instant claims. It would have been obvious to one of ordinary skill in the art at the time of the invention to use the formulations of the instant claims in the methods of the copending application, since the claims recite that the

formulations are eye drops, and the instant abstract also teaches some of the conditions treated of the copending application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Donna Jagoe whose telephone number is (571) 272-0576. The examiner can normally be reached on Monday through Friday from 8:00 A.M. - 4:30 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne (Bonnie) Eyler can be reached on (571) 272-0871. 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.

/YVONNE L. EYLER/
Supervisory Patent Examiner, Art Unit 1619

Donna Jagoe /D. J./
Examiner
Art Unit 1619

December 17, 2009

UNITED STATES PATENT AND TRADEMARK OFFICE

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/525,006	03/28/2005	Shirou Sawa	2005_0232A	1756

513 7590 10/08/2009

WENDEROTH, LIND & PONACK, L.L.P.
1030 15th Street, N.W.,
Suite 400 East
Washington, DC 20005-1503

EXAMINER	
JAGOE, DONNA A	
ART UNIT	PAPER NUMBER
1614	

MAIL DATE	DELIVERY MODE
10/08/2009	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.

Interview Summary	Application No.	Applicant(s)	
	10/525,006	SAWA ET AL.	
	Examiner	Art Unit	
	Donna Jagoe	1614	

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

(1) *Donna Jagoe*. (3)_____.

(2) *Warren Cheek*. (4)_____.

Date of Interview: *07 October 2009*.

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: *exemplary claims 41 and 63*.

Identification of prior art discussed: *Hellberg et al., Nolan et al., Gamache et al.,*.

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: *Hellberg teaches any NSAIA including bromfenac covalently linked to an antioxidant. Applicant presented arguments that there is no motivation to replace the Hellberg compound with the Nolan compound.*.

(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.

/Donna Jagoe/ Examiner, Art Unit 1614	

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.

OIPE MAPS
OCT 05 2009
PATENT & TRADEMARK OFFICE

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of	:	Attorney Docket No. 2005_0232A
Shirou SAWA et al.	:	Confirmation No. 1756
Serial No. 10/525,006	:	Group Art Unit 1614
Filed March 28, 2005	:	Examiner Donna A. Jagoe
AQUEOUS LIQUID PREPARATION CONTAINING 2-AMINO-3-(4-BROMOBENZOYL)PHENYLACETIC ACID	:	**Mail Stop: RCE**

PRELIMINARY AMENDMENT

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

Sir:

Please amend the above-identified application as follows:

The Commissioner is authorized to charge any deficiency or to credit any overpayment associated with this communication to Deposit Account No. 23-0975, with the EXCEPTION of deficiencies in fees for multiple dependent claims in new applications.

Amendments to the Claims

1-18. (Cancelled)

19. (Currently amended) An aqueous liquid preparation comprising at least the following two components, the first component comprising 2-amino-3-(4-bromobenzoyl)phenylacetic acid or a pharmacologically acceptable salt thereof or a hydrate thereof, and the second component comprising an alkyl aryl polyether alcohol type polymer or a polyethylene glycol fatty acid ester, wherein said liquid preparation is formulated for ophthalmic administration~~in the form of an eye drop~~.

20. (Previously presented) The aqueous liquid preparation according to claim 19, wherein the alkyl aryl polyether alcohol type polymer is tyloxapol;

wherein the concentration of the tyloxapol is selected from a range of about 0.01 w/v % to about 0.5 w/v %; and

wherein the concentration of the 2-amino-3-(4-bromobenzoyl)phenylacetic acid or a pharmacologically acceptable salt thereof or a hydrate thereof is selected from a range of about 0.01 to about 0.5 w/v %.

21. (Previously presented) The aqueous liquid preparation according to claim 20, wherein the pharmacologically acceptable salt of 2-amino-3-(4-bromobenzoyl)phenylacetic acid is a sodium salt.

22. (Previously presented) The aqueous liquid preparation according to claim 21, wherein the concentration of the 2-amino-3-(4-bromobenzoyl)phenylacetic acid sodium salt is selected from a range of about 0.05 to about 0.2 w/v %.

23. (Previously presented) The aqueous liquid preparation according to claim 22, wherein the concentration of the tyloxapol is selected from a range of about 0.01 w/v % to about 0.3 w/v %.

24. (Previously presented) The aqueous liquid preparation according to claim 23, wherein the concentration of the 2-amino-3-(4-bromobenzoyl)phenylacetic acid sodium salt is about 0.1 w/v %.

25. (Previously presented) The aqueous liquid preparation according to claim 24, wherein the concentration of the tyloxapol is about 0.02 w/v %.

26. (Previously presented) The aqueous liquid preparation according to claim 25, wherein the formulation further includes one or more additives selected from the group consisting of a preservative, buffer, thickener, stabilizer, chelating agent, and pH controlling agent.

27. (Previously presented) The aqueous liquid preparation according to claim 26, wherein said preservative is benzalkonium chloride; wherein said buffer is boric acid and/or sodium borate; wherein said thickener is polyvinylpyrrolidone; wherein said stabilizer is sodium sulfite; wherein said chelating agent is sodium edetate; and wherein said pH controlling agent is sodium hydroxide.

28. (Previously presented) The aqueous liquid preparation according to claim 27, wherein the pH is from about 7 to about 9.

29. (Previously presented) The aqueous liquid preparation according to claim 28, wherein the pH is from about 7.5 to about 8.5.

30. (Cancelled)

31. (Previously presented) The aqueous liquid preparation according to claim 23, wherein the concentration of the 2-amino-3-(4-bromobenzoyl)phenylacetic acid sodium salt is about 0.2 w/v %.

32. (Previously presented) The aqueous liquid preparation according to claim 31, wherein the concentration of the tyloxapol is about 0.3 w/v %.

33. (Previously presented) The aqueous liquid preparation according to claim 32, wherein the formulation further includes one or more additives selected from the group consisting of a preservative, buffer, thickener, stabilizer, chelating agent, and pH controlling agent.

34. (Previously presented) The aqueous liquid preparation according to claim 33, wherein said preservative is benzalkonium chloride; wherein said buffer is boric acid and/or sodium borate; wherein said thickener is polyvinylpyrrolidone; wherein said stabilizer is sodium sulfite; wherein said chelating agent is sodium edetate; and wherein said pH controlling agent is sodium hydroxide.

35. (Cancelled)

36. (Previously presented) The aqueous liquid preparation according to claim 31, wherein the concentration of the tyloxapol is about 0.02 w/v %.

37. (Previously presented) The aqueous liquid preparation according to claim 36, wherein the formulation further includes one or more additives selected from the group consisting of a preservative, buffer, thickener, stabilizer, chelating agent, and pH controlling agent.

38. (Previously presented) The aqueous liquid preparation according to claim 37, wherein said preservative is benzalkonium chloride; wherein said buffer is boric acid and/or sodium borate; wherein said thickener is polyvinylpyrrolidone; wherein said chelating agent is sodium edetate; and wherein said pH controlling agent is sodium hydroxide.

39. (Withdrawn-currently amended) A method for stabilizing 2-amino-3-(4-bromobenzoyl)phenylacetic acid or a pharmacologically acceptable salt thereof or a hydrate

thereof in an aqueous liquid preparation, which comprises incorporating tyloxapol or polyethylene glycol monostearate into an aqueous liquid preparation containing 2-amino-3-(4-bromobenzoyl)phenylacetic acid or a pharmacologically acceptable salt thereof or a hydrate thereof, to obtain an aqueous liquid preparation comprising at least the following two components, the first component comprising 2-amino-3-(4-bromobenzoyl)phenylacetic acid or a pharmacologically acceptable salt thereof or a hydrate thereof, and the second component comprising tyloxapol or polyethylene glycol monostearate, wherein said liquid preparation is formulated for ophthalmic administration~~in the form of an eye drop~~.

40. (Withdrawn-currently amended) A method for inhibiting decrease in preservative effect of a preservative in an aqueous liquid preparation of 2-amino-3-(4-bromobenzoyl)phenylacetic acid or a pharmacologically acceptable salt thereof or a hydrate thereof, which comprises incorporating tyloxapol or polyethylene glycol monostearate into an aqueous liquid preparation containing 2-amino-3-(4-bromobenzoyl)phenylacetic acid or a pharmacologically acceptable salt thereof or a hydrate thereof and a preservative, to obtain an aqueous liquid preparation comprising at least the following two components, the first component comprising 2-amino-3-(4- bromobenzoyl)phenylacetic acid or a pharmacologically acceptable salt thereof or a hydrate thereof, and the second component comprising tyloxapol or polyethylene glycol monostearate, together with a preservative, wherein said liquid preparation is formulated for ophthalmic administration~~in the form of an eye drop~~.

41. (Currently amended) An aqueous liquid preparation consisting essentially of at least the following two components, wherein the first component comprising is 2-amino-3-(4-bromobenzoyl)phenylacetic acid or a pharmacologically acceptable salt thereof or a hydrate thereof, and the second component comprising is an alkyl aryl polyether alcohol type polymer or a polyethylene glycol fatty acid ester, wherein said liquid preparation is formulated for ophthalmic administration~~in the form of an eye drop~~.

42. (Previously presented) The aqueous liquid preparation according to claim 41, wherein the alkyl aryl polyether alcohol type polymer is tyloxapol;

wherein the concentration of the tyloxapol is selected from a range of about 0.01 w/v % to about 0.5 w/v %; and

wherein the concentration of the 2-amino-3-(4-bromobenzoyl)phenylacetic acid or a pharmacologically acceptable salt thereof or a hydrate thereof is selected from a range of about 0.01 to about 0.5 w/v %.

43. (Previously presented) The aqueous liquid preparation according to claim 42, wherein the pharmacologically acceptable salt of 2-amino-3-(4-bromobenzoyl)phenylacetic acid is a sodium salt.

44. (Previously presented) The aqueous liquid preparation according to claim 43, wherein the concentration of the 2-amino-3-(4-bromobenzoyl)phenylacetic acid sodium salt is selected from a range of about 0.05 to about 0.2 w/v %.

45. (Previously presented) The aqueous liquid preparation according to claim 44, wherein the concentration of the tyloxapol is selected from a range of about 0.01 w/v % to about 0.3 w/v %.

46. (Previously presented) The aqueous liquid preparation according to claim 45, wherein the concentration of the 2-amino-3-(4-bromobenzoyl)phenylacetic acid sodium salt is about 0.1 w/v %.

47. (Previously presented) The aqueous liquid preparation according to claim 46, wherein the concentration of the tyloxapol is about 0.02 w/v %.

48. (Previously presented) The aqueous liquid preparation according to claim 47, wherein the formulation further includes one or more additives selected from the group consisting of a preservative, buffer, thickener, stabilizer, chelating agent, and pH controlling agent.

49. (Previously presented) The aqueous liquid preparation according to claim 48, wherein said preservative is benzalkonium chloride; wherein said buffer is boric acid and/or sodium borate; wherein said thickener is polyvinylpyrrolidone; wherein said stabilizer is sodium sulfite; wherein said chelating agent is sodium edetate; and wherein said pH controlling agent is sodium hydroxide.

50. (Previously presented) The aqueous liquid preparation according to claim 49, wherein the pH is from about 7 to about 9.

51. (Previously presented) The aqueous liquid preparation according to claim 50, wherein the pH is from about 7.5 to about 8.5.

52. (Cancelled)

53. (Previously presented) The aqueous liquid preparation according to claim 45, wherein the concentration of the 2-amino-3-(4-bromobenzoyl)phenylacetic acid sodium salt is about 0.2 w/v %.

54. (Previously presented) The aqueous liquid preparation according to claim 53, wherein the concentration of the tyloxapol is about 0.3 w/v %.

55. (Previously presented) The aqueous liquid preparation according to claim 54, wherein the formulation further includes one or more additives selected from the group consisting of a preservative, buffer, thickener, stabilizer, chelating agent, and pH controlling agent.

56. (Previously presented) The aqueous liquid preparation according to claim 55, wherein said preservative is benzalkonium chloride; wherein said buffer is boric acid and/or sodium borate; wherein said thickener is polyvinylpyrrolidone; wherein said stabilizer is sodium sulfite; wherein said chelating agent is sodium edetate; and wherein said pH controlling agent is sodium hydroxide.

57. (Cancelled)

58. (Previously presented) The aqueous liquid preparation according to claim 53, wherein the concentration of the tyloxapol is about 0.02 w/v %.

59. (Previously presented) The aqueous liquid preparation according to claim 58, wherein the formulation further includes one or more additives selected from the group consisting of a preservative, buffer, thickener, stabilizer, chelating agent, and pH controlling agent.

60. (Previously presented) The aqueous liquid preparation according to claim 59, wherein said preservative is benzalkonium chloride; wherein said buffer is boric acid and/or sodium borate; wherein said thickener is polyvinylpyrrolidone; wherein said chelating agent is sodium edetate; and wherein said pH controlling agent is sodium hydroxide.

61. (Withdrawn-currently amended) A method for stabilizing 2-amino-3-(4-bromobenzoyl)phenylacetic acid or a pharmacologically acceptable salt thereof or a hydrate thereof in an aqueous liquid preparation, which comprises incorporating tyloxapol or polyethylene glycol monostearate into an aqueous liquid preparation containing 2-amino-3-(4-bromobenzoyl)phenylacetic acid or a pharmacologically acceptable salt thereof or a hydrate thereof, to obtain an aqueous liquid preparation consisting essentially of at least the following two components, the first component comprising 2-amino-3-(4-bromobenzoyl)phenylacetic acid or a pharmacologically acceptable salt thereof or a hydrate thereof, and the second component comprising tyloxapol or polyethylene glycol monostearate, wherein said liquid preparation is formulated for ophthalmic administration~~in the form of an eye drop~~.

62. (Currently amended) A method for inhibiting decrease in preservative effect of a preservative in an aqueous liquid preparation of 2-amino-3-(4-bromobenzoyl)phenylacetic acid or a pharmacologically acceptable salt thereof or a hydrate thereof, which comprises incorporating tyloxapol or polyethylene glycol monostearate into an aqueous liquid preparation

containing 2-amino-3-(4-bromobenzoyl)phenylacetic acid or a pharmacologically acceptable salt thereof or a hydrate thereof and a preservative, to obtain an aqueous liquid preparation consisting essentially of at least the following two components, the first component comprising 2-amino-3-(4-bromobenzoyl)phenylacetic acid or a pharmacologically acceptable salt thereof or a hydrate thereof, and the second component comprising tyloxapol or polyethylene glycol monostearate, together with a preservative, wherein said liquid preparation is formulated for ophthalmic administration~~in the form of an eye drop~~.

63. (Currently amended) An aqueous liquid preparation consisting of the following two components, the first component comprising is 2-amino-3-(4-bromobenzoyl)phenylacetic acid or a pharmacologically acceptable salt thereof or a hydrate thereof, and the second component comprising is an alkyl aryl polyether alcohol type polymer or a polyethylene glycol fatty acid ester, and water, and optionally at least one preservative, isotonic, buffer, thickener, stabilizer, chelating agent, pH controlling agent, or perfume, wherein said liquid preparation is formulated for ophthalmic administration~~in the form of an eye drop~~.

REMARKS

A verified English translation of the Japanese priority application is concurrently submitted herewith under separate cover letter.

In addition, claims 19, 39-41, 61-63 have been amended as suggested by the Examiner in the Official Action dated June 3, 2009.

Accordingly, the rejection of the claims under 35 USC 112, second paragraph, is deemed to be overcome.

Applicants express their appreciation to the Examiner for the personal interview scheduled for October 7, 2009.

Respectfully submitted,

Shirou SAWA et al.

By _____
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Attorney for Applicants

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October 5, 2009

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/525,006	03/28/2005	Shirou Sawa	2005_0232A	1756

513 7590 06/03/2009

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EXAMINER	
JAGOE, DONNA A	
ART UNIT	PAPER NUMBER
1614	

MAIL DATE	DELIVERY MODE
06/03/2009	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)	
	10/525,006	SAWA ET AL.	
	Examiner	Art Unit	
	Donna Jagoe	1614	

-- 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 January 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) *19-29,31-34,36-51,53-56 and 58-63* is/are pending in the application.

4a) Of the above claim(s) *39,40,61 and 62* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *19-29,31-34,36-38,41-51,53-56,58-60 and 63* 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 *3/11/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 19-29, 31-34, 36-51, 53-56 and 58-63 are pending in this application.

Claims 39, 40, 61 and 62 are withdrawn from further consideration.

Claims 19-29, 31-34, 36-38, 41-51, 53-56, 58-60 and 63 are rejected.

Applicants' arguments filed January 15, 2009 have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Change of Examiner

The examiner assigned to the instant application has changed. The new examiner is Donna Jagoe. Contact information is provided at the end of this Office Action.

Priority

As recited in the Office Action dated September 27, 2007, Applicant is reminded that a certified translation has not been proved for the claim to foreign priority of JP2003-012427, filed 1/21/2003. Since no translation has been provided, prior art

dates have been determined with reference to the priority date for the PCT application date, PCT/JP04/00350, filed 1/16/2004.

Claim Rejections - 35 USC § 112

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

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 19-29, 31-34, 36-38, 41-51, 53-56, 58-60 and 63, are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 19 and 41 recite an aqueous liquid preparation comprising at least 2-amino-3-(4-bromobenzoyl)phenylacetic acid (bromfenac) and an alkyl aryl polyether alcohol type polymer or polyethylene glycol fatty acid ester “wherein said liquid preparation is in the form of an eye drop”. It is unclear what is meant by “in the form of an eye drop. Is this aqueous liquid preparation in a container shaped like an eye drop? It is suggested that the claim be amended to recite "wherein said liquid preparation is formulated for ophthalmic administration".

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 19-29, 31-34, 36-38, 41-51, 53-56, 58-60 and 63 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hellberg et al. (US 5,998,465; 1999) and

Nolan, et al. ("The topical anti-inflammatory and analgesic properties of bromfenac in rodents; Agents and Actions; 1988 Aug; 25(1-2):77-85; cited with previous Interview Summary).

Hellberg teaches pharmaceutical compositions of anti-inflammatory compounds (abstract); the compounds include a non-steroidal anti-inflammatory moiety (NSAIA) and an antioxidant moiety linked through an ester bond formed by the carboxylic acid moiety of the NSAIA (col. 2, lines 20-24); NSAIA moieties include bromfenac (col. 3, line 57; claim 5); examples 2 and 3 (col. 11) teach topical ophthalmic formulations useful for treating inflammation, both of these formulations include tyloxapol at 0.01-0.05 w/v %, HPMC (thickener), benzalkonium chloride (preservative), edetate disodium (chelating agent) (col. 11, Examples 2-3); the pH is adjusted to 7.4 (about 7.5; col. 11, line 64); topical formulations administered by drops (eye drops; col. 10, lines 15-18). Hellberg does not teach bromfenac (only the ester of bromfenac). Nolan teaches bromfenac (the sodium salt, sesquihydrate form) was effective as a topical analgesic at concentrations of 0.1-0.32 % in mice and more potent than the other drugs tested (abstract). It would have been obvious for one of ordinary skill in the art at the time of the invention to substitute bromfenac, taught by Nolan for the compounds of Hellberg in the example formulation giving formulations of the instant claims and to select concentrations of bromfenac sodium, sesquihydrate of 0.1, about 0.2 and about 0.32 %, in the invention of Gamache, since these values have demonstrated efficacy for topical use. It would also have been obvious to adjust the concentration of tyloxapol, to optimize the formulations for the effect would on the solubility and stability of the aqueous

preparations, which would have resulted in the effective tyloxapol concentrations of about 0.02 and 0.3 w/v%, recited in claims 25 and 32. The motivation to substitute bromfenac in the Hellberg formulations would have bee the art-recognized equivalent activity of bromfenac as an anti-inflammatory agent in topical usage. The motivation to adjust concentrations would have been the routine optimization of these topical ophthalmic formulations for anti-inflammatory use in the eye.

Claims 19-29, 31-34 and 36-38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gamache, et al. (WO 01/15677 A2; 03/2001; previously cited) and ISTA Pharmaceuticals ("New Drug Applications: Xibrom", http://www.drugs.com/nda/xibrom_040525.html, accessed online 9/19/2007; previously cited) or Nolan, et al. ("The topical anti-inflammatory and analgesic properties of bromfenac in rodents; Agents and Actions; 1988 Aug; 25(1-2):77-85; provided with Interview Summary).

