IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

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| In re application of | : | **Confirmation No. 2612** |
| Masayo HIGASHIYAMA | : | Attorney Docket No. 2004_1016A |
| Serial No. 10/500,354 | : | Group Art Unit 1614 |
| Filed June 30, 2004 | : | Examiner Charlesworth E. Rae |
| AQUEOUS LIQUID PREPARATIONS AND LIGHT-STABILIZED AQUEOUS LIQUID PREPARATIONS | | **Mail Stop: Amendment** |

**SUPPLEMENTAL AMENDMENT**

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

Sir:

Further to Applicants' Response dated October 9, 2007, please amend the above-identified application as follows:

## Amendments to the Specification

**Page 10, lines 5-17, please rewrite as follows:**

The appearance after light irradiation did not change from that immediately after preparation and was pale yellow and clear for Formulation 10 (pH 4) and Formulation 11 (pH 8.5) comprising sodium chloride. In addition, the appearance did not change from that immediately after preparation and was colorless and clear for Formulation 12 having a bepotastine besilate concentration of 0.1 w/v%. These results and the results of Formulation 7 (pH 6.8) in Experimental Example 2 indicate that addition of sodium chloride, which is a water-soluble metal chloride, improves light stability of bepotastine besilate at pH 4-8.5. In addition, they indicate that the light-stability of bepotastine besilate is improved in the concentration range of 0.1 w/v% - 1.5 w/v%.

## Amendments to the Claims

**1. (Currently amended)** An aqueous liquid preparation comprising (+)-(S)-4-[4-[(4-chlorophenyl)(2-pyridyl)methoxy]piperidino]butyric acid or a pharmacologically acceptable acid addition salt thereof, and a water-soluble metal chloride in an aqueous solution.

**2. (Original)** The aqueous liquid preparation of claim 1, wherein the metal chloride has a concentration selected from the range of a lower limit concentration of 0.15 w/v% and an upper limit concentration of 1.5 w/v%.

**3. (Previously presented)** The aqueous liquid preparation of claim 1, wherein the metal chloride is at least one kind selected from sodium chloride, potassium chloride and calcium chloride.

**4. (Previously presented)** The aqueous liquid preparation of claim 1, wherein the (+)-(S)-4-[4-[(4-chlorophenyl)(2-pyridyl)methoxy]piperidino]butyric acid or the pharmacologically acceptable acid addition salt thereof has a concentration selected from the range of a lower limit concentration of 0.1 w/v% and an upper limit concentration of 2.0 w/v%.

**5. (Previously presented)** The aqueous liquid preparation of claim 1, which is an acid addition salt of (+)-(S)-4-[4-[(4-chlorophenyl)(2-pyridyl)methoxy]piperidino]butyric acid.

**6. (Original)** The aqueous liquid preparation of claim 5, wherein the acid addition salt is monobenzenesulfonate.

**7. (Previously presented)** The aqueous liquid preparation of claim 1, wherein the aqueous liquid preparation has a pH in the range of 4-8.5.

**8. (Previously presented)** The aqueous liquid preparation of claim 1, which is an eye drop.

**9. (Previously presented)** The aqueous liquid preparation of claim 1, which is a nasal drop.

**10. (Currently amended)** An aqueous eye drop comprising (+)-(S)-4-[4-[(4-chlorophenyl)(2-pyridyl)methoxy]piperidino]butyric acid monobenzenesulfonate and sodium chloride at not less than 0.2 w/v% and not more than 0.8 w/v% in an aqueous solution.

**11. (Original)** A method of light-stabilizing (+)-(S)-4-[4-[(4-chlorophenyl)(2-pyridyl)methoxy]piperidino]butyric acid in an aqueous solution, which comprises adding a water-soluble metal chloride to an aqueous solution comprising (+)-(S)-4-[4-[(4-chlorophenyl)(2-pyridyl)methoxy]piperidino]butyric acid or a pharmacologically acceptable acid addition salt thereof.

## REMARKS

A further editorial change has been effected to the paragraph appearing on page 10, line 5.

Claims 1 and 10 have been further amended to specify that the preparation is "in an aqueous solution". This is responsive to the Examiner's statement on page 4, lines 3-4 of the Action that no patentable weight is given to the preamble of the former claims.

In addition, there is submitted herewith an executed Rule 132 Declaration of Dr. Higashiyama. The Declaration sets forth the experiments of Experimental Examples 1-4 of the specification. As discussed in Applicants' response of October 9, 2007, these experiments show the unexpected effect of this invention.

In view of the foregoing, favorable consideration and allowance is solicited.

Respectfully submitted,

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