DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
1401 Rockville Pike
Rockville MD 20852-1448

DEC 21 2000

Submission Tracking No. (STN) **103000/1004**
(Replaces Reference Number: 91-0184)

Mr. Peter A. Kresel
Allergan, Inc.
2525 Dupont Drive
P.O. Box 195
Irvine, CA 92713-9534

Dear Mr. Kresel:

The Supplement to your License Application for Botulinum Toxin Type A (BOTOX), to include the indication of treatment of cervical dystonia, submitted under Section 351 of the Public Health Service Act, has been approved.

Under this approval, BOTOX is indicated for the treatment of cervical dystonia in adults to decrease the severity of abnormal head position and neck pain associated with cervical dystonia.

We acknowledge your commitments dated December 13, 2000, and December 15, 2000, for the following postmarketing clinical study:

1. You have agreed to initiate a postmarketing study to evaluate the safety and immunogenicity of BOTOX in patients with cervical dystonia. You have made the following commitments for timeframes of conducting the study and submission of related materials to the Center for Biologics Evaluation and Research (CBER):

    a. The study protocol will be finalized and submitted to CBER for review and comment by the end of January 2001.

    b. The study will be initiated by the end of March 2001.

    c. A sufficient number of study subjects will be enrolled such that a minimum of 250 subjects will complete the two years of follow-up monitoring.

d. Enrollment of study subjects will be completed in approximately 3.5 years, with the last subject to be entered by the end of December 2004.

e. All study subjects will be followed until the 2-year clinical observation period for the last enrolled patient is completed in December 2006.

f. Database closure and initiation of data analysis will occur in December 2006.

g. The clinical study final report will be completed and submitted to CBER by April 2007.

h. In addition, you have agreed to include interim data analyses in the annual reports on the status of this study.

Be advised that as of April 1, 1999, all applications for new active ingredients, new dosage forms, new indications, new routes of administration and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred (63 FR 66632). A waiver for pediatric studies for this application is granted under 21 CFR 601.27.

This information will be placed in your biologics license application file for this product.

Changes in the manufacturing process, manufacturing facility, product testing, packaging or labeling for Botulinum Toxin Type A (BOTOX) may require the submission of a supplement to your biologics license application for review and approval prior to implementation.

It is required that adverse experience reports be submitted in accordance with the adverse events reporting requirements for licensed biological products (21 CFR 600.80) and that distribution reports be submitted as described (21 CFR 600.81). All adverse experience reports should be prominently identified according to 21 CFR 600.80 and be submitted to the Center for Biologics Evaluation and Research, HFM-210, Food and Drug Administration, 1401 Rockville Pike, MD 20852-1448.

It is required that reports of errors and accidents in manufacture be submitted in accordance with the error and accident reporting requirements for licensed biological products (21 CFR 600.14). All error and accident reports should be identified promptly according to 21 CFR 600.14 and submitted to the Director, Office of Compliance, Center for Biologics Evaluation and Research, HFM-600, 1401 Rockville Pike, Rockville, MD 20852-1448.

Please submit final printed labeling at the time of use and include implementation information on FDA Form 2567. Please provide a PDF-format electronic copy as well as original paper copies (ten for circulars and five for other labels). In addition, you may wish to submit draft copies of the proposed introductory advertising and promotional labeling with an FDA Form 2567 or Form 2253 to the Center for Biologics Evaluation and Research, Advertising and Promotional Labeling Branch, HFM-602, 1401 Rockville Pike, Rockville, MD 20852-1448. Final printed advertising and promotional labeling should be submitted at the time of initial dissemination, accompanied by a FDA Form 2567 or Form 2253.

All promotional claims must be consistent with and not contrary to approved labeling. No comparative promotional claim or claim of superiority over other similar products should be made unless data to support such claims are submitted to and approved by the Center for Biologics Evaluation and Research.

Please acknowledge receipt of this letter to the Director, Division of Vaccines and Related Products Applications, HFM-475, Center for Biologics Evaluation and Research.

Sincerely yours,

Donna K. Chandler, Ph.D.

for Karen L. Goldenthal, M.D.
Director
Division of Vaccines and
Related Products Applications
Office of Vaccines
Research and Review
Center for Biologics
Evaluation and Research