Gamache teaches compositions for otic and intranasal use (p.6, lines 5-6) that contain a combination of a 5-HT agonist and an anti-inflammatory agent (p. 6, lines 1-4; p. 12 lines 9-10) or alternatively sequential or concurrent dosing of separate compositions that contain the 5-HT antagonist in one composition and the anti-inflammatory agent in a second composition (p. 12, lines 9-11); specifically claimed is the anti-inflammatory specie bromfenac (2-amino-3-(4-bromobenzoyl)phenylacetic acid). Typical concentrations of anti-inflammatory agents, such as bromfenac, are taught in the range 0.01-1.0 % (w/v) (overlapping with 0.01-0.5; p. 13, lines 6-8);

aqueous formulations are preferred (p. 10, lines 11-14); tyloxapol is taught in a concentration of 0.05 % (w/v) (p. 16, line 30). It is noted that instant claim 21 and further dependent claims limit the options for the salt of bromfenac to the sodium salt, and that the specific concentrations recited in dependent claims apply to the sodium salt; the other options (bromfenac or a hydrate of bromfenac) are still viable choices that are part of instant claim 21 claims depending therefrom (which depend on and include the options of claim 20). Gamache teaches bromfenac in the concentration range of claim 20 (which is also an option of claims 21-24 and 31). The salt form of bromfenac in solution will be the same when the acid is dissolved in a solution followed by adjustment to the desired pH with NaOH/HCl (Gamache, p. 15, line 33) as when the sodium salt is dissolved in solution adjusted to the same pH; in this case Gamache also teaches the sodium salt limitation of instant claim 21, albeit not the sodium salt concentration limitation of instant claim 22 and further dependent claims, since the claim is drawn to an aqueous liquid preparation, irrespective of how it is prepared. However, the concentration range of 0.01-1.0% overlaps and encompasses the claimed concentration range of the sodium salt of bromfenac instantly claimed.

The ISTA Pharmaceuticals news release demonstrates that products containing 0.1 % bromfenac sodium acquired US marketing rights for Xibrom in May 2002 (were known by others in this country before applicant's priority date, a 35 USC 102(a) date). Nolan teaches bromfenac (the sodium salt, sesquihydrate form) was effective as a topical analgesic at concentrations of 0.1-0.32 % in mice and more potent than the other drugs tested (abstract). It would have been obvious for one of ordinary skill in the art at

the time of the invention to select concentrations of bromfenac sodium, sesquihydrate of 0.1, about 0.2 and about 0.32 %, in the invention of Gamache, since these values have demonstrated efficacy for topical use. It would have been obvious to adjust the concentration of tyloxapol, to see what the effect would be on the solubility and stability of the aqueous preparations, which would have resulted in the effective concentrations of the instant claims. It would also have been obvious to adjust the pH to values in the 7.5 to 8.5 range, with the potential of dissolving and/or stabilizing more of the acidic drug, bromfenac, in a more aqueous soluble ionic form. The motivation would have been to prepare pharmaceutical products with optimal drug dosage and stability.

Double Patenting

Claims 19-29, 31-34, 36-38, 41-51, 53-56, 58-60 and 63 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-43 of copending Application No. 11/755662.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the copending application contains claims drawn to method of treating pain and/or inflammation associated with an ocular condition, by administering the aqueous solutions of the instant claims. It would have been obvious to one of ordinary skill in the art at the time of the invention to use the formulations of the instant claims in the methods of the copending application, since the claims recite that the

formulations are eye drops, and the instant abstract also teaches some of the conditions treated of the copending application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Response to Arguments

Applicant asserts that Gamache et al. in view of ISTA or Nolan et al. does not teach the claimed invention because the amended claims require that the aqueous liquid preparation is in the form of an eye drop. In response, please see the rejection supra regarding claims drawn to the composition "in the form of an eye drop". Further, Gamache teaches the composition to be employed intranasally and intraotically. There is nothing differentiating the composition of the instant claims from the composition of Gamache other than the claim that it is "in the form of an eye drop". Drops that are formulated for intranasal use and otic use are sterile and isotonic. The intended use must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. Since the drops of Gamache are capable of performing the intended use, then it meets the claim. Regarding the inclusion of other agents in the drops of Gamache, The claim language *comprising* leaves the claim open for the inclusion of unspecified ingredients, even in major amounts. Applicant asserts that the tyloxapol is only mentioned as being added to an 1B/1D agonist and moxifloxacin in example 4 with no explanation of why it is

included. In response, a reference is not limited to working examples. *In re Fracalossi* 215 USPQ 569 (CCPA 1982). Applicant asserts that Gamache et la. Is silent regarding the alkyl aryl polyether alcohol type polymer or a polyethylene glycol fatty acid ester component according to the claimed eye drop. In response, Gamache et al. teach polysorbate 20, 60, and 80 as a surfactant or co-solvent (see page 12).

Applicant asserts that the intended purpose of the invention disclosed in Hellberg et al. is to provide compounds having anti-inflammatory activity and antioxidant activity and further asserts it would not be obvious to substitute bromfenac. In response, bromfenac is clearly disclosed as a compound that is contemplated for use in the invention of Hellberg et al. (see claims 5 and 19 of the patent). "Products of identical chemical composition (i.e. bromfenac) can not have mutually exclusive properties." A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims (i.e. anti inflammatory and antioxidant activity) are necessarily present. In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990) (Applicant argued that the claimed composition was a pressure sensitive adhesive containing a tacky polymer while the product of the reference was hard and abrasion resistant. "The Board correctly found that the virtual identity of monomers and procedures sufficed to support a prima facie case of unpatentability of Spada's polymer latexes for lack of novelty.").

In response to applicant's argument that Hellberg et al. is nonanalogous art, it has been held that a prior art reference must either be in the field of applicant's endeavor or, if not, then be reasonably pertinent to the particular problem with which the

applicant was concerned, in order to be relied upon as a basis for rejection of the claimed invention. See *In re Oetiker*, 977 F.2d 1443, 24 USPQ2d 1443 (Fed. Cir. 1992). In this case, Hellberg et al. teach a composition for intraocular administration comprising inter alia, a compound (bromfenac) and tyloxapol (see examples).

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.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Donna Jagoe whose telephone number is (571) 272-

0576. The examiner can normally be reached on Monday through Friday from 8:00 A.M. - 4:30 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on (571) 272-0718. 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.

Donna Jagoe /D. J./
Examiner
Art Unit 1614

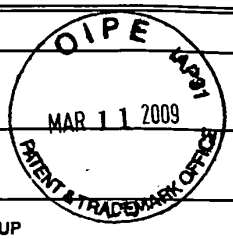
May 30, 2009

/Ardin Marschel/
Supervisory Patent Examiner, Art Unit 1614

March 11, 2009

Sheet 1 of 1

INFORMATION DISCLOSURE STATEMENT



FORM PTO 1449 (*modified*)

U.S. DEPARTMENT OF COMMERCE
PATENT AND TRADEMARK OFFICE

LIST OF REFERENCES CITED BY APPLICANT(S)
(*Use several sheets if necessary*)

Date Submitted to PTO: March 11, 2009

ATTY DOCKET NO.	SERIAL NO.
2005_0232A	10/525,006

APPLICANT
Shirou SAWA et al.

FILING DATE	GROUP
March 28, 2005	1614

U.S. PATENT DOCUMENTS

*EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE
	AA	5,597,560	1/1997	Bergamini et al.			
	AB						
	AC						
	AD						
	AE						
	AF						
	AG						
	AH						
	AI						

FOREIGN PATENT DOCUMENTS

		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION YES	TRANSLATION NO
	BA	01/15677	3/2001	WO				
	BB	2 013 188	9/1990	CA				
	BC	02/13804	2/2002	WO				
	BD	707 119	9/1995	AU				
	BE							

OTHER DOCUMENT(S) (*Including Author, Title, Date, Pertinent Pages, Etc.*)

	CA	Notice of Opposition dated February 19, 2009 issued by EPO in connection with the corresponding European patent application and Opposition.
	CB	
	CC	

EXAMINER	/Donna Jagoe/ (05/30/2009)	DATE CONSIDERED	

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

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /D.J./ (05/30/2009)

OIPE
MAR 11 2009
PATENT & TRADEMARK OFFICE

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of	:	**Confirmation No. 1756**
Shirou SAWA et al.	:	Attorney Docket No. 2005_0232A
Serial No. 10/525,006	:	Group Art Unit 1614
Filed March 28, 2005	:	Examiner Timothy P. Thomas

AQUEOUS LIQUID PREPARATION CONTAINING 2-AMINO-3-(4-BROMOBENZOYL)PHENYLACETIC ACID

Mail Stop: Amendment

INFORMATION DISCLOSURE STATEMENT

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

Sir:

Pursuant to the provisions of 37 CFR 1.56, 1.97 and 1.98, Applicants request consideration of the references listed on attached form PTO-1449 and any additional information identified below in paragraph 3. A legible copy of each reference listed on the Form PTO-1449 is enclosed, except a copy is not provided for:

[X] each U.S. Patent and U.S. Patent application publication;

[] each reference previously cited in prior parent application Serial No. _____.

1a. [] This Information Disclosure Statement is submitted:

within three months of the filing date (or of entry into the National Stage) of the above-entitled application, **or**

before the mailing of a first Office Action on the merits or the mailing of a first Office Action after the filing of an RCE,

and thus no certification and/or fee is required.

1b. [X] This Information Disclosure Statement is submitted

after the events of above paragraph 1a and prior to the mailing date of a final Office Action or a Notice of Allowance or an action which otherwise closes prosecution in the application, and thus:

(1) [X] the certification of paragraph 2 below is provided, **or**

(2) [] the fee of $180.00 specified in 37 CFR 1.17(p) is enclosed.

1c. [] This Information Disclosure Statement is submitted:

after the mailing date of a final Office Action or Notice of Allowance or action which otherwise closes prosecution in the application, and prior to payment of the issue fee, and thus:

the certification of paragraph 2 below is provided, and

the fee of $180.00 specified in 37 CFR 1.17(p) is enclosed.

2. It is hereby certified

a. [X] that each item of information contained in this Information Disclosure Statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of the Statement, or

b. [] that no item of information contained in the Information Disclosure Statement was cited in a communication from a foreign patent office in a counterpart foreign application and, to the knowledge of the person signing the certification after making reasonable inquiry, was known to any individual designated in §1.56(c) more than three months prior to the filing of the Statement.

3. [] Consideration of the following list of additional information (including any copending or abandoned U.S. application, prior uses and/or sales, etc.) is requested.

4. For each non-English language reference listed on the attached form PTO-1449, reference is made to:

   a. [] a full or partial English language translation submitted herewith,

   b. [] a foreign patent office search report (in the English language) submitted herewith,

   c. [] the concise explanation contained in the specification of the present application at page,

   d. [] the concise explanation set forth in the attached English language abstract,

   e. [] the concise explanation set forth below or on a separate sheet attached to the reference:

5. [X] A Notice of Opposition citing one or more of the references is enclosed. References D1 and D7 of the Notice of Opposition are not cited because they are already of record.

6. [] Statement Under 37 CFR 1.704(d)

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

The Commissioner is authorized to charge any deficiency or to credit any overpayment associated with this communication to Deposit Account No. 23-0975, with the EXCEPTION of deficiencies in fees for multiple dependent claims in new applications.

Respectfully submitted,

Shirou SAWA et al.

By _____
Warren M. Cheek
Registration No. 33,367
Attorney for Applicants

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March 11, 2009

Sheet 1 of 1

INFORMATION DISCLOSURE STATEMENT

FORM PTO 1449 (*modified*)

U.S. DEPARTMENT OF COMMERCE
PATENT AND TRADEMARK OFFICE

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(*Use several sheets if necessary*)

Date Submitted to PTO: March 11, 2009

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APPLICANT: Shirou SAWA et al.

FILING DATE	GROUP
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OIPE MAR 11 2009 PATENT & TRADEMARK OFFICE

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EXAMINER	DATE CONSIDERED

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

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of	:	**Confirmation No. 1756**
Shirou SAWA et al.	:	Attorney Docket No. 2005_0232A
Serial No. 10/525,006	:	Group Art Unit 1614
Filed March 28, 2005	:	Examiner Timothy P. Thomas
AQUEOUS LIQUID PREPARATION CONTAINING 2-AMINO-3-(4-BROMOBENZOYL)PHENYLACETIC ACID	:	**Mail Stop: Amendment**

AMENDMENT

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

Sir:

Responsive to the Official Action dated July 18, 2007, the time for responding thereto being extended for three months in accordance with a petition for extension submitted concurrently herewith, please amend the above-identified application as follows:

Amendments to the Claims

1-18. (Cancelled)

19. (Currently amended) An aqueous liquid preparation comprising at least the following two components, the first component comprising 2-amino-3-(4-bromobenzoyl)phenylacetic acid or a pharmacologically acceptable salt thereof or a hydrate thereof, and the second component comprising an alkyl aryl polyether alcohol type polymer or a polyethylene glycol fatty acid ester, wherein said liquid preparation is in the form of an eye drop.

20. (Previously presented) The aqueous liquid preparation according to claim 19, wherein the alkyl aryl polyether alcohol type polymer is tyloxapol;

wherein the concentration of the tyloxapol is selected from a range of about 0.01 w/v % to about 0.5 w/v %; and

wherein the concentration of the 2-amino-3-(4-bromobenzoyl)phenylacetic acid or a pharmacologically acceptable salt thereof or a hydrate thereof is selected from a range of about 0.01 to about 0.5 w/v %.

21. (Previously presented) The aqueous liquid preparation according to claim 20, wherein the pharmacologically acceptable salt of 2-amino-3-(4-bromobenzoyl)phenylacetic acid is a sodium salt.

22. (Previously presented) The aqueous liquid preparation according to claim 21, wherein the concentration of the 2-amino-3-(4-bromobenzoyl)phenylacetic acid sodium salt is selected from a range of about 0.05 to about 0.2 w/v %.

23. (Previously presented) The aqueous liquid preparation according to claim 22, wherein the concentration of the tyloxapol is selected from a range of about 0.01 w/v % to about 0.3 w/v %.

24. (Previously presented) The aqueous liquid preparation according to claim 23, wherein the concentration of the 2-amino-3-(4-bromobenzoyl)phenylacetic acid sodium salt is about 0.1 w/v %.

25. (Previously presented) The aqueous liquid preparation according to claim 24, wherein the concentration of the tyloxapol is about 0.02 w/v %.

26. (Previously presented) The aqueous liquid preparation according to claim 25, wherein the formulation further includes one or more additives selected from the group consisting of a preservative, buffer, thickener, stabilizer, chelating agent, and pH controlling agent.

27. (Previously presented) The aqueous liquid preparation according to claim 26, wherein said preservative is benzalkonium chloride; wherein said buffer is boric acid and/or sodium borate; wherein said thickener is polyvinylpyrrolidone; wherein said stabilizer is sodium sulfite; wherein said chelating agent is sodium edetate; and wherein said pH controlling agent is sodium hydroxide.

28. (Previously presented) The aqueous liquid preparation according to claim 27, wherein the pH is from about 7 to about 9.

29. (Previously presented) The aqueous liquid preparation according to claim 28, wherein the pH is from about 7.5 to about 8.5.

30. (Cancelled)

31. (Previously presented) The aqueous liquid preparation according to claim 23, wherein the concentration of the 2-amino-3-(4-bromobenzoyl)phenylacetic acid sodium salt is about 0.2 w/v %.

32. (Previously presented) The aqueous liquid preparation according to claim 31, wherein the concentration of the tyloxapol is about 0.3 w/v %.

33. (Previously presented) The aqueous liquid preparation according to claim 32, wherein the formulation further includes one or more additives selected from the group consisting of a preservative, buffer, thickener, stabilizer, chelating agent, and pH controlling agent.

34. (Previously presented) The aqueous liquid preparation according to claim 33, wherein said preservative is benzalkonium chloride; wherein said buffer is boric acid and/or sodium borate; wherein said thickener is polyvinylpyrrolidone; wherein said stabilizer is sodium sulfite; wherein said chelating agent is sodium edetate; and wherein said pH controlling agent is sodium hydroxide.

35. (Cancelled)

36. (Previously presented) The aqueous liquid preparation according to claim 31, wherein the concentration of the tyloxapol is about 0.02 w/v %.

37. (Previously presented) The aqueous liquid preparation according to claim 36, wherein the formulation further includes one or more additives selected from the group

consisting of a preservative, buffer, thickener, stabilizer, chelating agent, and pH controlling agent.

38. (Previously presented) The aqueous liquid preparation according to claim 37, wherein said preservative is benzalkonium chloride; wherein said buffer is boric acid and/or sodium borate; wherein said thickener is polyvinylpyrrolidone; wherein said chelating agent is sodium edetate; and wherein said pH controlling agent is sodium hydroxide.

39. (Withdrawn-currently amended) A method for stabilizing 2-amino-3-(4-bromobenzoyl)phenylacetic acid or a pharmacologically acceptable salt thereof or a hydrate thereof in an aqueous liquid preparation, which comprises incorporating tyloxapol or polyethylene glycol monostearate into an aqueous liquid preparation containing 2-amino-3-(4-bromobenzoyl)phenylacetic acid or a pharmacologically acceptable salt thereof or a hydrate thereof, to obtain an aqueous liquid preparation comprising at least the following two components, the first component comprising 2-amino-3-(4- bromobenzoyl)phenylacetic acid or a pharmacologically acceptable salt thereof or a hydrate thereof, and the second component comprising tyloxapol or polyethylene glycol monostearate, wherein said liquid preparation is in the form of an eye drop.

40. (Withdrawn-currently amended) A method for inhibiting decrease in preservative effect of a preservative in an aqueous liquid preparation of 2-amino-3-(4-bromobenzoyl)phenylacetic acid or a pharmacologically acceptable salt thereof or a hydrate thereof, which comprises incorporating tyloxapol or polyethylene glycol monostearate into an aqueous liquid preparation containing 2-amino-3-(4-bromobenzoyl)phenylacetic acid or a pharmacologically acceptable salt thereof or a hydrate thereof and a preservative, to obtain an aqueous liquid preparation comprising at least the following two components, the first component comprising 2-amino-3-(4- bromobenzoyl)phenylacetic acid or a pharmacologically acceptable salt thereof or a hydrate thereof, and the second component comprising tyloxapol or

polyethylene glycol monostearate, together with a preservative, wherein said liquid preparation is in the form of an eye drop.

41. (Currently amended) An aqueous liquid preparation consisting essentially of ~~at least~~ the following two components, wherein the first component ~~comprising~~ is 2-amino-3-(4-bromobenzoyl)phenylacetic acid or a pharmacologically acceptable salt thereof or a hydrate thereof, and the second component ~~comprising~~ is an alkyl aryl polyether alcohol type polymer or a polyethylene glycol fatty acid ester, wherein said liquid preparation is in the form of an eye drop.

42. (Previously presented) The aqueous liquid preparation according to claim 41, wherein the alkyl aryl polyether alcohol type polymer is tyloxapol;

wherein the concentration of the tyloxapol is selected from a range of about 0.01 w/v % to about 0.5 w/v %; and

wherein the concentration of the 2-amino-3-(4-bromobenzoyl)phenylacetic acid or a pharmacologically acceptable salt thereof or a hydrate thereof is selected from a range of about 0.01 to about 0.5 w/v %.

43. (Previously presented) The aqueous liquid preparation according to claim 42, wherein the pharmacologically acceptable salt of 2-amino-3-(4-bromobenzoyl)phenylacetic acid is a sodium salt.

44. (Previously presented) The aqueous liquid preparation according to claim 43, wherein the concentration of the 2-amino-3-(4-bromobenzoyl)phenylacetic acid sodium salt is selected from a range of about 0.05 to about 0.2 w/v %.

45. (Previously presented) The aqueous liquid preparation according to claim 44, wherein the concentration of the tyloxapol is selected from a range of about 0.01 w/v % to about 0.3 w/v %.

46. (Previously presented) The aqueous liquid preparation according to claim 45, wherein the concentration of the 2-amino-3-(4-bromobenzoyl)phenylacetic acid sodium salt is about 0.1 w/v %.

47. (Previously presented) The aqueous liquid preparation according to claim 46, wherein the concentration of the tyloxapol is about 0.02 w/v %.

