DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

sBLA 103000/5251

SUPPLEMENT APPROVAL

Allergan, Inc.
Attention: Gus Aromin
Director, Global Regulatory Affairs
2525 Dupont Drive, P.O. Box 19534
Irvine, CA 92623-9534

Dear Mr. Aromin:

Please refer to your Supplemental Biologics License Application (sBLA), dated March 19, 2012, and received March 20, 2012, submitted under section 351 of the Public Health Service Act for BOTOX® (onabotulinumtoxinA) for injection.

We acknowledge receipt of your amendments dated April 25, May 25, July 17, August 22, September 10, October 10, November 6, December 6 and 14, 2012; January 3, and 17, 2013.

This Prior Approval supplemental biologics application provides for the treatment of overactive bladder with symptoms of urinary incontinence, urgency, and frequency, in adults who have had an inadequate response to or are intolerant of an anticholinergic medication.

We have completed our review of this supplemental application, as amended. It is approved, effective on the date of this letter, for use as recommended in the enclosed, agreed-upon labeling text.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit, via the FDA automated drug registration and listing system (eLIST), the content of labeling [21 CFR 601.14(b)] in structured product labeling (SPL) format, as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm, that is identical to the enclosed labeling text for the package insert and the Medication Guide and include the labeling changes proposed in any pending "Changes Being Effected" (CBE) supplements. Information on submitting SPL files using eLIST may be found in the guidance for industry titled "SPL Standard for Content of Labeling Technical Qs and As" at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf.

The SPL will be accessible via publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications for this BLA, including pending "Changes Being Effected" (CBE) supplements, for which FDA has not yet issued an action letter, with the content of labeling [21 CFR 601.12(f)] in MS Word format that includes the changes approved in this supplemental application.

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable.

We are waiving the pediatric study requirement for ages less than 12 years old because there is evidence suggesting that the risk/benefit profile of the drug product would be unfavorable in this age group. The Division believes that it is imprudent to treat overactive bladder symptoms with an invasive therapy in patients who may be unable to manage the attendant risks, such as urinary retention.

We are deferring submission of your pediatric study for ages 12 to 17 years, inclusive, for this application because the product is ready for approval in adults and the pediatric studies have not been completed.

Your deferred pediatric studies required by section 505B(a) of the Federal Food, Drug, and Cosmetic Act are required postmarketing studies. The status of these postmarketing studies must be reported annually according to 21 CFR 601.28 and section 505B(a)(3)(B) of the Federal Food, Drug, and Cosmetic Act. These required studies are listed below.

#1 Initial double-blind single treatment base study to evaluate the safety and efficacy of intradetrusor injection of BOTOX for the treatment of overactive bladder with urinary incontinence in patients $\geq$12 to $\leq$ 17 years who have not been adequately managed with anticholinergic therapy.

Final Protocol Submission:	August 2013
Study/Trial Completion:	October 2017
Final Report Submission:	January 2018

#2 Extension study to enroll all patients who complete the initial study. Patients in this study may be treated up to 48-weeks and may receive multiple re-treatments during that period to further evaluate the long term safety and efficacy of BOTOX in the treatment of pediatric patients with overactive bladder and urinary incontinence.

Final Protocol Submission:	November 2013
Study/Trial Completion:	December 2018
Final Report Submission:	March 2019

active - relevant for this BLA

Submit the protocols to your IND 012430, with a cross-reference letter to this BLA.

Reports of these required pediatric postmarketing studies must be submitted as a BLA or as a supplement to your approved BLA with the proposed labeling changes you believe are warranted based on the data derived from these studies. When submitting the reports, please clearly mark your submission "**SUBMISSION OF REQUIRED PEDIATRIC ASSESSMENTS**" in large font, bolded type at the beginning of the cover letter of the submission.

RISK EVALUATION AND MITIGATION STRATEGY REQUIREMENTS

This supplement also contained a proposed REMS modification. However, we refer to our July 17, 2012, supplemental BLA approval letter informing you that your request to eliminate REMS has been approved and that maintaining the Medication Guide as part of the labeling is adequate to address the serious and significant public health concerns and meets the standard in 21 CFR 208.1.

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit, in triplicate, a cover letter requesting advisory comments, the proposed materials in draft or mock-up form with annotated references, and the package insert(s) to:

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Prescription Drug Promotion
5901-B Ammendale Road
Beltsville, MD 20705-1266

As required under 21 CFR 601.12(f)(4), you must submit final promotional materials, and the package insert(s), at the time of initial dissemination or publication, accompanied by a Form FDA 2253. For instruction on completing the Form FDA 2253, see page 2 of the Form. For more information about submission of promotional materials to the Office of Prescription Drug Promotion (OPDP), see http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm.

REPORTING REQUIREMENTS

We remind you that you must comply with reporting requirements for an approved BLA (21 CFR 600.80 and 600.81).

In addition, we request that you submit semi-annual safety analyses based on all postmarketing serious adverse event reports in pediatric patients <18 years of age treated with intradetrusor injection of Botox for the indication of overactive bladder (non-neurogenic). We request that you submit these reports for a period of at least three years following the launch of Botox in the United States for treatment of overactive bladder in adults.

If you have any questions, please call Nenita Crisostomo, R.N., Regulatory Health Project Manager, at (301) 796-0875.

Sincerely,

{See appended electronic signature page}

Hylton V. Joffe, M.D., M.M.Sc.
Director
Division of Reproductive and Urologic Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

ENCLOSURE:
Content of Labeling

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

HYLTON V JOFFE
01/18/2013