APPENDIX A

REMS MODIFICATION: Addition of BOTOX® Upper Limb Spasticity Indication

BLA 103000 BOTOX® / BOTOX® Cosmetic (OnabotulinumtoxinA)

Botulinum Toxin Type A

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RISK EVALUATION AND MITIGATION STRATEGY (REMS)

I. GOAL(S)

The goals of the REMS are to:

- minimize the risks of medication errors related to the lack of interchangeability of **BOTOX®/BOTOX® Cosmetic** Units with those of licensed botulinum toxins of other manufacturers; and
- inform prescribers and patients about the potential occurrence of spread of toxin effect beyond the injection site.

II. REMS ELEMENTS

The **BOTOX®/BOTOX® Cosmetic** REMS includes a Medication Guide for patients and a Communication Plan for Healthcare Providers.

A. Medication Guide

In compliance with 21 CFR 208.24, Allergan will institute the following measures:

- o A Medication Guide will be included inside each **BOTOX®/BOTOX® Cosmetic** carton (all vial sizes).
- o The carton will include a prominent notice to “Dispense the enclosed Medication Guide to each patient".
- o Allergan’s standard packaging quality assurance procedures will ensure the most recent Medication Guide is packaged in each carton.
- o The “Dear Healthcare Provider” letter (DHCPL) will include instructions to dispense a Medication Guide to every patient at each **BOTOX®/BOTOX® Cosmetic** treatment session.
- o Ten (10) copies of the Medication Guide will be included with the DHCPL for each physician.

- Medication Guides will also be available via sales and/or medical affairs representatives, the product website and through the Sponsor toll-free medical information line.

Because the Medication Guide is included as part of the secondary package for **BOTOX®/BOTOX® Cosmetic**, Allergan has met the requirements of 21 CFR 208.24 for distribution and dispensing of the Medication Guide.

Please refer to the proposed Medication Guide in Appendix 1.

B. Communication Plan

Allergan will implement a communication plan to healthcare providers to support implementation of the REMS. A Dear Healthcare Provider Letter (DHCPL) was distributed in September 2009 with the FDA-approved labeling and Medication Guide for **BOTOX®/BOTOX® Cosmetic** to all purchasers of **BOTOX®** and/or **BOTOX® Cosmetic** based on Allergan's Customer Lists.

C. Elements to Assure Safe Use

The **BOTOX®/BOTOX® Cosmetic** REMS does not require Elements to Assure Safe Use.

D. Implementation System

The **BOTOX®/BOTOX® Cosmetic** REMS does not require an Implementation System.

E. Timetable for Submissions of Assessments

The timetable for Submission of Assessments is as follows:

- 1st Assessment: 18 months from REMS approval
- 2nd Assessment: 3 years from REMS approval
- 3rd Assessment: 7 years from REMS approval

The assessment period will close no earlier than 60 days prior to the date respective assessment is due. The assessment is to be received by the FDA on the due date.