48. (Previously presented) The aqueous liquid preparation according to claim 47, wherein the formulation further includes one or more additives selected from the group consisting of a preservative, buffer, thickener, stabilizer, chelating agent, and pH controlling agent.

49. (Previously presented) The aqueous liquid preparation according to claim 48, wherein said preservative is benzalkonium chloride; wherein said buffer is boric acid and/or sodium borate; wherein said thickener is polyvinylpyrrolidone; wherein said stabilizer is sodium sulfite; wherein said chelating agent is sodium edetate; and wherein said pH controlling agent is sodium hydroxide.

50. (Previously presented) The aqueous liquid preparation according to claim 49, wherein the pH is from about 7 to about 9.

51. (Previously presented) The aqueous liquid preparation according to claim 50, wherein the pH is from about 7.5 to about 8.5.

52. (Cancelled)

53. (Previously presented) The aqueous liquid preparation according to claim 45, wherein the concentration of the 2-amino-3-(4-bromobenzoyl)phenylacetic acid sodium salt is about 0.2 w/v %.

54. (Previously presented) The aqueous liquid preparation according to claim 53, wherein the concentration of the tyloxapol is about 0.3 w/v %.

55. (Previously presented) The aqueous liquid preparation according to claim 54, wherein the formulation further includes one or more additives selected from the group consisting of a preservative, buffer, thickener, stabilizer, chelating agent, and pH controlling agent.

56. (Previously presented) The aqueous liquid preparation according to claim 55, wherein said preservative is benzalkonium chloride; wherein said buffer is boric acid and/or sodium borate; wherein said thickener is polyvinylpyrrolidone; wherein said stabilizer is sodium sulfite; wherein said chelating agent is sodium edetate; and wherein said pH controlling agent is sodium hydroxide.

57. (Cancelled)

58. (Previously presented) The aqueous liquid preparation according to claim 53, wherein the concentration of the tyloxapol is about 0.02 w/v %.

59. (Previously presented) The aqueous liquid preparation according to claim 58, wherein the formulation further includes one or more additives selected from the group

consisting of a preservative, buffer, thickener, stabilizer, chelating agent, and pH controlling agent.

60. (Previously presented) The aqueous liquid preparation according to claim 59, wherein said preservative is benzalkonium chloride; wherein said buffer is boric acid and/or sodium borate; wherein said thickener is polyvinylpyrrolidone; wherein said chelating agent is sodium edetate; and wherein said pH controlling agent is sodium hydroxide.

61. (Withdrawn-currently amended) A method for stabilizing 2-amino-3-(4-bromobenzoyl)phenylacetic acid or a pharmacologically acceptable salt thereof or a hydrate thereof in an aqueous liquid preparation, which comprises incorporating tyloxapol or polyethylene glycol monostearate into an aqueous liquid preparation containing 2-amino-3-(4-bromobenzoyl)phenylacetic acid or a pharmacologically acceptable salt thereof or a hydrate thereof, to obtain an aqueous liquid preparation consisting essentially of at least the following two components, the first component comprising 2-amino-3-(4- bromobenzoyl)phenylacetic acid or a pharmacologically acceptable salt thereof or a hydrate thereof, and the second component comprising tyloxapol or polyethylene glycol monostearate, wherein said liquid preparation is in the form of an eye drop.

62. (Currently amended) A method for inhibiting decrease in preservative effect of a preservative in an aqueous liquid preparation of 2-amino-3-(4-bromobenzoyl)phenylacetic acid or a pharmacologically acceptable salt thereof or a hydrate thereof, which comprises incorporating tyloxapol or polyethylene glycol monostearate into an aqueous liquid preparation containing 2-amino-3-(4-bromobenzoyl)phenylacetic acid or a pharmacologically acceptable salt thereof or a hydrate thereof and a preservative, to obtain an aqueous liquid preparation consisting essentially of at least the following two components, the first component comprising 2-amino-3-(4- bromobenzoyl)phenylacetic acid or a pharmacologically acceptable salt thereof or a hydrate

thereof, and the second component comprising tyloxapol or polyethylene glycol monostearate, together with a preservative, wherein said liquid preparation is in the form of an eye drop.

63. (Currently amended) An aqueous liquid preparation consisting of the following two components, the first component ~~comprising~~ is 2-amino-3-(4- bromobenzoyl)phenylacetic acid or a pharmacologically acceptable salt thereof or a hydrate thereof, and the second component ~~comprising~~ is an alkyl aryl polyether alcohol type polymer or a polyethylene glycol fatty acid ester, and water, and optionally at least one preservative, isotonic, buffer, thickener, stabilizer, chelating agent, pH controlling agent, or perfume, wherein said liquid preparation is in the form of an eye drop.

REMARKS

Favorable reconsideration is respectfully solicited in view of the following remarks.

Initially, Applicant wishes to express its sincere thanks for the courtesy and cooperation provided to its undersigned representative by Examiner Timothy Thomas and Supervisory Examiner Ardin Marschel during the personal interview held on November 20, 2008. The following is a summary of the items discussed during the interview.

Claims 19, 39, 40, 41, 61, 62 and 63 have been amended to require that the aqueous liquid preparation is in the form of an eye drop. Claims 30, 35, 52 and 57 have accordingly been cancelled.

Claim 41 has been amended to delete "at least" and to change "comprising" to – is –.

Claim 63 has been amended to change "comprising" to – is – and to add --and water --.

Turning to the Official Action, Applicants acknowledge with thanks the Examiner's indication that numerous former grounds of rejection have been withdrawn in view of Applicants' last response.

On page 3, claims 19-29, 31-34, 36-38, 41-51, 53-56, 58-60 and 63 are rejected under 35 U.S.C. 103 as obvious over Gamache et al. (WO 01/15677) in view of ISTA or Nolan et al. This ground of rejection is respectfully traversed as applied to the amended claims.

Claims 19, 39, 40, 41, 61, 62 and 63 have been amended to require that the aqueous liquid preparation is in the form of an eye drop according to claims 30, 35, 52 and 57. None of claims 30, 35, 52 or 57 were encompassed by the rejection.

Accordingly this ground of rejection is deemed to be overcome.

Furthermore, Applicants take the opportunity to provide additional remarks for the Examiner's consideration against a potential 103 rejection based upon a different combination of references.

The subject matter of the claimed invention is directed to an eye drop having a specific combination of 2-amino-3-(4- bromobenzoyl)phenylacetic acid or a pharmacologically acceptable salt thereof or a hydrate thereof, and an alkyl aryl polyether alcohol type polymer or a

polyethylene glycol fatty acid ester.

On the other hand, Gamache et al. do not disclose or suggest this specific combination. The cited reference is directed to compositions comprising of 5-HT_{1D} and/or HT_{1B} agonists. The cited reference states that these agonists may be combined with an extensive list of other pharmaceutical agents, i.e. (1) anti-microbial agent, (2) anti-inflammatory agents or (3) anti-allergy agent (please see page 6, lines 1-3 of Gamache). Gamache et al. only describes "bromfenac" as one of many examples of anti-inflammatory agents enumerated on page 12, lines 11-24. Gamache et al. does not concretely describe nor suggest the claimed preparation containing bromfenac.

Further, tyloxapol (0.05% w/v) is only mentioned as being added to an 1B/1D agonist (0.1-1.0% w/v) and moxifloxacin (0.3% w/v) in Example 4 (an Example of an otic/nasal suspension). There is no explanation about tyloxapol in the description of Gamache et al. or why it is included. Moreover in this Example, moxifloxacin is incorporated as a well-known antibacterial agent but is not an anti-inflammatory agent like bromfenac. Thus it is unclear from Gamache et al. why tyloxapol is added to the otic/nasal suspension containing 1B/1D agonist and moxifloxacin.

"Tyloxapol" described in Example 4 is just a single word description and does not give any clues and hints to the present invention. Therefore, the word "tyloxapol" described only in Example 4 does not destroy the novelty of the present invention.

Further, Gamache et al. is silent about an alkyl aryl polyether alcohol type polymer or a polyethylene glycol fatty acid ester component according to the claimed eye drop.

Thus the disclosure of Gamache et al. would suggest to the skilled artisan thousands of possible combinations of ingredients to include with an IB/ID agonist. Such disclosure does not lead the artisan to the claimed specific combination nor does such disclosure render the claimed combination obvious. The prior art must motivate one skilled in the art to make the claimed combination. There is no teachings or suggestion in Gamache of selecting bromfenac in combination with an alkyl aryl polyether alcohol type polymer or a polyethylene glycol fatty acid ester.

Furthermore, Gamache et al. is directed to compositions for relieving otic pain (abstract) by apply the compositions to the ear or nasally (page 10, lines 6-9 and Example 4). There is no teaching or motivation to make the claimed eye drop.

Regarding claims 41-51, 53-56 and 58-60, the claims are directed to an eye drop which consists essentially of the recited specific combination of ingredients. The claim recites the transitional phrase "consisting essentially of" means that the claim is open to include the specified ingredients and additional ingredients that do not materially affect the basic and novel characteristics of the claimed invention. See M.P.E.P. 2111.03.

It is respectfully submitted that the principal IB/ID agonist of the Gamache composition would affect the basic novel properties of the claimed preparation.

One skilled in the art would not have been motivated to modify the Gamache et al. composition in view of ISTA and Nolan, to arrive at the claimed eye drop. The primary object of Gamache et al. is to make a composition containing an IB/ID agonist. The artisan would not have been motivated by the reference to make a composition lacking the IB/ID agonist. An IB/ID agonist is excluded from claims 41-51, 53-56 and 58-60 by the "consisting essentially of" transitional phrase.

Regarding claim 63, the claim is limited to an eye drop which "consists of" the recited bromfenac, recited an alkyl aryl polyether alcohol type polymer or a polyethylene glycol fatty acid ester, and water. Such claim explicitly excludes other ingredients, such as an IB/ID agonist.

For the foregoing reasons, Applicant submits that the present invention is unobvious from Gamache et al. and ISTA or Nolan to those skilled in the art.

Claims 41-60 and 63 are rejected under 35 USC 112, second paragraph, as being indefinite for the reasons set forth on pages 6-7 of the Action.

Based upon the Examiner's remarks during the personal interview, it is believed that this ground of rejection is overcome by the foregoing amendments.

Claims 19-38, 41-60 and 63 are rejected under 35 USC 103 as being unpatentable over Hellberg et al. and Nolan et al. This ground of rejection is respectfully traversed as applied to the amended claims.

The Examiner asserts that it would have been obvious to substitute the compounds having anti-inflammatory and anti-oxidant activity used in the ophthalmic compositions of Hellberg et al. with bromfenac used in the dermal applications disclosed in Nolan et al. Applicants respectfully disagree.

The intended purpose of the invention disclosed in Hellberg et al. is to provide "[c]ompounds having anti-inflammatory ***and*** antioxidant activity." See Hellberg et al., Abstract (emphasis added); see also Hellberg at column 2, lines 13-18 ("***The present invention provides*** new compounds having potent anti-inflammatory ***and*** anti-oxidant activity.") (emphasis added). Indeed, Hellberg et al. explicitly state that the principle of operation of the anti-inflammatory and antixodixant compounds is to provide a two-pronged therapeutic approach not previously available in the art:

> The compounds of the present invention are capable of protecting against cellular damage by a wide range of insults. Since the compounds provide this protection by decreasing free radical or oxidative damage, reducing cyclooxygenase or lipoxygenase mediated inflammation, and improving site delivery, this therapy represents an improved two-pronged approach to cytoprotection.

See Hellberg et al. at Column 2, lines 57-63. Therefore, the intended purpose of the invention disclosed in Hellberg et al. is to provide compounds with not only anti-inflammatory activity, but also anti-oxidant activity for improved therapeutic functionality:

> The compounds also include an anti-oxidant component. As oxidative stress has been implicated in inflammatory responses, the presence of an anti-oxidant will further help treat the target tissue.
>
> The compounds of the present invention also exhibit properties present only in the combined molecule, ***not in the individual components***. One such property is the inhibitory efficacy against 5-lipoxygenase, an enzyme known to be involved in inflammation.

See Hellberg et al. at Column 2, lines 38-45 (emphasis added).

The USPTO has made clear that "[i]f [the] proposed modification would render the prior art invention being modified unsatisfactory for its intended purpose, then there is no suggestion or motivation to make the proposed modification." See MPEP section 2143.01 V, citing *In re*

Gordon, 733 F.2d 900 (Fed. Cir. 1984). Additionally, section 2143.01 VI of the MPEP plainly states: "The proposed modification cannot change the principle of operation of a reference. If the proposed modification or combination of the prior art would change the principle of operation of the prior art invention being modified, then the teachings of the references are not sufficient to render the claims *prima facie* obvious." See also *In re Ratti*, 270 F.2d 810, 123 USPQ 349 (CCPA 1959).

Here, the Examiner asserts that it would have been obvious to substitute the anti-inflammatory and anti-oxidant compounds disclosed in Hellberg et al. with bromfenac as disclosed in Nolan et al. because of "the art recognized equivalent activity of bromfenac as an anti-inflammatory agent in topical usage." See Official Action date July 18, 2008 at page 9. But as indicated in the Official Action and in Hellberg et al., bromfenac is an anti-inflammatory and not an antioxidant. The proposed substitution of the dual action anti-inflammatory and anti-oxidant compounds disclosed in Hellberg et al. with bromfenac would render the Hellberg et al. invention unsatisfactory for its intended purpose of providing "compounds having potent anti-inflammatory and anti-oxidant activity." The proposed substitution would result in a bromfenac composition having only anti-inflammatory activity. This proposed modification would radically change the principle of operation of Hellberg et al. from "an improved two-pronged approach to cytoprotection" to a mere one-pronged approach based on anti-inflammatory action alone.

Therefore, because the proposed substitution of the anti-inflammatory and anti-oxidant compounds disclosed in Hellberg et al. with bromfenac as disclosed in Nolan et al. would render the Hellberg et al. invention unsatisfactory for its intended purpose and radically change the principle of operation of Hellberg et al., Applicants respectfully submit a prima facie case of obviousness cannot be based on the combination of Hellberg et al. and Nolan et al.

In addition to the argument that the proposed modification changes the principle operation and intended purpose of Hellberg et al., Applicants submit that Hellberg et al. explicitly teach away from the use of a compound, such as bromfenac, having only anti-inflammatory activity. Hellberg et al. clearly recite deficiencies in the use of non-steroidal anti-inflammatory agents such as bromfenac:

> Non-steroidal anti-inflammatory agents (NSAIA) have been used for the treatment of inflammatory disorders. The following references may be referred to for further background concerning this use of NSAIAs:
>
> Ophthalmoscope, volume 8, page 257 (1910);
>
> FASEB Journal, volume 1, page 89 (1987); and
>
> Inflammation and Mechanisms and Actions of Traditional Drugs, vol. I Anti-inflammatory and Anti-rheumatic drugs. Boca Raton, Fla., CRC Press, (1985).
>
> However, ***there are some problems associated with NSAIA treatment including delivery to the appropriate site of action and side effects*** (Goodman and Gilman's The Pharmacological Basis of Therapeutics, pages 638-669, Pergman Press, NY (1990)).

See Hellberg et al. at Column 1, lines 28-37 (emphasis added).

According to the USTPO guidelines, "[i]t is improper to combine references where the references teach away from their combination." See MPEP § 2145, citing *In re Grasselli*, 713 F.2d 731, 743 (Fed. Cir. 1983); see also *McGinley v. Franklin Sports, Inc.*, 262 F.3d 1339, 1354 (Fed.Cir. 2001) ("It is well-established that references which "teach away cannot serve to create a prima facie case of obviousness.") (citations omitted).

Here, Hellberg et al. plainly state that NSAIA treatment is associated with "problems" such as "side effects" and "delivery to the appropriate site of action." In light of this teaching away from the use of a non-steroidal anti-inflammatory agent (NSAIA), one skilled in the art would not substitute bromfenac, a known NSAIA, for the anti-inflammatory and anti-oxidant compounds disclosed in Hellberg et al. Therefore, because Hellberg et al. teach away from the use of bromfenac, Applicants respectfully submit a prima facie case of obviousness cannot be based on the combination of Hellberg et al. and Nolan et al.

For the reasons detailed above, Applicants respectfully request withdrawal of the rejection of claims 19-38, 41-60 and 63 under 35 USC 103 as being unpatentable over Hellberg et al. and Nolan et al.

Lastly, claims 19-38 are provisionally rejected on the ground of non-statutory obviousness-type double patenting as being unpatentable over claims 1-43 of copending

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/525,006	03/28/2005	Shirou Sawa	2005_0232A	1756

513 7590 12/03/2008

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EXAMINER	
THOMAS, TIMOTHY P	
ART UNIT	PAPER NUMBER
1614	
MAIL DATE	DELIVERY MODE
12/03/2008	PAPER

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

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

Interview Summary	Application No.	Applicant(s)	
	10/525,006	SAWA ET AL.	
	Examiner	Art Unit	
	TIMOTHY P. THOMAS	1614	

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

(1) *TIMOTHY P. THOMAS*. (3)*Warren Cheek*.

(2) *Ardin Marschel*. (4)*Naoko Kishida*.

Date of Interview: *20 November 2008*.

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: *19 and 41*.

Identification of prior art discussed: *Gamache, et al. (WO 01/15677 A2); Nolan, et al. ("The topical anti-inflammatory and analgesic properties of bromfenic in rodents; Agents and Actions; 1988 Aug; 25(1-2):77-85); Hellberg et al. (US 5,998,465)*.

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: *Potential claim amendments were discussed that might potentially overcome the prior art-based rejections; potential designs of experimental studies were also discussed that might yield unexpected results to overcome the 103 rejections*.

(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.

/Timothy P Thomas/ Examiner, Art Unit 1614	

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/525,006	03/28/2005	Shirou Sawa	2005_0232A	1756

513 7590 07/18/2008

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EXAMINER	
THOMAS, TIMOTHY P	
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1614	
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07/18/2008	PAPER

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Office Action Summary	Application No.	Applicant(s)	
	10/525,006	SAWA ET AL.	
	Examiner	Art Unit	
	TIMOTHY P. THOMAS	1614	

-- 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 *26 March 2008*.

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

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

Disposition of Claims

4)☒ Claim(s) *19-63* is/are pending in the application.

4a) Of the above claim(s) *39,40,61 and 62* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *19-38,41-60 and 63* is/are rejected.

7)☒ Claim(s) *41-60* 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 *3/26/2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. New claims 61-62 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 8/20/2007.

Response to Arguments

2. Applicants' arguments, filed 3/26/2008, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

3. Applicant's arguments, see pp. 11-14, filed 3/26/2008, with respect to the rejections of claims 19-24 and 31, of claim 19 and of claims 19-38 under 35 USC 102 have been fully considered and are persuasive. The rejections of claims 19-24 and 31, 19 and 19-38 have been withdrawn.

Applicant's arguments that neither Gamache nor Dobrozsi concretely describe the combination of bromfenac and tyloxapol, recited in the amended claims, are persuasive. Therefore the rejections based on Gamache and Dobrozsi are withdrawn. Applicant's argument that Sawa does not have a proper 102(e) date is also persuasive.

4. Applicant's arguments, see pp. 15-17, filed 3/26/2008, with respect to rejection of claims 19-29, 31-34 and 36-38 under 35 USC 103 have been fully considered and are persuasive. The rejection of claims 19-29, 31-34 and 36-38 has been withdrawn.

Applicant's arguments that neither Gamache nor Dobrozsi concretely describe the combination of bromfenac and tyloxapol, recited in the amended claims, are persuasive. Therefore the rejections based on Gamache and Dobrozsi are withdrawn. Applicant's arguments that Sawa does not have a 102(e) date is persuasive.

5. Applicant's arguments with respect to the rejection of claims 19-29, 31-34 and 36-38 as being unpatentable over Gamache and ISTA Pharmaceuticals or Nolan have been fully considered but they are not persuasive:

6. Claims 19-29, 31-34, 36-38, 41-51, 53-56, 58-60 and 63 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gamache, et al. (WO 01/15677 A2; 03/2001; previously cited) and ISTA Pharmaceuticals ("New Drug Applications: Xibrom", http://www.drugs.com/nda/xibrom_040525.html, accessed online 9/19/2007; previously cited) or Nolan, et al. ("The topical anti-inflammatory and analgesic properties of bromfenic in rodents; Agents and Actions; 1988 Aug; 25(1-2):77-85; provided with Interview Summary).

The rejection is maintained for the reasons of record and the following reasons.

Applicant argues that Gamache does not suggest the claimed invention, because Gamache is directed to 5-HT agonists compositions with a great number of other possible ingredients; the reference does not suggest the required combination of bromfenac and tyloxapol. This is not persuasive. Gamache clearly teaches combinations of 5-$HT_{1B/1D}$ agonists with one or more anti-inflammatory agents, dosed concurrently or sequentially with anti-inflammatory agent compositions. (p. 12, lines 9-11); bromfenac is clearly taught as an anti-inflammatory compound specie (p. 12, line

17; claim 11). This implies two different compositions as embodiments: 1) a composition containing a 1B/1D agonist and an anti-inflammatory agent (such as in claims 7, 10-11) and 2) two different compositions, where the first contains only an anti-inflammatory agent as the active compound, the second contains only a 1B/1D agonist as active agent (implied by sequential dosing). Taking Example 4 as the model formulation, it would have been obvious to one of ordinary skill in the art at the time of the invention to substitute bromfenac for Moxifloxin taught in the example, giving an aqueous liquid preparation containing both required ingredients of the instant claims, bromfenac and tyloxapol (along with the 5-$HT_{1B/1D}$ agonists). Alternatively, it would have been obvious to substitute bromfenac for both Moxifloxin and the 1B/1D agonist, giving an aqueous liquid preparation containing both required ingredients of the instant claims, bromfenac and tyloxapol (without a 5-$HT_{1B/1D}$ agonist). The motivation to prepare the combination formulation (with two active ingredients) would have been for the treatment of otic inflammatory reactions and responses, taught by Gamache (on p. 12, lines 8-11). The motivation to prepare the single active formulation (without a 5-$HT_{1B/1D}$ agonist) would have been for the sequential treatment of otic inflammatory reactions and responses, taught by Gamache. The motivation to select bromfenac as the anti-inflammatory agent would have been the art-recognized usefulness for the purpose of treating inflammatory reactions and responses, recognized by Gamache, and bomfenac sodium at the concentrations of the claims is taught by ISTA Pharmaceuticals and Nolan, also suitable for the purpose of Gamache's formulations. With respect to the tyloxapol concentrations recited in instant claims 25 and 32, of “about 0.02 w/v%” and

"about 0.3 w/v%", the amount taught is considered to be close, if not within the unspecified range implied by "about". Alternatively, it would have been obvious to optimize concentrations of tyloxapol, which one of ordinary skill in the art would have recognized is a surfactant, to optimize the conditions of the formulations for solubility of other ingredients, stability and efficacy in the anti-inflammatory action of the formulation, which would have given tyloxapol concentrations of the instant claims. The motivation would have been the routine optimization of conditions.

Applicant argues that ISTA Pharmaceuticals press release about Xibrom has a different composition than the instant formulation. This point is not at issue; the reference was cited to demonstrate salts and hydrates of bromfenac and concentrations of the instant claims. Applicant also argues the ISTA reference of the Nolan reference in combination with Gamache does not suggest the claimed invention comprising the at least two components. This is not persuasive because Gamache alone suggests the combination of the two required components, as outlined above.

Applicant argues that the combination of a 1B/1D agonist with bromfenac would not read on claims 41-60 because of the recitation of the "consisting essentially of" transitional phrase. This is not persuasive, since the phrase "at least" after "consisting essentially of" in claim 41 opens the subject matter to any additional ingredients. Even if the "at least" were absent from the claim language, the embodiment suggested by Gamache of only one single active anti-inflammatory agent (useful in a sequential treatment method) would obviate such a claim construction. With respect to claim 63, even if the "comprising" language was replaced by "consisting of" language, the

substitution of bromfenac for the active ingredients in Example 4 as suggested by Gamache would produce a composition that reads on the specific components recited in claim 63, assuming water would be required in that claim.

7. Applicant's arguments, see pp. 17-18, with respect to the rejection of claims 19-30 as being unpatentable over Yakuji Nippo Ltd. and Xia; and claims 19-38 as being unpatentable over Yakuji Nippo Ltd., Xia, and Nolan have been fully considered and are persuasive. Therefore, the rejections have been withdrawn. However, upon further consideration, a new ground(s) of rejection is made as follows.

8. Claims 19-38, 41-60 and 63 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-43 of copending Application No. 11/755662.

Claim Rejections - 35 USC § 112

9. 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.

10. Claims 41-60 and 63 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

This rejection is necessitated by the amendment introducing new claims.

11. With respect to claims 41-60, the recitation of the transitional phrase generally considered to refer to closed claim language, "consisting essentially of" together with the open language term, "at least" in the 1st line of claim 41, is not clear whether open construction or closed construction is meant by the claim; additionally the language of

the 1st and 2nd components, “comprising”, an open construction term is also unclear and inconsistent with the closed construction phrase, “consisting essentially of”. It is not clear whether formulations containing the recited components and additional components would fall within or outside of the metes and bounds of the instant claims. For other rejections the phrase "consisting essentially of at least" is construed to have the same meaning as "comprising", consistent with the broadest reasonable interpretation of these claims.

12. With respect to claim 63, the recitation of the transitional phrase, “consisting of" the two components, each of which use the term, “comprising” to recite the compounds present in each components, does not make clear whether the claim construction is closed or open; i.e., it is not clear whether a formulation containing one compound from the 1st component, one compound from the 2nd component, one or more of the optional components recited and at least one non-component compound (not recited in the claim), such as water or an alcohol, would fall within the scope of or be excluded from the subject matter of the claim. For prior art rejections, the claims are construed in the broader meaning, i.e., the presence of "comprising” in the claim has the meaning of open ended claim construction.

13. Additionally, claim 63 recites “an aqueous liquid preparation” consisting of two required components, and optionally containing at least one additional component, none of the required or optional components recite water. The presence of an “aqueous” preparation along with the absence of water is inconsistent, and does not make clear whether water is required, optional or absent.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

14. Claims 19-38, 41-60 and 63 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hellberg et al. (US 5,998,465; 1999) and Nolan, et al. ("The topical anti-inflammatory and analgesic properties of bromfenac in rodents; Agents and Actions; 1988 Aug; 25(1-2):77-85; cited with previous Interview Summary).

15. Hellberg teaches pharmaceutical compositions of anti-inflammatory compounds (abstract); the compounds include a non-steroidal anti-inflammatory moiety (NSAIA) and an antioxidant moiety linked through an ester bond formed by the carboxylic acid moiety of the NSAIA (col. 2, lines 20-24); NSAIA moieties include bromfenac (col. 3, line 57; claim 5); examples 2 and 3 (col. 11) teach topical ophthalmic formulations useful for treating inflammation, both of these formulations include tyloxapol at 0.01-0.05 w/v %, HPMC (thickener), benzalkonium chloride (preservative), edetate disodium (chelating agent) (col. 11, Examples 2-3); the pH is adjusted to 7.4 (about 7.5; col. 11, line 64); topical formulations administered by drops (eyedrops; col. 10, lines 15-18). Hellberg does not teach bromfenac (only the ester of bromfenac). Nolan teaches bromfenac (the sodium salt, sesquihydrate form) was effective as a topical analgesic at concentrations of 0.1-0.32 % in mice and more potent than the other drugs tested (abstract). It would have been obvious for one of ordinary skill in the art at the time of the invention to substitute bromfenac, taught by Nolan for the compounds of Hellberg in the example formulation giving formulations of the instant claims and to select concentrations of

bromfenac sodium, sesquihydrate of 0.1, about 0.2 and about 0.32 %, in the invention of Gamache, since these values have demonstrated efficacy for topical use. It would also have been obvious to adjust the concentration of tyloxapol, to optimize the formulations for the effect would on the solubility and stability of the aqueous preparations, which would have resulted in the effective tyloxapol concentrations of about 0.02 and 0.3 w/v%, recited in claims 25 and 32. The motivation to substitute bromfenac in the Hellberg formulations would have bee the art-recognized equivalent activity of bromfenac as an anti-inflammatory agent in topical usage. The motivation to adjust concentrations would have been the routine optimization of these topical ophthalmic formulations for anti-inflammatory use in the eye.

Double Patenting

16. A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

17. Claims 41-60 are objected to under 37 CFR 1.75 as being a substantial duplicate of claims 19-38. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

This objection is necessitated by the amendment adding new claims. Claim 41 uses the transitional phrase in the preamble, "consisting essentially of at least", whereas claim 19 uses the transitional phrase, "comprising"; all other wording is identical. "Consisting essentially of" is generally closed language, excluding components not recited in the claim. However, the presence of the open language term, "at least" removes the closed language of "consisting essentially of", giving the meaning that the recited components are required, but additional components no recited may optionally be present, which is the same meaning possessed by the term, "comprising". Therefore, though the two sets of claims use slightly different wording, the meanings are the same.

Conclusion

18. No claim is allowed.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to TIMOTHY P. THOMAS whose telephone number is (571)272-8994. The examiner can normally be reached on Monday-Thursday 6:30 a.m. - 5:00 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on (571) 272-0718. 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.

/Timothy P Thomas/
Examiner, Art Unit 1614

/Ardin Marschel/
Supervisory Patent Examiner, Art Unit 1614

Notice of References Cited	Application/Control No. 10/525,006	Applicant(s)/Patent Under Reexamination SAWA ET AL.	
	Examiner TIMOTHY P. THOMAS	Art Unit 1614	Page 1 of 1

U.S. PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Name	Classification
*	A	US-5,998,465	12-1999	Hellberg et al.	514/432
	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

In re application of	:	**Confirmation No. 1756**
Shirou SAWA et al.	:	Attorney Docket No. 2005_0232A
Serial No. 10/525,006	:	Group Art Unit 1614
Filed March 28, 2005	:	Examiner Timothy P. Thomas
AQUEOUS LIQUID PREPARATION CONTAINING 2-AMINO-3-(4-BROMOBENZOYL)PHENYLACETIC ACID	:	**Mail Stop: Amendment**

THE COMMISSIONER IS AUTHORIZED TO CHARGE ANY DEFICIENCY IN THE FEES FOR THIS PAPER TO DEPOSIT ACCOUNT NO 23-0975

AMENDMENT

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

Sir:

Responsive to the Official Action dated September 27, 2007, the time for responding thereto being extended for three months in accordance with a petition for extension submitted concurrently herewith, please amend the above-identified application as follows:

Amendments to the Claims

1-18. (Cancelled)

19. (Currently amended) An aqueous liquid preparation comprising at least the following two components, the first component comprising 2-amino-3-(4-bromobenzoyl)phenylacetic acid or a pharmacologically acceptable salt thereof or a hydrate thereof, and the second component comprising an alkyl aryl polyether alcohol type polymer or a polyethylene glycol fatty acid ester.

20. (Previously presented) The aqueous liquid preparation according to claim 19, wherein the alkyl aryl polyether alcohol type polymer is tyloxapol;

wherein the concentration of the tyloxapol is selected from a range of about 0.01 w/v % to about 0.5 w/v %; and

wherein the concentration of the 2-amino-3-(4-bromobenzoyl)phenylacetic acid or a pharmacologically acceptable salt thereof or a hydrate thereof is selected from a range of about 0.01 to about 0.5 w/v %.

21. (Previously presented) The aqueous liquid preparation according to claim 20, wherein the pharmacologically acceptable salt of 2-amino-3-(4-bromobenzoyl)phenylacetic acid is a sodium salt.

22. (Previously presented) The aqueous liquid preparation according to claim 21, wherein the concentration of the 2-amino-3-(4-bromobenzoyl)phenylacetic acid sodium salt is selected from a range of about 0.05 to about 0.2 w/v %.

23. (Previously presented) The aqueous liquid preparation according to claim 22, wherein the concentration of the tyloxapol is selected from a range of about 0.01 w/v % to about 0.3 w/v %.

24. (Previously presented) The aqueous liquid preparation according to claim 23, wherein the concentration of the 2-amino-3-(4-bromobenzoyl)phenylacetic acid sodium salt is about 0.1 w/v %.

25. (Previously presented) The aqueous liquid preparation according to claim 24, wherein the concentration of the tyloxapol is about 0.02 w/v %.

26. (Previously presented) The aqueous liquid preparation according to claim 25, wherein the formulation further includes one or more additives selected from the group consisting of a preservative, buffer, thickener, stabilizer, chelating agent, and pH controlling agent.

27. (Previously presented) The aqueous liquid preparation according to claim 26, wherein said preservative is benzalkonium chloride; wherein said buffer is boric acid and/or sodium borate; wherein said thickener is polyvinylpyrrolidone; wherein said stabilizer is sodium sulfite; wherein said chelating agent is sodium edetate; and wherein said pH controlling agent is sodium hydroxide.

28. (Previously presented) The aqueous liquid preparation according to claim 27, wherein the pH is from about 7 to about 9.

29. (Previously presented) The aqueous liquid preparation according to claim 28, wherein the pH is from about 7.5 to about 8.5.

30. (Previously presented) The aqueous liquid preparation according to claim 27, wherein said liquid preparation is in the form of an eye drop.

31. (Previously presented) The aqueous liquid preparation according to claim 23, wherein the concentration of the 2-amino-3-(4-bromobenzoyl)phenylacetic acid sodium salt is about 0.2 w/v %.

32. (Previously presented) The aqueous liquid preparation according to claim 31, wherein the concentration of the tyloxapol is about 0.3 w/v %.

33. (Previously presented) The aqueous liquid preparation according to claim 32, wherein the formulation further includes one or more additives selected from the group consisting of a preservative, buffer, thickener, stabilizer, chelating agent, and pH controlling agent.

34. (Previously presented) The aqueous liquid preparation according to claim 33, wherein said preservative is benzalkonium chloride; wherein said buffer is boric acid and/or sodium borate; wherein said thickener is polyvinylpyrrolidone; wherein said stabilizer is sodium sulfite; wherein said chelating agent is sodium edetate; and wherein said pH controlling agent is sodium hydroxide.

35. (Previously presented) The aqueous liquid preparation according to claim 34, wherein said liquid preparation is in the form of an eye drop.

36. (Previously presented) The aqueous liquid preparation according to claim 31, wherein the concentration of the tyloxapol is about 0.02 w/v %.

37. (Previously presented) The aqueous liquid preparation according to claim 36, wherein the formulation further includes one or more additives selected from the group consisting of a preservative, buffer, thickener, stabilizer, chelating agent, and pH controlling agent.

38. (Previously presented) The aqueous liquid preparation according to claim 37, wherein said preservative is benzalkonium chloride; wherein said buffer is boric acid and/or sodium borate; wherein said thickener is polyvinylpyrrolidone; wherein said chelating agent is sodium edetate; and wherein said pH controlling agent is sodium hydroxide.

39. (Withdrawn-currently amended) A method for stabilizing 2-amino-3-(4-bromobenzoyl)phenylacetic acid or a pharmacologically acceptable salt thereof or a hydrate thereof in an aqueous liquid preparation, which comprises incorporating tyloxapol or polyethylene glycol monostearate into an aqueous liquid preparation containing 2-amino-3-(4-bromobenzoyl)phenylacetic acid or a pharmacologically acceptable salt thereof or a hydrate thereof, to obtain an aqueous liquid preparation comprising at least the following two components, the first component comprising 2-amino-3-(4- bromobenzoyl)phenylacetic acid or a pharmacologically acceptable salt thereof or a hydrate thereof, and the second component comprising tyloxapol or polyethylene glycol monostearate.

40. (Withdrawn-currently amended) A method for inhibiting decrease in preservative effect of a preservative in an aqueous liquid preparation of 2-amino-3-(4-bromobenzoyl)phenylacetic acid or a pharmacologically acceptable salt thereof or a hydrate thereof, which comprises incorporating tyloxapol or polyethylene glycol monostearate into an aqueous liquid preparation containing 2-amino-3-(4-bromobenzoyl)phenylacetic acid or a pharmacologically acceptable salt thereof or a hydrate thereof and a preservative, to obtain an aqueous liquid preparation comprising at least the following two components, the first component comprising 2-amino-3-(4- bromobenzoyl)phenylacetic acid or a pharmacologically

acceptable salt thereof or a hydrate thereof, and the second component comprising tyloxapol or polyethylene glycol monostearate, together with a preservative.

41. (New) An aqueous liquid preparation consisting essentially of at least the following two components, the first component comprising 2-amino-3-(4-bromobenzoyl)phenylacetic acid or a pharmacologically acceptable salt thereof or a hydrate thereof, and the second component comprising an alkyl aryl polyether alcohol type polymer or a polyethylene glycol fatty acid ester.

42. (New) The aqueous liquid preparation according to claim 41, wherein the alkyl aryl polyether alcohol type polymer is tyloxapol;

wherein the concentration of the tyloxapol is selected from a range of about 0.01 w/v % to about 0.5 w/v %; and

wherein the concentration of the 2-amino-3-(4-bromobenzoyl)phenylacetic acid or a pharmacologically acceptable salt thereof or a hydrate thereof is selected from a range of about 0.01 to about 0.5 w/v %.

43. (New) The aqueous liquid preparation according to claim 42, wherein the pharmacologically acceptable salt of 2-amino-3-(4-bromobenzoyl)phenylacetic acid is a sodium salt.

44. (New) The aqueous liquid preparation according to claim 43, wherein the concentration of the 2-amino-3-(4-bromobenzoyl)phenylacetic acid sodium salt is selected from a range of about 0.05 to about 0.2 w/v %.

45. (New) The aqueous liquid preparation according to claim 44, wherein the concentration of the tyloxapol is selected from a range of about 0.01 w/v % to about 0.3 w/v %.

46. (New) The aqueous liquid preparation according to claim 45, wherein the concentration of the 2-amino-3-(4-bromobenzoyl)phenylacetic acid sodium salt is about 0.1 w/v %.

47. (New) The aqueous liquid preparation according to claim 46, wherein the concentration of the tyloxapol is about 0.02 w/v %.

48. (New) The aqueous liquid preparation according to claim 47, wherein the formulation further includes one or more additives selected from the group consisting of a preservative, buffer, thickener, stabilizer, chelating agent, and pH controlling agent.

49. (New) The aqueous liquid preparation according to claim 48, wherein said preservative is benzalkonium chloride; wherein said buffer is boric acid and/or sodium borate; wherein said thickener is polyvinylpyrrolidone; wherein said stabilizer is sodium sulfite; wherein said chelating agent is sodium edetate; and wherein said pH controlling agent is sodium hydroxide.

50. (New) The aqueous liquid preparation according to claim 49, wherein the pH is from about 7 to about 9.

51. (New) The aqueous liquid preparation according to claim 50, wherein the pH is from about 7.5 to about 8.5.

52. (New) The aqueous liquid preparation according to claim 49, wherein said liquid preparation is in the form of an eye drop.

53. (New) The aqueous liquid preparation according to claim 45, wherein the

concentration of the 2-amino-3-(4-bromobenzoyl)phenylacetic acid sodium salt is about 0.2 w/v %.

54. (New) The aqueous liquid preparation according to claim 53, wherein the concentration of the tyloxapol is about 0.3 w/v %.

55. (New) The aqueous liquid preparation according to claim 54, wherein the formulation further includes one or more additives selected from the group consisting of a preservative, buffer, thickener, stabilizer, chelating agent, and pH controlling agent.

56. (New) The aqueous liquid preparation according to claim 55, wherein said preservative is benzalkonium chloride; wherein said buffer is boric acid and/or sodium borate; wherein said thickener is polyvinylpyrrolidone; wherein said stabilizer is sodium sulfite; wherein said chelating agent is sodium edetate; and wherein said pH controlling agent is sodium hydroxide.

57. (New) The aqueous liquid preparation according to claim 56, wherein said liquid preparation is in the form of an eye drop.

58. (New) The aqueous liquid preparation according to claim 53, wherein the concentration of the tyloxapol is about 0.02 w/v %.

59. (New) The aqueous liquid preparation according to claim 58, wherein the formulation further includes one or more additives selected from the group consisting of a preservative, buffer, thickener, stabilizer, chelating agent, and pH controlling agent.

60. (New) The aqueous liquid preparation according to claim 59, wherein said preservative is benzalkonium chloride; wherein said buffer is boric acid and/or sodium borate;

wherein said thickener is polyvinylpyrrolidone; wherein said chelating agent is sodium edetate; and wherein said pH controlling agent is sodium hydroxide.

61. (New) A method for stabilizing 2-amino-3-(4-bromobenzoyl)phenylacetic acid or a pharmacologically acceptable salt thereof or a hydrate thereof in an aqueous liquid preparation, which comprises incorporating tyloxapol or polyethylene glycol monostearate into an aqueous liquid preparation containing 2-amino-3-(4-bromobenzoyl)phenylacetic acid or a pharmacologically acceptable salt thereof or a hydrate thereof, to obtain an aqueous liquid preparation consisting essentially of at least the following two components, the first component comprising 2-amino-3-(4- bromobenzoyl)phenylacetic acid or a pharmacologically acceptable salt thereof or a hydrate thereof, and the second component comprising tyloxapol or polyethylene glycol monostearate.

62. (New) A method for inhibiting decrease in preservative effect of a preservative in an aqueous liquid preparation of 2-amino-3-(4-bromobenzoyl)phenylacetic acid or a pharmacologically acceptable salt thereof or a hydrate thereof, which comprises incorporating tyloxapol or polyethylene glycol monostearate into an aqueous liquid preparation containing 2-amino-3-(4-bromobenzoyl)phenylacetic acid or a pharmacologically acceptable salt thereof or a hydrate thereof and a preservative, to obtain an aqueous liquid preparation consisting essentially of at least the following two components, the first component comprising 2-amino-3-(4-bromobenzoyl)phenylacetic acid or a pharmacologically acceptable salt thereof or a hydrate thereof, and the second component comprising tyloxapol or polyethylene glycol monostearate, together with a preservative.

63. (New) An aqueous liquid preparation consisting of the following two components, the first component comprising 2-amino-3-(4- bromobenzoyl)phenylacetic acid or a pharmacologically acceptable salt thereof or a hydrate thereof, and the second component comprising an alkyl aryl polyether alcohol type polymer or a polyethylene glycol fatty acid ester,

and optionally at least one preservative, isotonic, buffer, thickener, stabilizer, chelating agent, pH controlling agent, or perfume.

REMARKS

Favorable reconsideration is respectfully solicited in view of the following remarks.

Initially, Applicant wishes to express its sincere thanks for the courtesy and cooperation provided to its undersigned representative by Examiner Thomas and Examiner Marschel during the personal interview held on March 13, 2008. The following is a summary of the items discussed during the interview.

Claim 19 has been amended as suggested by the Examiners to clarify that the claimed preparation has at least two components, the first component and the second component as described above.

Claims 39 and 40 have been amended consistent with the amendments to claim 19, to allow for rejoinder of these claims upon an allowance of claims 19-38.

New claims 41-63 have been added for additional patent protection. Claims 41-62 correspond to claims 19-40, respectively, except in reciting that the preparation "consists essentially of" the recited components. New claim 63 correponds to claim 19, except that the claim recites "consisting of" the recited components, together with optional components which are supported on page 12, lines 3-11 of the specification.

Turning to the Official Action, item 7 of the Official Action states that the Oath or Declaration is defective because it was not executed. An executed copy of the Declaration was filed on March 28, 2005. A check of the PTO image file history during the interview revealed that an executed copy of the Declaration has been received.

Accordingly, this defect is believed to be overcome.

Claims 19-24 and 31 are rejected under 35 U.S.C. 102 as anticipated by Gamache et al., WO 01/15677. This ground of rejection is respectfully traversed.

The subject matter of the present invention is directed to the specific combination of 2-amino-3-(4- bromobenzoyl)phenylacetic acid or a pharmacologically acceptable salt thereof or a hydrate thereof and an alkyl aryl polyether alcohol type polymer or a polyethylene glycol fatty acid ester.

On the other hand, Gamache et al. do not disclose this specific combination. Moreover the cited reference is directed to compositions comprising of 5-HT_{1D} and/or HT_{1B} agonists. The cited reference states that these agonists may be combined with an extensive list of other pharmaceutical agents, i.e. (1) anti-microbial agent, (2) anti-inflammatory agents or (3) anti-allergy agent (please see page 6, lines 1-3 of Gamache).

In addition, Gamache et al. only describes "bromfenac" as one of many examples of anti-inflammatory agents enumerated on page 12, lines 11-24. Gamache et al. does not concretely describe nor suggest the claimed preparation containing bromfenac.

Further, although tyloxapol (0.05% w/v) is added to an 1B/1D agonist (0.1-1.0% w/v) and moxifloxacin (0.3% w/v) in Example 4 (an Example of an otic/nasal suspension), there is no explanation about tyloxapol in the description of Gamache et al. or why it is included. Moreover in this Example, moxifloxacin is incorporated as a well-known antibacterial agent but is not an anti-inflammatory agent like bromfenac. Thus it is unclear from Gamache et al. why tyloxapol is added to the otic/nasal suspension containing 1B/1D agonist and moxifloxacin.

"Tyloxapol" described in Example 4 is just a single word description and does not give any clues and hints to the present invention. Therefore, the word "tyloxapol" described only in Example 4 does not destroy the novelty of the present invention.

Besides, Gamache et al. is silent about an alkyl aryl polyether alcohol type polymer or a polyethylene glycol fatty acid ester component according to the preparation of the present invention.

Thus, Gamache et al. neither describe or suggest the specific claimed preparation of the present invention.

As discussed during the interview, it is respectfully submitted that the disclosure of Gamache et al. does not constitute an "anticipation" of the claimed invention under 35 U.S.C. 102. It is not possible to envision the specific claimed combination from the great number of possible combinations suggested by the cited reference.

As stated by the Board of Appeals in a similar case many years ago,

"While the invention here claimed in its broader aspect is doubtless embraced within the

speculative teachings of the references, we doubt if references which are not directed to the same purpose and do not have the same inventive concept, can be fairly applied in rejecting claims such as those on appeal where anticipation can be found only by making one of a very great number of possible permutations which are covered by the reference disclosures. The likelihood of producing a composition such as here claimed from a disclosure such as shown by the Dykstra patent would be about the same as the likelihood of discovering the combination of a safe from a mere inspection of the dials thereof."

Ex parte Garvey, 41 USPQ 583 (POBA 1939). See also Ex parte Starr, 44 USPQ 545 (POBA 1938); and Application of Luvisi, 52 CCPA 1063 (CCPA 1963).

See also M.P.E.P. 2131.02, discussing In re Meyer, 202 USPQ 175 (CCPA 1979) (A reference disclosing "alkaline chlorine or bromine solution" embraces a large number of species and cannot be said to anticipate claims to "alkali metal hypochlorite.").

For the foregoing reasons, it is respectfully submitted that the claimed invention is novel over Gamache et al.

Applicant gratefully acknowledges the Examiners' indication during the interview that this ground of rejection would be withdrawn.

Claim 19 is rejected under 35 U.S.C. 102 as anticipated by Dobrozsi, U.S. 6,319,513. This ground of rejection is respectfully traversed for the same reasons as stated above regarding the rejection over Gamache et al.

Dobrozsi discloses compositions comprising colloidal particles selected from the group consisting of silica, titanium dioxide, clay, and mixtures thereof. To the colloidal particle compositions may be added a great number of additional ingredients such as (1) analgesics, (2) decongestants, (3) expectorants, (4) antitussives, (5) antihistamines, (6) broncholilator, (7) topical anesthetics, (8) sensory agents, (9) oral care agents, (10) miscellaneous respiratory agents, (11) gastrointestinal agents, and mixtures thereof (please see column 2, lines 33-45 of Dobrozsi).

Dobrozsi describes on column 9, line 66 - column 10, line 11 that "[t]he analgesics useful for this invention include any narcotic and non-narcotic analgesics, such as --- bromfenac, ---". That is, Dobrozsi only describes "bromfenac" as one of so many examples of agents enumerated.

Further, Dobrozsi does not describe nor suggest an alkyl aryl polyether alcohol type polymer or a polyethylene glycol fatty acid ester component according to the preparation of the

present invention.

Besides, Dobrozsi neither describes nor suggests the specific combination of 2-amino-3-(4- bromobenzoyl)phenylacetic acid or a pharmacologically acceptable salt thereof or a hydrate thereof and an alkyl aryl polyether alcohol type polymer or a polyethylene glycol fatty acid ester of the claimed invention.

Although tyloxapol is added to oxymethazoline hydrochloride in the preparation of mucoretentive intrasal spray decongestant (Example 10) on column 23, line 46 in Dobrozsi, no explanation about tyloxapol is given.

Besides, oxymethazoline hydrochloride is a well known adrenergic, and is not an anti-inflammatory agent like bromfenac.

For the same reasons as the 102 rejection over Gamache et al., it is respectfully submitted that the present invention is novel over Dobrozsi.

Applicant gratefully acknowledges the Examiners' indication during the interview that this ground of rejection would be withdrawn.

Claims 19-38 are further rejected under 35 U.S.C. 102(e) as being anticipated by Sawa, U.S. 2007/0082857. This ground of rejection is respectfully traversed.

The cited reference is a published U.S. patent application of a U.S. national stage application based upon PCT/JP04/16849 filed November 12, 2004. International Application No. PCT/JP2004/016849 was published in Japanese language under Publication No. WO2005/046700. Please see Appendix A. Accordingly, the published patent application has no 102(e) date, nor does the published international application WO2005/046700 have a 102(e) date. Please see Appendix B, which is a copy of Example 5 of the Examination Guidelines for 35 U.S.C. 102(e) published by the USPTO.

Accordingly, the earliest effective date of the cited reference as a prior art reference is its publication date of April 12, 2007. Moreover, the earliest effective date of the published international application WO2005/046700 is its publication date of May 26, 2005.

In conclusion, the cited reference is not available as prior art against the present invention, and this ground of rejection should be withdrawn.

Applicant gratefully acknowledges the Examiners' indication during the interview that this ground of rejection would be withdrawn.

Claims 19-29, 31-34 and 36-38 are rejected under 35 U.S.C. 103 as being unpatentable over Gamache et al. and ISTA Pharmaceuticals or Nolan et al. (abstract). This ground of rejection is respectfully traversed.

The essential features of the preparation of the present invention cannot be derived from the combination of Gamache et al. and ISTA Pharmaceuticals or Nolan (abstract).

Gamache et al. is discussed above. This reference does not suggest the claimed invention. Gamache et al. is directed to 5-HT agonist compositions with a great number of other possible ingredients. The reference does not suggest the claimed aqueous liquid preparation comprises at least the following two components according to claims 19-38, the first component comprising 2-amino-3-(4- bromobenzoyl)phenylacetic acid or a pharmacologically acceptable salt thereof or a hydrate thereof, and the second component comprising an alkyl aryl polyether alcohol type polymer or a polyethylene glycol fatty acid ester.

Regarding claims 41-60, the claim recites the transitional phrase "consisting essentially of" means that the claim is limited to the specified ingredients and those that do not materially affect the basic and novel characteristics of the claimed invention. See M.P.E.P. 2111.03.

It is respectfully submitted that the principal 5-HT agonist of the Gamache composition would affect the basic novel properties of the claimed preparation.

The Examiners indicated during the interview that this amendment would be helpful to overcome this ground of rejection.

The cited ISTA publication was discussed during the interview. Although the cited reference has a publication date of May 25, 2004 after the effective U.S. filing date of the instant application, the reference is cited for its statement that "ISTA acquired U.S. marketing rights for Xibrom in May 2002 under a license from Senju." Thus the rejection is based upon the position that the claimed invention was known by others in the U.S. prior to the effective filing date of the instant application in the U.S. of January 16, 2004. And since the knowledgeable person(s) of ISTA is not an inventor of the invention, the reference is available as a reference under 35 U.S.C.

102(a), i.e. there is no one year grace period under 35 U.S.C. 102(b).

It should be noted that the cited reference does not disclose the claimed preparation. It does disclose a "bromfenac sodium ophthalmic solution", but it does not disclose the second claimed component comprising an alkyl aryl polyether alcohol type polymer or a polyethylene glycol fatty acid ester. Nevertheless, it is understood that the PTO position is that the reference is being cited for the proposition that the claimed preparation was known in the U.S. by ISTA before the effective filing date of the instant application.

Upon inquiry, it has been determined that Xibrom has a different composition from the claimed preparation. Enclosed is a copy of the Product Insert and Material Safety Data Sheet as Appendix C. An examination of these documents show that Xibrom contains no alkyl aryl polyether alcohol type polymer or polyethylene glycol fatty acid ester, which is the second component of the claimed preparation.

There is also enclosed a ISTA Press Release about Xibrom, which states that "Xibrom, under a different trade name but identical formulation, was launched in Japan in 2000 by Senju Pharmaceuticals Co. Ltd. ISTA acquired U.S. marketing rights for Xibrom in 2002 and launched the product in the U.S. in 2005." Please see the attached Appendix D.

In summary, the cited ISTA reference fails to suggest that the claimed preparation was known in the U.S. prior to the effective filing date of the instant application. Moreover the cited ISTA reference in combination with Gamache et al. does not suggest the claimed invention.

Regarding the alternative secondary reference Nolan, only the abstract of Nolan was cited in the rejection and included with the Office Action. The abstract only teaches that bromfenac is a potent anti-inflammatory agent. It does not disclose the claimed second component. Therefore the combination of Nolan (abstract) with Gamache et al. does not suggest the claimed preparation comprising the at least two components.

Applicant acknowledges that a complete copy of Nolan was provided to the Applicant's representative during the interview. The complete copy of the reference will be studied for its relevance and additional comments will be provided if possible.

Nevertheless, it is respectfully submitted that neither Gamache et al., ISTA

Pharmaceuticals and/or Nolan disclose or suggest the claimed preparation as amended, because they do not disclose the claimed preparation comprises the at least first and second claimed components.

Regarding new claims 41-60, even if one skilled in the art would have been motivated to modify the Gamache et al. composition in view of ISTA and Nolan, the artisan would have still obtained a 5-HT agonist composition, which is excluded from the amended claims by the "consisting essentially of" transitional phrase.

For the foregoing reasons, Applicant submits that the present invention is unobvious from Gamache et al. and ISTA Pharmaceuticals or Nolan to those skilled in the art.

Claims 19-30 are rejected under 35 U.S.C. 103 as unpatentable over Yakuji Nippo Ltd. and Xia, U.S. 6,369,112. This ground of rejection is respectfully traversed.

As stated in the rejection, the Yakuji reference teaches a bromfenac solution. It does not teach tyloxapol. Xia teaches adding tyloxapol to a contact lens solution to improve stability of the solution.

However Xia teaches adding tyloxapol to the contact lens solution for the purpose of improving stability of the biguanide disinfection agent in the solution. See the abstract and column 1, lines 10-12.

On the other hand, the claimed invention does not contain a biguanide. Furthermore the preparation of Yakuji contains bromfenac and does not contain any biguanide, according to the partial translation of record. Bromfenac is structurally very different from a biguanide.

Therefore it is respectfully submitted that one skilled in the art would not have been motivated to add tyloxapol taught by Xia to the composition of Yakuji for the purpose of stabilizing bromfenac.

Therefore, it is respectfully submitted that the present invention is unobvious from Yakuji Nippo Ltd. and Xia.

There is concurrently filed herewith an Information Disclosure Statement. As suggested by the Examiners, a complete English Translation of Yakuji is cited in the IDS and enclosed herewith. Also enclosed and cited is a corrected partial English translation of Yakuji.

Claims 19-38 are further rejected under 35 U.S.C. 103 as unpatentable over Yakuji Nippo Ltd. and Xia and Nolan (abstract). This ground of rejection is respectfully traversed.

The teachings of Yakuji and Xia are discussed above. Nolan (abstract) fails to remedy the deficiencies of Yakuji and Xia. There is no teaching or suggestion in the cited references for combining tyloxapol, or any alkyl aryl polyether alcohol type polymer or polyethylene glycol fatty acid ester, with bromfenac, or a 2-amino-3-(4- bromobenzoyl)phenylacetic acid or a pharmacologically acceptable salt thereof or a hydrate thereof, to obtain the claimed preparation.

Accordingly, this ground of rejection is respectfully submitted to be overcome.

Applicant gratefully acknowledges the Examiners' indication during the interview that this ground of rejection should be overcome.

Lastly, claims 19-38 are provisionally rejected on the ground of non-statutory obviousness-type double patenting as being unpatentable over claims 1-43 of copending application Serial No. 11/755,662.

The Examiner is respectfully requested to hold this provisional ground of rejection in abeyance until a later date. Upon overcoming all other grounds of rejection, it is respectfully submitted that this provisional ground of rejection should be withdrawn and the application passed on to allowance.

In summary, it is believed that each ground of rejection set forth in the Official Action has been overcome, and that the application is now in condition for allowance. Accordingly such allowance is solicited.

Respectfully submitted,

Shirou SAWA et al.

By: _____

Warren M. Cheek
Registration No. 33,367
Attorney for Applicants

WMC/dlk
Washington, D.C. 20006-1021
Telephone (202) 721-8200
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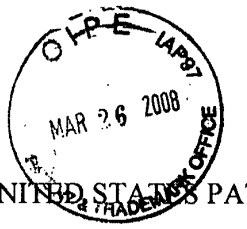
March 26, 2008



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of	:	**Confirmation No. 1756**
Shirou SAWA et al.	:	Attorney Docket No. 2005_0232A
Serial No. 10/525,006	:	Group Art Unit 1614
Filed March 28, 2005	:	Examiner Timothy P. Thomas
AQUEOUS LIQUID PREPARATION CONTAINING 2-AMINO-3-(4-BROMOBENZOYL)PHENYLACETIC ACID	:	**Mail Stop: Amendment**

THE COMMISSIONER IS AUTHORIZED TO CHARGE ANY DEFICIENCY IN THE FEES FOR THIS PAPER TO DEPOSIT ACCOUNT NO 23-0975

INFORMATION DISCLOSURE STATEMENT

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

Sir:

Pursuant to the provisions of 37 CFR 1.56, 1.97 and 1.98, Applicants request consideration of the references listed on attached form PTO-1449 and any additional information identified below in paragraph 3. A legible copy of each reference listed on the Form PTO-1449 is enclosed, except a copy is not provided for:

[X] each U.S. Patent and U.S. Patent application publication;

[] each reference previously cited in the international application PCT/_____; and/or

[] each reference previously cited in prior parent application Serial No. _____.

1a. [] This Information Disclosure Statement is submitted:

within three months of the filing date (or of entry into the National Stage) of the above-entitled application, **or**

03/31/2008 LLANDGRA 00000061 10525006
04 FC:1806 180.00 OP

before the mailing of a first Office Action on the merits or the mailing of a first Office Action after the filing of an RCE,

and thus no certification and/or fee is required.

1b. [X] This Information Disclosure Statement is submitted

after the events of above paragraph 1a and prior to the mailing date of a final Office Action or a Notice of Allowance or an action which otherwise closes prosecution in the application, and thus:

(1) [] the certification of paragraph 2 below is provided, **or**

(2) [X] the fee of $180.00 specified in 37 CFR 1.17(p) is enclosed.

1c. [] This Information Disclosure Statement is submitted:

after the mailing date of a final Office Action or Notice of Allowance or action which otherwise closes prosecution in the application, and prior to payment of the issue fee, and thus:

the certification of paragraph 2 below is provided, and

the fee of $180.00 specified in 37 CFR 1.17(p) is enclosed.

2. It is hereby certified

a. [] that each item of information contained in this Information Disclosure Statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of the Statement, or

b. [] that no item of information contained in the Information Disclosure Statement was cited in a communication from a foreign patent office in a counterpart foreign application and, to the knowledge of the person signing the certification after making reasonable inquiry, was known to any individual designated in §1.56(c) more than three months prior to the filing of the Statement.

3. [] Consideration of the following list of additional information (including any copending or abandoned U.S. application, prior uses and/or sales, etc.) is requested.

4. For each non-English language reference listed on the attached form PTO-1449, reference is made to:

   a. [] a full or partial English language translation submitted herewith,

   b. [] a foreign patent office search report (in the English language) submitted herewith,

   c. [] the concise explanation contained in the specification of the present application at page,

   d. [] the concise explanation set forth in the attached English language abstract,

   e. [] the concise explanation set forth below or on a separate sheet attached to the reference:

5. [] A foreign patent office search report citing one or more of the references is enclosed.

6. [] Statement Under 37 CFR 1.704(d)

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

Respectfully submitted,

Shirou SAWA et al.

By _____
Warren M. Cheek
Registration No. 33,367
Attorney for Applicants

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Washington, D.C. 20006-1021
Telephone (202) 721-8200
Facsimile (202) 721-8250
March 26, 2008

Sheet 1 of 1

INFORMATION DISCLOSURE STATEMENT

FORM PTO 1449 (*modified*)

U.S. DEPARTMENT OF COMMERCE
PATENT AND TRADEMARK OFFICE

LIST OF REFERENCES CITED BY APPLICANT(S)
(*Use several sheets if necessary*)

Date Submitted to PTO: March 26, 2008

ATTY DOCKET NO.	SERIAL NO.
2005_0232A	10/525,006

APPLICANT: Shirou SAWA et al.

FILING DATE	GROUP
March 28, 2005	1614

U.S. PATENT & TRADEMARK OFFICE MAR 26 2008

U.S. PATENT DOCUMENTS

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

FOREIGN PATENT DOCUMENTS

		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION YES	TRANSLATION NO
	BA							
	BB							
	BC							
	BD							
	BE							

OTHER DOCUMENT(S) (*Including Author, Title, Date, Pertinent Pages, Etc.*)

	CA	Corrected partial English translation of New Drugs in Japan, 2001, 2001 Edition, Published by Yakuji Nippo Ltd., May 11, 2001, pp. 27-29, previously submitted on April 11, 2005.
	CB	Complete English translation of New Drugs in Japan, 2001, 2001 Edition, Published by Yakuji Nippo Ltd., May 11, 2001, pp. 27-29.
	CC	

EXAMINER | DATE CONSIDERED

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

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
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Alexandria, Virginia 22313-1450
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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/525,006	03/28/2005	Shirou Sawa	2005_0232A	1756

513 7590 03/20/2008

WENDEROTH, LIND & PONACK, L.L.P.
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SUITE 800
WASHINGTON, DC 20006-1021

EXAMINER	
THOMAS, TIMOTHY P	
ART UNIT	PAPER NUMBER
1614	
MAIL DATE	DELIVERY MODE
03/20/2008	PAPER

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

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

Interview Summary	Application No.	Applicant(s)	
	10/525,006	SAWA ET AL.	
	Examiner	Art Unit	
	TIMOTHY P. THOMAS	1614	

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

(1) *TIMOTHY P. THOMAS*. (3)*Warren Cheek*.

(2) *Ardin Marschel*. (4)_____.

Date of Interview: *13 March 2008*.

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: *19 and 20*.

Identification of prior art discussed: *See Continuation Sheet*.

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: *the objection to the oath and rejections under 35 USC 102 and 103 were discussed with possible claim amendments that might be adopted. See attached 892 and copy of reference.*.

(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.

/Timothy P. Thomas/
Patent Examiner
Examiner's signature, if required

Examiner Note: You must sign this form unless it is an Attachment to a signed Office action.

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.

Continuation of Identification of prior art discussed: Gamache, et al. (WO 01/15677 A2); Dobrozsi (US 6,319,513 B1); Sawa (US 2007/0082857 A1); ISTA Pharmaceuticals ("New Drug Applications: Xibrom"; http://www.drugs.com/nda/xibrom_040525.html; accessed 9/19/2007); Nolan, et al. (Agents and Actions; 25 (1-2): 77-85, abstract); Yakuji Nippo Ltd ("New Drugs in Japan", 2001, IDS reference AP, English section translation); Xia (US 6,369,112 B1).

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Notice of References Cited	Application/Control No. 10/525,006	Applicant(s)/Patent Under Reexamination SAWA ET AL.	
	Examiner TIMOTHY P. THOMAS	Art Unit 1614	Page 1 of 1

U.S. PATENT DOCUMENTS

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

FOREIGN PATENT DOCUMENTS

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

NON-PATENT DOCUMENTS

*		Include as applicable: Author, Title Date, Publisher, Edition or Volume, Pertinent Pages)
	U	Nolan, et al. ("The topicla anti-inflammatory and analgesic properties of bromfenac in rodents"; 1988; Agents and Actions; 25(1-2): 77-85
	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.
10/525,006	03/28/2005	Shirou Sawa	2005_0232A	1756

513 7590 09/27/2007

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SUITE 800
WASHINGTON, DC 20006-1021

EXAMINER	
THOMAS, TIMOTHY P	
ART UNIT	**PAPER NUMBER**
1614	

MAIL DATE	DELIVERY MODE
09/27/2007	PAPER

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

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

Office Action Summary	Application No.	Applicant(s)	
	10/525,006	SAWA ET AL.	
	Examiner	Art Unit	
	Timothy P. Thomas	1614	

-- 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 *20 August 2007*.

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

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

Disposition of Claims

4)☒ Claim(s) *19-40* is/are pending in the application.

4a) Of the above claim(s) *39 and 40* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *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 *See Continuation Sheet*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Attachment(s) 3). Information Disclosure Statement(s) (PTO/SB/08), Paper No(s)/Mail Date :2/17/2005, 4/11/2005, 7/12/2007.

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of group I, claims 19-38 in the reply filed on 8/20/2007 is acknowledged.

2. Applicant's election without traverse of claim 20 as the alkyl aryl polyether alcohol type polymer or polyethylene glycol fatty acid ester species (interpreted as tyloxapol, contained in the claim) in the reply filed on 8/20/2007 is acknowledged.

3. Claims 39-40 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 8/20/2007.

Status of Claims

4. Claims 19-40 are pending. Claims 39-40 are withdrawn. Claims 19-38 are examined on the basis of the merits.

Priority

5. Applicant is advised of possible benefits Applicant is advised of possible benefits under 35 U.S.C. 119(a)-(d), wherein an application for patent filed in the United States may be entitled to the benefit of the filing date of a prior application filed in a foreign country.

6. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Acknowledgement is made of applicant's claim to foreign priority and the receipt of a copy of the application, JP2003-012427, filed 1/21/2003. However, since no

translation has been provided, prior art dates have been determined with reference to the priority date for the PCT application date, PCT/JP04/00350, filed 1/16/2004.

Oath/Declaration

7. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:
It was not executed in accordance with either 37 CFR 1.66 or 1.68.

The oath or declaration contains no signatures of the inventors with date signed

Claim Rejections - 35 USC § 102

8. 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 –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (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.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

9. Claims 19-24 and 31 are rejected under 35 U.S.C. 102(b) as being anticipated by Gamache, et al. (WO 01/15677 A2; 03/2001).

Gamache teaches all of the components of the claims: compositions for otic and intranasal use (p.6, lines 5-6) that contain a combination of a 5-HT agonist and an anti-

inflammatory agent (p. 6, lines 1-4; p. 12 lines 9-10) or alternatively sequential or concurrent dosing of separate compositions that contain the 5-HT antagonist in one composition and the anti-inflammatory agent in a second composition (p. 12, lines 9-11); specifically claimed is the anti-inflammatory specie bromfenac (the first compound of instant claim 19; claim 11;); typical concentrations of anti-inflammatory agents, such as bromfenac, are taught in the range 0.01-1.0 % (w/v) (overlapping with 0.01-0.5; p. 13, lines 6-8); aqueous formulations are preferred (p. 10, lines 11-14); tyloxapol is taught at the concentration of 0.05 % (w/v) (p. 16, line 30). It is noted that claim 21 and further dependent claims limit the options for the salt of bromfenac to the sodium salt, and that the specific concentrations recited in dependent claims apply to the sodium salt; the other options (bromfenac or a hydrate of bromfenac) are still viable choices that are part of the claims 21 and dependent claims (which depend on and include the options of claim 20). Gamache anticipates 1) the claim to bromfenac in the concentration range of claim 20 (which is also an option of claims 21-24 and 31). 2) The form of bromfenac in solution will be the same when the acid is dissolved in a solution followed by adjustment to the desired pH with NaOH/HCl (Gamache, p. 15, line 33) as when the sodium salt is dissolved in solution adjusted to the same pH; for this case Gamache also anticipates the sodium salt limitation of claim 21, albeit not the sodium salt concentration limitation of claim 22 and further dependent claims, since the claim is drawn to an aqueous liquid preparation, irrespective of how it is prepared.

10. Claim 19 is rejected under 35 U.S.C. 102(b) as being anticipated by Dobrozsi (US 6,319,513 B1; 11/2001).

Dobrozsi teaches aqueous liquid compositions comprising a pharmaceutically active agent selected from a group that includes analgesics (abstract); a specie taught is bromfenac (column 10, line 11); tyloxapol is taught at 0.15 and 0.035 % (Example 10).

11. Claims 19-38 are rejected under 35 U.S.C. 102(e) as being anticipated by Sawa (US 2007/0082857 A1; priority date 11/2003).

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

Sawa teaches the elements of the claims: aqueous solution preparations comprising an aminoglycoside antibiotic and bromfenac or a salt of bromfenac (abstract); bromfenac sodium and bromfenac sodium hydrate is taught at 0.1 and 0.2 % (Tables 1, 3, 6, 9-15); tyloxapol at 0.3 % resulted in solutions that were clear, when the control (no additive) was turbid (Table 5, 8), tyloxapol is also taught at 0,02 % (Table 15); additives taught include benzalkonium chloride (Table 8), boric acid (Tables 9, 12), sodium edentate (Table 15), and sodium hydroxide (Table 15); pH values include 7.5, 7.8 and 8.0 (Tables 9-15); eye drop formulations are also taught (Examples 1-7). It is noted that the aqueous preparations contain an active ingredient not in the instant

claims. However, Sawa still anticipates the instant claims, due to the open language construction of the claims (use of "comprising").

12. Applicant cannot rely upon the foreign priority papers to overcome this rejection because a translation of said papers has not been made of record in accordance with 37 CFR 1.55. See MPEP § 201.15.

Claim Rejections - 35 USC § 103

13. 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.

14. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

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

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

16. Claims 19-29, 31-34, and 36-38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gamache, et al. (WO 01/15677 A2; 03/2001) and ISTA Pharmaceuticals ("New Drug Applications: Xibrom", http://www.drugs.com/nda/xibrom_040525.html, accessed online 9/19/2007) or Nolan, et al. ("The topical anti-inflammatory and analgesic properties of bromfenic in rodents:; Agents and Actions; 1988 Aug; 25(1-2):77-85, abstract).

Claims 19-24 and 31 are rejected as outlined above. With respect to claims 21-38 (claims 21-24 and 31, with respect to the sodium salt of bromfenic and associated concentrations), in addition to the points made above, Gamache also teaches the additives and pH of the instant claims, edetate disodium, benzylalkonium chloride, sodium hydroxide, and a pH of 7.3-7.4 (Example 2); polyvinyl pyrrolidone (p. 14, line 5); and sodium borate buffer (p. 13, line 11). Gamache does not specifically teach the sodium salt of bromfenic, nor a hydrate, nor the concentration range or specific bromfenic sodium concentrations of 0.05-0.2, or at 0.1 or 0.2 %, nor the tyloxapol concentrations of 0.02 or 0.3 %. The ISTA Pharmaceuticals news release demonstrates that products containing 0.1 % bromfenac sodium acquired US marketing rights for Xibrom in May 2002 (were known by others in this country before applicant's priority date, a 35 USC 102(a) date). Nolan teaches bromfenac (the sodium salt, sesquihydrate form) was effective as a topical analgesic at concentrations of 0.1-0.32 % in mice and more potent than the other drugs tested (abstract). It would have been

obvious for one of ordinary skill in the art at the time of the invention to select concentrations of bromfenac sodium, sesquihydrate of 0.1, about 0.2 and about 0.32 %, in the invention of Gamache, since these values have demonstrated efficacy for topical use. It would have been obvious to adjust the concentration of tyloxapol, to see what the effect would be on the solubility and stability of the aqueous preparations, which would have resulted in the effective concentrations of the instant claims. It would also have been obvious to adjust the pH to values in the 7.5 to 8.5 range, with the potential of dissolving and/or stabilizing more of the acidic drug, bromfenic, in a more aqueous soluble ionic form. The motivation would have been to prepare pharmaceutical products with optimal drug dosage and stability.

17. Claims 19-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yakuji Nippo Ltd. ("New Drugs in Japan"; 2001; English translation provided; IDS Reference AP) and Xia (US 6,369,112 B1).

Yakuji Nippo teaches a bromfenac sodium sesquihydrate ophthalmic formulation that contains: 0.1% (w/v) bromfenac (items 1-3); boric acid buffer, sodium sulfite, disodium eentate, polyvinylpyrrolidone, and benzalkonium chloride (item 2, additives); a pH of 8.0-8.6 (item 2, pH). Yakuji Nippo does not teach tyloxapol. Xia teaches a solution useful for contact lenses that provides enhanced cleaning and disinfecting efficacy of the contact lens (abstract), which contains tyloxapol as one of three ingredients (abstract; column 3, lines 7-21); tyloxapol is taught at concentrations of 0.25 and 0.025 (about 0.02 and 0.3; Table 1). Xia teaches the addition of tyloxapol to the solution improves the stability and therefore the disinfecting efficacy over time of the

active component (column 7, lines 8-18). It would have been obvious to one of ordinary skill in the art at the time of the invention to add tyloxapol to the ophthalmic formulation of Yakuji Nippo. The motivation to do so is that taught by Xia, the stability enhancing effect of this component on the active ingredient. There would have been an expectation of success, since tyloxapol has demonstrated efficacy with the contact lens cleaning solutions.

18. Claim19-38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yakuji Nippo Ltd. ("New Drugs in Japan"; 2001; English translation provided; IDS Reference AP) and Xia (US 6,369,112 B1) as applied to claims 19-30 above, and further in view of Nolan, et al. ("The topical anti-inflammatory and analgesic properties of bromfenic in rodents:; Agents and Actions; 1988 Aug; 25(1-2):77-85, abstract).

Neither Yakuji Nippo or Xia teach the bromfenac sodium hydrate solutions at a bromfenac concentration of 0.2 %. Nolan teaches topical solutions are efficacious in the concentration range of 0.1-0.32 %. It would have been obvious to one of ordinary skill in the art at the time of the invention to use a concentration of about 0.2% bromfenic sodium hydrate (right in the middle of the range Nolan teaches is effective), in the modified Yakuji Nippo ophthalmic solution with tyloxapol added. The motivation to use a higher bromfenac concentration would be to provide an option of a more concentrated solution for patients in cases where a physician determines that higher anti-inflammatory concentration is desirable, such as when the lower dosage does not completely relieve the inflammation or pain.

Double Patenting

19. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

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

20. Claims 19-38 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-43 of copending Application No. 11/755662. Although the conflicting claims are not identical, they are not patentably distinct from each other because the copending application contains claims drawn to method of treating pain and/or inflammation associated with an ocular condition, by administering the aqueous solutions of the instant claims. It would have been obvious to one of ordinary skill in the art at the time of the invention to use the formulations of the instant claims in the methods of the copending application, since the claims recite that the formulations are eye drops, and the instant abstract also teaches some of the conditions treated of the copending application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

21. No claim is allowed.

22. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Timothy P. Thomas whose telephone number is (571) 272-8994. The examiner can normally be reached on Monday-Thursday 6:30 a.m. - 5:00 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on (571) 272-0718. 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.

/TPT/

Timothy P. Thomas
Patent Examiner

9/22/07
ARDIN H. MARSCHEL
SUPERVISORY PATENT EXAMINER

Sheet 1 of 1 | INFORMATION DISCLOSURE STATEMENT | DT12 Rec'd PCT/PTO 17 FEB 2005

FORM PTO 1449 (*modified*)

U.S. DEPARTMENT OF COMMERCE
PATENT AND TRADEMARK OFFICE

LIST OF REFERENCES CITED BY APPLICANT(S)
(*Use several sheets if necessary*)

Date Submitted to PTO: February 17, 2005

ATTY DOCKET NO.	SERIAL NO.
2005_0232A	NEW 10/525006

APPLICANT	
Shirou SAWA et al.	
FILING DATE	**GROUP**
February 17, 2005	

U.S. PATENT DOCUMENTS

*EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE
	AA						
	AB						
	AC						
	AD						

FOREIGN PATENT DOCUMENTS

		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION YES	TRANSLATION NO
	AE	9-503791	4/1997	JP				
	AF	2-124817	5/1990	JP				
	AG	1-104023	4/1989	JP				
	AH	00/59475	10/2000	WO				
	AI	11-228404	8/1999	JP	copies not provided			
	AJ							
	AK							
	AL							

OTHER DOCUMENT(S) (*Including Author, Title, Date, Pertinent Pages, Etc.*)

	AM	
	AN	
	AO	

EXAMINER	/Timothy Thomas/	DATE CONSIDERED	09/19/2007

*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 form with next communication to applicant.

Sheet 1 of 1 — INFORMATION DISCLOSURE STATEMENT

FORM PTO 1449 (*modified*)

U.S. DEPARTMENT OF COMMERCE
PATENT AND TRADEMARK OFFICE

LIST OF REFERENCES CITED BY APPLICANT(S)
(*Use several sheets if necessary*)

Date Submitted to PTO: April 11, 2005

ATTY DOCKET NO.	SERIAL NO.
2005_0232A	10/525,006

APPLICANT: Shirou SAWA et al.

FILING DATE	GROUP
February 17, 2005	

U.S. PATENT DOCUMENTS

*EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE
/T.P.T./	AA	5,603,929	2/1997	Desai et al.			Corresponds to Ref AH
	AB	5,653,972	8/1997	Desai et al.			Corresponds to Ref AH
	AC	4,910,225	3/1990	Ogawa et al.			Corresponds to Ref AI
	AD	5,110,493	5/1992	Cherng-Chyi et al.			Corresponds to Ref AJ
	AE	6,383,471	5/2002	Chen et al.			Corresponds to Ref AK
	AF	4,045,576	8/1977	Welstead, Jr. et al.			Corresponds to Ref AM
	AG	4,683,242	7/1987	Poser			Corresponds to Ref AN

FOREIGN PATENT DOCUMENTS

		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION YES NO.
	AH	~~9-503791~~	4/1997	JP			
	AI	2-124817	5/1990	JP			
	AJ	1-104023	4/1989	JP			
	AK	00/59475	10/2000	~~WO~~	copies not provided		
/T.P.T./	AL	11-228404	8/1999	JP			Yes
/T.P.T./	AM	5-223052	8/1993	JP			Abstract
	~~AN~~	~~62-126124~~	~~6/1987~~	~~JP~~	not in English		No
	AO						

OTHER DOCUMENT(S) (*Including Author, Title, Date, Pertinent Pages, Etc.*)

/T.P.T./	AP	New Drugs in Japan, 2001, 2001 Edition, Published by Yakuji Nippo Ltd., May 11, 2001, pp. 27-29, and its English translation of the material portions.
	AQ	

EXAMINER	/Timothy Thomas/	DATE CONSIDERED	09/19/2007

*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.

Sheet 1 of 1 — INFORMATION DISCLOSURE STATEMENT

FORM PTO 1449 (*modified*)

U.S. DEPARTMENT OF COMMERCE
PATENT AND TRADEMARK OFFICE

LIST OF REFERENCES CITED BY APPLICANT(S)
(*Use several sheets if necessary*)

Date Submitted to PTO: July 12, 2007

ATTY DOCKET NO.	SERIAL NO.
2005_0232A	10/525,006

APPLICANT: Shirou SAWA et al.

FILING DATE	GROUP
March 28, 2005	1609

OIPE IAP92 JUL 12 2007 PATENT & TRADEMARK OFFICE

U.S. PATENT DOCUMENTS

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

FOREIGN PATENT DOCUMENTS

		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION YES	TRANSLATION NO
/T.P.T./	AJ	96/14829	5/1996	WO				
	AK							
	AL							
	AM							
	AN							

OTHER DOCUMENT(S) (*Including Author, Title, Date, Pertinent Pages, Etc.*)

	AO	
	AP	
	AQ	

EXAMINER	/Timothy Thomas/	DATE CONSIDERED	09/19/2007

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

Notice of References Cited	Application/Control No. 10/525,006	Applicant(s)/Patent Under Reexamination SAWA ET AL.	
	Examiner Timothy P. Thomas	Art Unit 1614	Page 1 of 1

U.S. PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Name	Classification
*	A	US-6,319,513	11-2001	Dobrozsi, Douglas Joseph	424/434
*	B	US-2007/0082857 A1	04-2007	Sawa, Shirou	514/035
*	C	US-6,369,112	04-2002	Xia, Erning	514/635
	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	WO 01/15677 A2	03-2001	PCT/US	Gamache, et al.	A61K 31/00
	O					
	P					
	Q					
	R					
	S					
	T					

NON-PATENT DOCUMENTS

*		Include as applicable: Author, Title Date, Publisher, Edition or Volume, Pertinent Pages)
	U	ISTA Pharmaceuticals; "New Drug Applications: Xibrom", http://www.drugs.com/nda/xibrom_040525.html, accessed online 9/19/2007
	V	Nolan, et al.; "The topical anti-inflammatory and analgesic properties of bromfenic in rodents:; Agents and Actions; 1988 Aug; 25(1-2):77-85, abstract
	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.

OIPE IAP97 AUG 20 2007 PATENT & TRADEMARK OFFICE

IPW

THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of	:	**Confirmation No. 1756**
Shirou SAWA et al.	:	Attorney Docket No. 2005_0232A
Serial No. 10/525,006	:	Group Art Unit 1614
Filed March 28, 2005	:	Examiner Timothy P. Thomas
AQUEOUS LIQUID PREPARATION CONTAINING 2-AMINO-3-(4-BROMOBENZOYL)PHENYLACETIC ACID	:	**Mail Stop: Amendment**

RESPONSE

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

Sir:

This is responsive to the Official Action dated July 24, 2007.

The Official Action constitutes a requirement for restriction and a species requirement.

Applicants elect to prosecute the invention of Group I, claims 19-38.

Applicants elect claim 20 as the single species.

The claims readable on the elected species are claims 19-40.

Favorable action on the merits is solicited.

Respectfully submitted,

Shirou SAWA et al.

By: Warren Cheek

Warren M. Cheek, Jr.
Registration No. 33,367
Attorney for Applicants

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August 20, 2007

UNITED STATES PATENT AND TRADEMARK OFFICE

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www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/525,006	03/28/2005	Shirou Sawa	2005_0232A	1756

513 7590 07/24/2007

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EXAMINER	
THOMAS, TIMOTHY P	
ART UNIT	**PAPER NUMBER**
1614	

MAIL DATE	DELIVERY MODE
07/24/2007	PAPER

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

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

Office Action Summary	Application No.	Applicant(s)	
	10/525,006	SAWA ET AL.	
	Examiner	Art Unit	
	Timothy P. Thomas	1614	

-- 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 *04 June 2007*.

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

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

Disposition of Claims

4)☒ Claim(s) *19-40* is/are pending in the application.

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

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

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

8)☒ Claim(s) *19-40* 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

Status of Application

1. Acknowledgement of a second set of preliminary amendments to the claims, filed 4/3/2007, is made. Claims 1-18 are cancelled. New claims 19-40 have been added and are pending.

2. The previous restriction requirement is modified as follows for application to the 4/3/2007 set of claims.

Election/Restrictions

3. Restriction is required under 35 U.S.C. 121 and 372.

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 accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

Group I, claim(s) 19-38, drawn to an aqueous liquid preparation.

Group II, claim(s) 39, drawn to a method for stabilizing 2-amino-3-(4-bromobenzoyl)phenylacetic acid in an aqueous liquid preparation.

Group III, claim(s) 40, drawn to a method for inhibiting decrease in preservative effect of a preservative.

The inventions listed as Groups I-III 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 features for the following reasons: the technical feature common to the claims is 2-amino-3-(4-bromobenzoyl)phenylacetic acid (bromfenac) with a second component (an alkyl aryl polyether alcohol type polymer or a polyethylene glycol fatty acid ester) in an aqueous liquid preparation. Desai et al. (WO 96/14829; IDS Ref. AJ) teaches aqueous ophthalmic compositions (example 1) consisting of, inter alia, bromfenac (claim 5), with optional components, including tyloxapol (an alkyl aryl

polyether alcohol type polymer (p.4, line 29). Since the technical feature has previously been disclosed, there is no unifying corresponding technical feature.

4. This application contains claims directed to more than one species of the generic invention. These species are deemed to lack unity of invention because they are not so linked as to form a single general inventive concept under PCT Rule 13.1.

The species are as follows:

A single disclosed alkyl aryl polyether alcohol type polymer or polyethylene glycol fatty acid ester (e.g., tyloxapol or polyethylene glycol monostearate)

Applicant is required, in reply to this action, to elect a single species to which the claims shall be restricted if no generic claim is finally held to be allowable. The reply must also identify the claims readable on the elected species, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered non-responsive unless accompanied by an election.

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

5. The claims are deemed to correspond to the species listed above in the following manner:

tyloxapol (claims 20-40)
polyethylene glycol monostearate (claims 39-40)

The following claim(s) are generic: Claim 19.

6. The species listed above do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, the species lack the same or corresponding special technical features for the following reasons: As outlined above, tyloxapol has been disclosed in aqueous compositions containing bromfenac by Desai. While both may be useful as stabilizers, the species fall within different types of compounds with different chemical structures and chemical properties.

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

The election of an invention or species may be made with or without traverse. To reserve a right to petition, the election must be made with traverse. If the reply does not distinctly and specifically point out supposed errors in the restriction requirement, the election shall be treated as an election without traverse.

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

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

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Timothy P. Thomas whose telephone number is (571) 272-8994. The examiner can normally be reached on Monday-Thursday 6:30 a.m. - 5:00 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on (571) 272-0718. 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.

/TPT/
Timothy P. Thomas
Patent Examiner

Frederick Krass
Primary Examiner
Art Unit 1614

OIPE IAP97 JUL 12 2007 PATENT & TRADEMARK OFFICE

IFW

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of	:	**Confirmation No. 1756**
Shirou SAWA et al.	:	Attorney Docket No. 2005_0232A
Serial No. 10/525,006	:	Group Art Unit 1609
Filed March 28, 2005	:	Examiner Timothy P. Thomas

AQUEOUS LIQUID PREPARATION CONTAINING 2-AMINO-3-(4-BROMOBENZOYL)PHENYLACETIC ACID

Mail Stop: Amendment

SECOND SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT

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

Sir:

Pursuant to the provisions of 37 CFR 1.56, 1.97 and 1.98, Applicants request consideration of the references listed on attached form PTO-1449 and any additional information identified below in paragraph 3. A legible copy of each reference listed on the Form PTO-1449 is enclosed, except a copy is not provided for:

[X] each U.S. Patent and U.S. Patent application publication;

[] each reference previously cited in the international application PCT/_____; and/or

[] each reference previously cited in prior parent application Serial No. _____.

1a. [X] This Information Disclosure Statement is submitted:

within three months of the filing date (or of entry into the National Stage) of the above-entitled application, **or**

before the mailing of a first Office Action on the merits or the mailing of a first Office Action after the filing of an RCE,

and thus no certification and/or fee is required.

1b. [] This Information Disclosure Statement is submitted

after the events of above paragraph 1a and prior to the mailing date of a final Office Action or a Notice of Allowance or an action which otherwise closes prosecution in the application, and thus:

(1) [] the certification of paragraph 2 below is provided, **or**

(2) [] the fee of $180.00 specified in 37 CFR 1.17(p) is enclosed.

1c. [] This Information Disclosure Statement is submitted:

after the mailing date of a final Office Action or Notice of Allowance or action which otherwise closes prosecution in the application, and prior to payment of the issue fee, and thus:

the certification of paragraph 2 below is provided, and

the fee of $180.00 specified in 37 CFR 1.17(p) is enclosed.

2. It is hereby certified

a. [] that each item of information contained in this Information Disclosure Statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of the Statement, or

b. [] that no item of information contained in the Information Disclosure Statement was cited in a communication from a foreign patent office in a counterpart foreign application and, to the knowledge of the person signing the certification after making reasonable inquiry, was known to any individual designated in §1.56(c) more than three months prior to the filing of the Statement.

3. [] Consideration of the following list of additional information (including any copending or abandoned U.S. application, prior uses and/or sales, etc.) is requested.

4. For each non-English language reference listed on the attached form PTO-1449, reference is made to:

   a. [] a full or partial English language translation submitted herewith,

   b. [X] a foreign patent office search report (in the English language) submitted herewith,

   c. [] the concise explanation contained in the specification of the present application at page,

   d. [] the concise explanation set forth in the attached English language abstract,

   e. [] the concise explanation set forth below or on a separate sheet attached to the reference:

5. [X] A foreign patent office search report citing one or more of the references is enclosed.

6. [] Statement Under 37 CFR 1.704(d)

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

Respectfully submitted,

Shirou SAWA et al.

By _____
Warren M. Cheek, Jr.
Registration No. 33,367
Attorney for Applicants

WMC/dlk
Washington, D.C. 20006-1021
Telephone (202) 721-8200
Facsimile (202) 721-8250
July 12, 2007

Sheet 1 of 1 | INFORMATION DISCLOSURE STATEMENT

FORM PTO 1449 (*modified*)

U.S. DEPARTMENT OF COMMERCE
PATENT AND TRADEMARK OFFICE

LIST OF REFERENCES CITED BY APPLICANT(S)
(Use several sheets if necessary)

Date Submitted to PTO: July 12, 2007

ATTY DOCKET NO.	SERIAL NO.
2005_0232A	10/525,006

APPLICANT: Shirou SAWA et al.

FILING DATE	GROUP
March 28, 2005	1609

OIPE IAP97 JUL 12 2007 PATENT & TRADEMARK OFFICE

U.S. PATENT DOCUMENTS

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

FOREIGN PATENT DOCUMENTS

		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION YES	TRANSLATION NO
	AJ	96/14829	5/1996	WO				
	AK							
	AL							
	AM							
	AN							

OTHER DOCUMENT(S) *(Including Author, Title, Date, Pertinent Pages, Etc.)*

	AO	
	AP	
	AQ	

EXAMINER	DATE CONSIDERED

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

INTERNATIONAL SEARCH REPORT

Int ional Application No
PCT/US 95/14910

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 A61K9/00 A61K47/18

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.
A	EP,A,0 306 984 (SYNTEX INC.,U.S.A.) 15 March 1989 cited in the application see the whole document ---	1-26
A	WO,A,94 15597 (ALLERGAN INC.,U.S.A.) 21 July 1994 cited in the application see the whole document ---	1-26
A	US,A,4 960 799 (I.E.NAGY) 2 October 1990 cited in the application see the whole document ---	1-26

-/--

[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
7 March 1996	22.03.96

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	Scarponi, U

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

INTERNATIONAL SEARCH REPORT

Int ional Application No
PCT/US 95/14910

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	EP,A,0 076 136 (ALCON LABORATORIES INC.,U.S.A.) 6 April 1983 cited in the application see the whole document see claims see examples -----	1-26

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

INTERNATIONAL SEARCH REPORT

national application No.
PCT/US95/14910

Box I Observations where certain claims were found unsearchable (Continuation of item 1 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. [X] Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
Remark: Although claims 20-24 are directed to a method of treatment of the human/animal body by therapy (Rule 39.1 (iv) PCT), the search has been carried out and based on the alleged effects of the composition.

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 II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

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

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 searches without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

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.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

Form PCT/ISA/210 (continuation of first sheet (1)) (July 1992)

INTERNATIONAL SEARCH REPORT

Int ·onal Application No
PCT/US 95/14910

Patent document cited in search report	Publication date	Patent family member(s)		Publication date
EP-A-306984	15-03-89	AU-B-	2204288	16-03-89
		CA-A-	1328614	19-04-94
		DE-A-	3870111	21-05-92
		FI-B-	94924	15-08-95
		IE-B-	60717	10-08-94
		JP-A-	1104023	21-04-89
		JP-B-	6096542	30-11-94
		NO-B-	175404	04-07-94
		US-A-	5414011	09-05-95
		US-A-	5110493	05-05-92
WO-A-9415597	21-07-94	AU-B-	6021794	15-08-94
US-A-4960799	02-10-90	NONE		
EP-A-76136	06-04-83	US-A-	4407791	04-10-83
		AU-B-	557817	08-01-87
		AU-B-	9050382	08-04-83
		CA-A-	1194421	01-10-85
		WO-A-	8301003	31-03-83
		US-A-	4525346	25-06-85

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

OIPE IAP97
JUN 04 2007
PATENT & TRADEMARK OFFICE

IFW

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of	:	**Confirmation No. 1756**
Shirou SAWA et al.	:	Attorney Docket No. 2005_0232A
Serial No. 10/525,006	:	Group Art Unit 1609
Filed March 28, 2005	:	Examiner Timothy P. Thomas
AQUEOUS LIQUID PREPARATION CONTAINING 2-AMINO-3-(4-BROMOBENZOYL)PHENYLACETIC ACID	:	**Mail Stop: Amendment**

RESPONSE

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

Sir:

This is responsive to the Official Action dated May 23, 2007.

The Official Action constitutes a requirement for restriction of claims 1-18.

However, claims 1-18 were cancelled without prejudice and new claims 19-40 were added in a Second Preliminary Amendment dated April 3, 2007. A copy of the amendment is enclosed.

Accordingly, the Examiner is respectfully requested to issue a new restriction requirement. Favorable action on the merits is solicited.

Respectfully submitted,

Shirou SAWA et al.

By: _____
Warren M. Cheek, Jr.
Registration No. 33,367
Attorney for Applicants

WMC/dlk
Washington, D.C. 20006-1021
Telephone (202) 721-8200
Facsimile (202) 721-8250
June 4, 2007

THE COMMISSIONER IS AUTHORIZED TO CHARGE ANY DEFICIENCY IN THE FEES FOR THIS PAPER TO DEPOSIT ACCOUNT NO. 23-0975

OIPE IAP87
JUN 04 2007
PATENT & TRADEMARK OFFICE

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of	:	**Confirmation No. 1756**
Shirou SAWA et al.	:	Attorney Docket No. 2005_0232A
Serial No. 10/525,006	:	Group Art Unit 1615
Filed March 28, 2005	:	Examiner **Not Yet Assigned**
AQUEOUS LIQUID PREPARATION CONTAINING 2-AMINO-3-(4-BROMOBENZOYL)PHENYLACETIC ACID	:	**Mail Stop: Amendment**

SECOND SUPPLEMENTAL PRELIMINARY AMENDMENT

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

Sir:

Please amend the above-identified application as follows:

COPY

Amendments to the Claims

1-18. (Cancelled)

19. (Previously presented) An aqueous liquid preparation comprising 2-amino-3-(4-bromobenzoyl)phenylacetic acid or a pharmacologically acceptable salt thereof or a hydrate thereof, and an alkyl aryl polyether alcohol type polymer or a polyethylene glycol fatty acid ester.

20. (Previously presented) The aqueous liquid preparation according to claim 19, wherein the alkyl aryl polyether alcohol type polymer is tyloxapol;

wherein the concentration of the tyloxapol is selected from a range of about 0.01 w/v % to about 0.5 w/v %; and

wherein the concentration of the 2-amino-3-(4-bromobenzoyl)phenylacetic acid or a pharmacologically acceptable salt thereof or a hydrate thereof is selected from a range of about 0.01 to about 0.5 w/v %.

21. (Previously presented) The aqueous liquid preparation according to claim 20, wherein the pharmacologically acceptable salt of 2-amino-3-(4-bromobenzoyl)phenylacetic acid is a sodium salt.

22. (Previously presented) The aqueous liquid preparation according to claim 21, wherein the concentration of the 2-amino-3-(4-bromobenzoyl)phenylacetic acid sodium salt is selected from a range of about 0.05 to about 0.2 w/v %.

23. (Previously presented) The aqueous liquid preparation according to claim 22, wherein the concentration of the tyloxapol is selected from a range of about 0.01 w/v % to about 0.3 w/v %.

24. (Previously presented) The aqueous liquid preparation according to claim 23, wherein the concentration of the 2-amino-3-(4-bromobenzoyl)phenylacetic acid sodium salt is about 0.1 w/v %.

25. (Previously presented) The aqueous liquid preparation according to claim 24, wherein the concentration of the tyloxapol is about 0.02 w/v %.

26. (Previously presented) The aqueous liquid preparation according to claim 25, wherein the formulation further includes one or more additives selected from the group consisting of a preservative, buffer, thickener, stabilizer, chelating agent, and pH controlling agent.

27. (Previously presented) The aqueous liquid preparation according to claim 26, wherein said preservative is benzalkonium chloride; wherein said buffer is boric acid and/or sodium borate; wherein said thickener is polyvinylpyrrolidone; wherein said stabilizer is sodium sulfite; wherein said chelating agent is sodium edetate; and wherein said pH controlling agent is sodium hydroxide.

28. (Previously presented) The aqueous liquid preparation according to claim 27, wherein the pH is from about 7 to about 9.

29. (Previously presented) The aqueous liquid preparation according to claim 28, wherein the pH is from about 7.5 to about 8.5.

30. (Previously presented) The aqueous liquid preparation according to claim 27, wherein said liquid preparation is in the form of an eye drop.

31. (Previously presented) The aqueous liquid preparation according to claim 23, wherein the concentration of the 2-amino-3-(4-bromobenzoyl)phenylacetic acid sodium salt is about 0.2 w/v %.

32. (Previously presented) The aqueous liquid preparation according to claim 31, wherein the concentration of the tyloxapol is about 0.3 w/v %.

33. (Previously presented) The aqueous liquid preparation according to claim 32, wherein the formulation further includes one or more additives selected from the group consisting of a preservative, buffer, thickener, stabilizer, chelating agent, and pH controlling agent.

34. (Previously presented) The aqueous liquid preparation according to claim 33, wherein said preservative is benzalkonium chloride; wherein said buffer is boric acid and/or sodium borate; wherein said thickener is polyvinylpyrrolidone; wherein said stabilizer is sodium sulfite; wherein said chelating agent is sodium edetate; and wherein said pH controlling agent is sodium hydroxide.

35. (Previously presented) The aqueous liquid preparation according to claim 34, wherein said liquid preparation is in the form of an eye drop.

36. (Previously presented) The aqueous liquid preparation according to claim 31, wherein the concentration of the tyloxapol is about 0.02 w/v %.

37. (Currently amended) The aqueous liquid preparation according to claim 36, wherein the formulation further includes one or more additives selected from the group consisting of a preservative, buffer, thickener, stabilizer, chelating agent, and pH controlling agent.

38. (Previously presented) The aqueous liquid preparation according to claim 37, wherein said preservative is benzalkonium chloride; wherein said buffer is boric acid and/or sodium borate; wherein said thickener is polyvinylpyrrolidone; wherein said chelating agent is sodium edetate; and wherein said pH controlling agent is sodium hydroxide.

39. (Previously presented) A method for stabilizing 2-amino-3-(4-bromobenzoyl)phenylacetic acid or a pharmacologically acceptable salt thereof or a hydrate thereof in an aqueous liquid preparation, which comprises incorporating tyloxapol or polyethylene glycol monostearate into an aqueous liquid preparation containing 2-amino-3-(4-bromobenzoyl)phenylacetic acid or a pharmacologically acceptable salt thereof or a hydrate thereof.

40. (Previously presented) A method for inhibiting decrease in preservative effect of a preservative in an aqueous liquid preparation of 2-amino-3-(4-bromobenzoyl)phenylacetic acid or a pharmacologically acceptable salt thereof or a hydrate thereof, which comprises incorporating tyloxapol or polyethylene glycol monostearate into an aqueous liquid preparation containing 2-amino-3-(4-bromobenzoyl)phenylacetic acid or a pharmacologically acceptable salt thereof or a hydrate thereof and a preservative.

REMARKS

Claim 37 has been amended to correct an inadvertent omission.

Favorable action on the merits is solicited.

Respectfully submitted,

Shirou SAWA et al.

By: _____
Warren M. Cheek, Jr.
Registration No. 33,367
Attorney for Applicants

WMC/dlk
Washington, D.C. 20006-1021
Telephone (202) 721-8200
Facsimile (202) 721-8250
April 3, 2007

UNITED STATES PATENT AND TRADEMARK OFFICE

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

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/525,006	03/28/2005	Shirou Sawa	2005_0232A	1756

513 7590 05/23/2007

WENDEROTH, LIND & PONACK, L.L.P.
2033 K STREET N. W.
SUITE 800
WASHINGTON, DC 20006-1021

EXAMINER	
THOMAS, TIMOTHY P	
ART UNIT	**PAPER NUMBER**
1609	
MAIL DATE	**DELIVERY MODE**
05/23/2007	PAPER

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

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

Office Action Summary	Application No.	Applicant(s)	
	10/525,006	SAWA ET AL.	
	Examiner	Art Unit	
	Timothy P. Thomas	1609	

-- 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 *17 February 2005*.

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) *1-18* 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) *1-18* 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

1. Restriction is required under 35 U.S.C. 121 and 372.

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 accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

Group I, claim(s) 1-16, drawn to an aqueous liquid preparation.

Group II, claim(s) 17, drawn to a method for stabilizing 2-amino-3-(4-bromobenzoyl) phenylacetic acid.

Group III, claim(s) 18, drawn to a method for inhibiting decrease in preservative effect of a preservative in an aqueous liquid preparation of 2-amino-3-(4-bromobenzoyl) phenylacetic acid.

2. The inventions listed as Groups I-III 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 features for the following reasons: the technical feature common to all the claims is the sodium salt/hydrate of 2-amino-3-(4-bromobenzoyl) phenylacetic acid (also known as bromfenac sodium hydrate) in an aqueous liquid preparation. Such a preparation has been disclosed in "New Drugs in Japan, 2001" (translation of table (2), provided by applicant). Therefore, since the technical feature common to the claims was known in the art at the time of the invention, no corresponding special technical feature is present in the claims.

3. This application contains claims directed to more than one species of the generic invention. These species are deemed to lack unity of invention because they are not so linked as to form a single general inventive concept under PCT Rule 13.1.

The species are as follows:

The polymer additive selected from: a) tyloxapol (claims 3, 15, 17, 18); b) polyethylene glycol monostearate (claims 5, 16, 17, 18); c) any other alkyl aryl polyether alcohol type polymer, not in a) (claim 1); or d) any other polyethylene glycol fatty acid ester, not in b) (claim 1).

Applicant is required, in reply to this action, to elect a single species to which the claims shall be restricted if no generic claim is finally held to be allowable. The reply must also identify the claims readable on the elected species, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered non-responsive unless accompanied by an election.

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

4. The claims are deemed to correspond to the species listed above in the following manner:

a) claims 1-3, 6, 8-15, 17-18
b) claims 1, 4-5, 7-14, 16-18
c) claims 1-2, 6, 8-14
d) claims 1, 4, 7-14

The following claim(s) are generic: 1, 8-14.

5. The species listed above do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, the species lack the same or corresponding special technical features for the following reasons: the group of polymer additives does not constitute a proper Markush group, different core polymer repeating groups are represented by the different species or possible other choices, each of which

consist of a range of polymer compounds with different chemical and physical properties.

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

The election of an invention or species may be made with or without traverse. To reserve a right to petition, the election must be made with traverse. If the reply does not distinctly and specifically point out supposed errors in the restriction requirement, the election shall be treated as an election without traverse.

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

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

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Timothy P. Thomas whose telephone number is (703)

272-8994. The examiner can normally be reached on Monday-Thursday 6:30 a.m. - 5:00 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisors, Cecilia Tsang or Janet Andres can be reached on (571) 272-0562 or (571) 272-0867. 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.

VICKIE KIM
PRIMARY EXAMINER

Timothy Thomas
Timothy P. Thomas, Ph.D.
Patent Examiner

OIPE IAP97 APR 03 2007 PATENT & TRADEMARK OFFICE

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of	:	**Confirmation No. 1756**
Shirou SAWA et al.	:	Attorney Docket No. 2005_0232A
Serial No. 10/525,006	:	Group Art Unit 1615
Filed March 28, 2005	:	Examiner **Not Yet Assigned**
AQUEOUS LIQUID PREPARATION CONTAINING 2-AMINO-3-(4-BROMOBENZOYL)PHENYLACETIC ACID	:	**Mail Stop: Amendment**

SECOND SUPPLEMENTAL PRELIMINARY AMENDMENT

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

THE COMMISSIONER IS AUTHORIZED TO CHARGE ANY DEFICIENCY IN THE FEES FOR THIS PAPER TO DEPOSIT ACCOUNT NO. 23-0975

Sir:

Please amend the above-identified application as follows:

Amendments to the Claims

1-18. (Cancelled)

19. (Previously presented) An aqueous liquid preparation comprising 2-amino-3-(4-bromobenzoyl)phenylacetic acid or a pharmacologically acceptable salt thereof or a hydrate thereof, and an alkyl aryl polyether alcohol type polymer or a polyethylene glycol fatty acid ester.

20. (Previously presented) The aqueous liquid preparation according to claim 19, wherein the alkyl aryl polyether alcohol type polymer is tyloxapol;

wherein the concentration of the tyloxapol is selected from a range of about 0.01 w/v % to about 0.5 w/v %; and

wherein the concentration of the 2-amino-3-(4-bromobenzoyl)phenylacetic acid or a pharmacologically acceptable salt thereof or a hydrate thereof is selected from a range of about 0.01 to about 0.5 w/v %.

21. (Previously presented) The aqueous liquid preparation according to claim 20, wherein the pharmacologically acceptable salt of 2-amino-3-(4-bromobenzoyl)phenylacetic acid is a sodium salt.

22. (Previously presented) The aqueous liquid preparation according to claim 21, wherein the concentration of the 2-amino-3-(4-bromobenzoyl)phenylacetic acid sodium salt is selected from a range of about 0.05 to about 0.2 w/v %.

23. (Previously presented) The aqueous liquid preparation according to claim 22, wherein the concentration of the tyloxapol is selected from a range of about 0.01 w/v % to about 0.3 w/v %.

24. (Previously presented) The aqueous liquid preparation according to claim 23, wherein the concentration of the 2-amino-3-(4-bromobenzoyl)phenylacetic acid sodium salt is about 0.1 w/v %.

25. (Previously presented) The aqueous liquid preparation according to claim 24, wherein the concentration of the tyloxapol is about 0.02 w/v %.

26. (Previously presented) The aqueous liquid preparation according to claim 25, wherein the formulation further includes one or more additives selected from the group consisting of a preservative, buffer, thickener, stabilizer, chelating agent, and pH controlling agent.

27. (Previously presented) The aqueous liquid preparation according to claim 26, wherein said preservative is benzalkonium chloride; wherein said buffer is boric acid and/or sodium borate; wherein said thickener is polyvinylpyrrolidone; wherein said stabilizer is sodium sulfite; wherein said chelating agent is sodium edetate; and wherein said pH controlling agent is sodium hydroxide.

28. (Previously presented) The aqueous liquid preparation according to claim 27, wherein the pH is from about 7 to about 9.

29. (Previously presented) The aqueous liquid preparation according to claim 28, wherein the pH is from about 7.5 to about 8.5.

30. (Previously presented) The aqueous liquid preparation according to claim 27, wherein said liquid preparation is in the form of an eye drop.

31. (Previously presented) The aqueous liquid preparation according to claim 23, wherein the concentration of the 2-amino-3-(4-bromobenzoyl)phenylacetic acid sodium salt is about 0.2 w/v %.

32. (Previously presented) The aqueous liquid preparation according to claim 31, wherein the concentration of the tyloxapol is about 0.3 w/v %.

33. (Previously presented) The aqueous liquid preparation according to claim 32, wherein the formulation further includes one or more additives selected from the group consisting of a preservative, buffer, thickener, stabilizer, chelating agent, and pH controlling agent.

34. (Previously presented) The aqueous liquid preparation according to claim 33, wherein said preservative is benzalkonium chloride; wherein said buffer is boric acid and/or sodium borate; wherein said thickener is polyvinylpyrrolidone; wherein said stabilizer is sodium sulfite; wherein said chelating agent is sodium edetate; and wherein said pH controlling agent is sodium hydroxide.

35. (Previously presented) The aqueous liquid preparation according to claim 34, wherein said liquid preparation is in the form of an eye drop.

36. (Previously presented) The aqueous liquid preparation according to claim 31, wherein the concentration of the tyloxapol is about 0.02 w/v %.

37. (Currently amended) The aqueous liquid preparation according to claim 36, wherein the formulation further includes one or more additives selected from the group consisting of a preservative, buffer, thickener, stabilizer, chelating agent, and pH controlling agent.

38. (Previously presented) The aqueous liquid preparation according to claim 37, wherein said preservative is benzalkonium chloride; wherein said buffer is boric acid and/or sodium borate; wherein said thickener is polyvinylpyrrolidone; wherein said chelating agent is sodium edetate; and wherein said pH controlling agent is sodium hydroxide.

39. (Previously presented) A method for stabilizing 2-amino-3-(4-bromobenzoyl)phenylacetic acid or a pharmacologically acceptable salt thereof or a hydrate thereof in an aqueous liquid preparation, which comprises incorporating tyloxapol or polyethylene glycol monostearate into an aqueous liquid preparation containing 2-amino-3-(4-bromobenzoyl)phenylacetic acid or a pharmacologically acceptable salt thereof or a hydrate thereof.

40. (Previously presented) A method for inhibiting decrease in preservative effect of a preservative in an aqueous liquid preparation of 2-amino-3-(4-bromobenzoyl)phenylacetic acid or a pharmacologically acceptable salt thereof or a hydrate thereof, which comprises incorporating tyloxapol or polyethylene glycol monostearate into an aqueous liquid preparation containing 2-amino-3-(4-bromobenzoyl)phenylacetic acid or a pharmacologically acceptable salt thereof or a hydrate thereof and a preservative.

REMARKS

Claim 37 has been amended to correct an inadvertent omission.

Favorable action on the merits is solicited.

Respectfully submitted,

Shirou SAWA et al.

By: _____
Warren M. Cheek, Jr.
Registration No. 33,367
Attorney for Applicants

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April 3, 2007

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of	:	**Confirmation No. 1756**
Shirou SAWA et al.	:	Attorney Docket No. 2005_0232A
Serial No. 10/525,006	:	Group Art Unit 1615
Filed March 28, 2005	:	Examiner **Not Yet Assigned**
AQUEOUS LIQUID PREPARATION CONTAINING 2-AMINO-3-(4-BROMOBENZOYL)PHENYLACETIC ACID	:	**Mail Stop: Amendment**

THE COMMISSIONER IS AUTHORIZED TO CHARGE ANY DEFICIENCY IN THE FEE FOR THIS PAPER TO DEPOSIT ACCOUNT NO. 23-0975.

SUPPLEMENTAL PRELIMINARY AMENDMENT

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

Sir:

Please amend the above-identified application as follows:

Amendments to the Claims

1-18. (Cancelled)

19. (New) An aqueous liquid preparation comprising 2-amino-3-(4-bromobenzoyl)phenylacetic acid or a pharmacologically acceptable salt thereof or a hydrate thereof, and an alkyl aryl polyether alcohol type polymer or a polyethylene glycol fatty acid ester.

20. (New) The aqueous liquid preparation according to claim 19, wherein the alkyl aryl polyether alcohol type polymer is tyloxapol;

wherein the concentration of the tyloxapol is selected from a range of about 0.01 w/v % to about 0.5 w/v %; and

wherein the concentration of the 2-amino-3-(4-bromobenzoyl)phenylacetic acid or a pharmacologically acceptable salt thereof or a hydrate thereof is selected from a range of about 0.01 to about 0.5 w/v %.

21. (New) The aqueous liquid preparation according to claim 20, wherein the pharmacologically acceptable salt of 2-amino-3-(4-bromobenzoyl)phenylacetic acid is a sodium salt.

22. (New) The aqueous liquid preparation according to claim 21, wherein the concentration of the 2-amino-3-(4-bromobenzoyl)phenylacetic acid sodium salt is selected from a range of about 0.05 to about 0.2 w/v %.

23. (New) The aqueous liquid preparation according to claim 22, wherein the concentration of the tyloxapol is selected from a range of about 0.01 w/v % to about 0.3 w/v %.

24. (New) The aqueous liquid preparation according to claim 23, wherein the concentration of the 2-amino-3-(4-bromobenzoyl)phenylacetic acid sodium salt is about 0.1 w/v %.

25. (New) The aqueous liquid preparation according to claim 24, wherein the concentration of the tyloxapol is about 0.02 w/v %.

26. (New) The aqueous liquid preparation according to claim 25, wherein the formulation further includes one or more additives selected from the group consisting of a preservative, buffer, thickener, stabilizer, chelating agent, and pH controlling agent.

27. (New) The aqueous liquid preparation according to claim 26, wherein said preservative is benzalkonium chloride; wherein said buffer is boric acid and/or sodium borate; wherein said thickener is polyvinylpyrrolidone; wherein said stabilizer is sodium sulfite; wherein said chelating agent is sodium edetate; and wherein said pH controlling agent is sodium hydroxide.

28. (New) The aqueous liquid preparation according to claim 27, wherein the pH is from about 7 to about 9.

29. (New) The aqueous liquid preparation according to claim 28, wherein the pH is from about 7.5 to about 8.5.

30. (New) The aqueous liquid preparation according to claim 27, wherein said liquid preparation is in the form of an eye drop.

31. (New) The aqueous liquid preparation according to claim 23, wherein the concentration of the 2-amino-3-(4-bromobenzoyl)phenylacetic acid sodium salt is about 0.2 w/v %.

32. (New) The aqueous liquid preparation according to claim 31, wherein the concentration of the tyloxapol is about 0.3 w/v %.

33. (New) The aqueous liquid preparation according to claim 32, wherein the formulation further includes one or more additives selected from the group consisting of a preservative, buffer, thickener, stabilizer, chelating agent, and pH controlling agent.

34. (New) The aqueous liquid preparation according to claim 33, wherein said preservative is benzalkonium chloride; wherein said buffer is boric acid and/or sodium borate; wherein said thickener is polyvinylpyrrolidone; wherein said stabilizer is sodium sulfite; wherein said chelating agent is sodium edetate; and wherein said pH controlling agent is sodium hydroxide.

35. (New) The aqueous liquid preparation according to claim 34, wherein said liquid preparation is in the form of an eye drop.

36. (New) The aqueous liquid preparation according to claim 31, wherein the concentration of the tyloxapol is about 0.02 w/v %.

37. (New) The aqueous liquid according to claim 36, wherein the formulation further includes one or more additives selected from the group consisting of a preservative, buffer, thickener, stabilizer, chelating agent, and pH controlling agent.

38. (New) The aqueous liquid preparation according to claim 37, wherein said preservative is benzalkonium chloride; wherein said buffer is boric acid and/or sodium borate; wherein said thickener is polyvinylpyrrolidone; wherein said chelating agent is sodium edetate; and wherein said pH controlling agent is sodium hydroxide.

39. (New) A method for stabilizing 2-amino-3-(4-bromobenzoyl)phenylacetic acid or a pharmacologically acceptable salt thereof or a hydrate thereof in an aqueous liquid preparation, which comprises incorporating tyloxapol or polyethylene glycol monostearate into an aqueous liquid preparation containing 2-amino-3-(4-bromobenzoyl)phenylacetic acid or a pharmacologically acceptable salt thereof or a hydrate thereof.

40. (New) A method for inhibiting decrease in preservative effect of a preservative in an aqueous liquid preparation of 2-amino-3-(4-bromobenzoyl)phenylacetic acid or a pharmacologically acceptable salt thereof or a hydrate thereof, which comprises incorporating tyloxapol or polyethylene glycol monostearate into an aqueous liquid preparation containing 2-amino-3-(4-bromobenzoyl)phenylacetic acid or a pharmacologically acceptable salt thereof or a hydrate thereof and a preservative.

REMARKS

Claims 1-18 are cancelled without prejudice and new claims 19-40 are added. The new claims are supported by the original claims and the disclosure of the specification.

Favorable action on the merits is solicited.

Respectfully submitted,

Shirou SAWA et al.

By: _____
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March 20, 2007

JC10 Rec'd PCT/PTO 11 APR 2005

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of	:	
Shirou SAWA et al.	:	**Mail Stop: PCT**
Serial No. 10/525,006	:	Attorney Docket No. 2005_0232A
Filed February 17, 2005	:	

AQUEOUS LIQUID PREPARATION CONTAINING
2-AMINO-3-(4-BROMOBENZOYL)PHENYLACETIC ACID
[Corresponding to PCT/JP2004/000350
Filed January 16, 2004]

SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT

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

Sir:

Pursuant to the provisions of 37 CFR 1.56, 1.97 and 1.98, Applicants request consideration of the references listed on attached form PTO-1449 and any additional information identified below in paragraph 3. A legible copy of each reference listed on the Form PTO-1449 is enclosed, except a copy is not provided for:

[X] each U.S. Patent and U.S. Patent application publication;

[] each reference previously cited in the international application PCT/_____; and/or

[] each reference previously cited in prior parent application Serial No. _____.

1a. [X] This Information Disclosure Statement is submitted:

within three months of the filing date (or of entry into the National Stage) of the above-entitled application, **or**

before the mailing of a first Office Action on the merits or the mailing of a first Office Action after the filing of an RCE,

and thus no certification and/or fee is required.

1b. [] This Information Disclosure Statement is submitted

after the events of above paragraph 1a and prior to the mailing date of a final Office Action or a Notice of Allowance or an action which otherwise closes prosecution in the application, and thus:

(1) [] the certification of paragraph 2 below is provided, **or**

(2) [] the fee of $180.00 specified in 37 CFR 1.17(p) is enclosed.

1c. [] This Information Disclosure Statement is submitted:

after the mailing date of a final Office Action or Notice of Allowance or action which otherwise closes prosecution in the application, and prior to payment of the issue fee, and thus:

the certification of paragraph 2 below is provided, and

the fee of $180.00 specified in 37 CFR 1.17(p) is enclosed.

2. It is hereby certified

a. [] that each item of information contained in this Information Disclosure Statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of the Statement, or

b. [] that no item of information contained in the Information Disclosure Statement was cited in a communication from a foreign patent office in a counterpart foreign application and, to the knowledge of the person signing the certification after making reasonable inquiry, was known to any individual designated in §1.56(c) more than three months prior to the filing of the Statement.

3. [] Consideration of the following list of additional information (including any copending or abandoned U.S. application, prior uses and/or sales, etc.) is requested.

4. For each non-English language reference listed on the attached form PTO-1449, reference is made to:

   a. [] a full or partial English language translation submitted herewith,

   b. [] a foreign patent office search report (in the English language) submitted herewith,

   c. [] the concise explanation contained in the specification of the present application at page,

   d. [] the concise explanation set forth in the attached English language abstract,

   e. [] the concise explanation set forth below or on a separate sheet attached to the reference:

5. [X] Enclosed are English language references corresponding to the foreign language references cited in the International Search Report and specification.

Respectfully submitted,

Shirou SAWA et al.

By _____
Warren M. Cheek, Jr.
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April 11, 2005

Sheet 1 of 1 — INFORMATION DISCLOSURE STATEMENT

FORM PTO 1449 (*modified*)

U.S. DEPARTMENT OF COMMERCE
PATENT AND TRADEMARK OFFICE

LIST OF REFERENCES CITED BY APPLICANT(S)
(*Use several sheets if necessary*)

Date Submitted to PTO: April 11, 2005

ATTY DOCKET NO.	SERIAL NO.
2005_0232A	10/525,006

APPLICANT	
Shirou SAWA et al.	
FILING DATE February 17, 2005	**GROUP**

U.S. PATENT DOCUMENTS

*EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE
	AA	5,603,929	2/1997	Desai et al.			Corresponds to Ref AH
	AB	5,653,972	8/1997	Desai et al.			Corresponds to Ref AH
	AC	4,910,225	3/1990	Ogawa et al.			Corresponds to Ref AI
	AD	5,110,493	5/1992	Cherng-Chyi et al.			Corresponds to Ref AJ
	AE	6,383,471	5/2002	Chen et al.			Corresponds to Ref AK
	AF	4,045,576	8/1977	Welstead, Jr. et al.			Corresponds to Ref AM
	AG	4,683,242	7/1987	Poser			Corresponds to Ref AN

FOREIGN PATENT DOCUMENTS

		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION YES NO.
	AH	9-503791	4/1997	JP			
	AI	2-124817	5/1990	JP			
	AJ	1-104023	4/1989	JP			
	AK	00/59475	10/2000	WO			
	AL	11-228404	8/1999	JP			Yes
	AM	5-223052	8/1993	JP			Abstract
	AN	62-126124	6/1987	JP			No
	AO						

OTHER DOCUMENT(S) (*Including Author, Title, Date, Pertinent Pages, Etc.*)

	AP	New Drugs in Japan, 2001, 2001 Edition, Published by Yakuji Nippo Ltd., May 11, 2001, pp. 27-29, and its English translation of the material portions.
	AQ	

EXAMINER	DATE CONSIDERED

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