DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

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

Reference Numbers: 97-0111 and 97-0924

AUG 31 1998

Dennis J. Foley, Ph.D.
Wyeth Laboratories, Inc.
Wasp & Biddle Streets
P.O. Box 34
Marietta, PA 17547

Dear Dr. Foley:

Enclosed please find Biologics License No. 3 issued in accordance with the provisions of Section 351(a) of the Public Health Service Act, as amended November 21, 1997 (FDAMA; Public Law 105-115), controlling the manufacture and sale of biological products. This license authorizes Wyeth Laboratories, Inc. to manufacture and ship for sale, barter, or exchange in interstate and foreign commerce Rotavirus Vaccine, Live, Oral, Tetravalent for which your company has demonstrated compliance with establishment and product standards.

Under this license, you are authorized to manufacture and distribute Rotavirus Vaccine, Live, Oral, Tetravalent for the immunization of infants at 2, 4, and 6 months of age. In accordance with your approved labeling, your product will bear the trade name Rotashield and will be marketed as a two component package containing lyophilized vaccine (4×10^5 pfu/dose) and 2.5 ml citrate bicarbonate buffer in a plastic dispette. The citrate bicarbonate buffer shall be filled into dispettes at [redacted] packaged at [redacted] and sterilized using [redacted]

You are requested to submit samples of the vaccine and diluent in final containers for testing together with protocols for final container and monovalent concentrates showing results of all applicable tests. No lots of product shall be distributed until notification of release is received from the Director, Center of Biologics Evaluation and Research (CBER).

The dating period for the vaccine shall be 24 months from the date of manufacture when stored at or below 25°C. The dating period for the diluent shall be 30 months from date of manufacture when stored at or below 25°C. The date of manufacture shall be defined as the date of the formulation of the tetravalent bulk in the case of the vaccine, and as the date of fill for the diluent.

If you wish to request extension of the dating period beyond that stated above, you may do so by submitting Supplements to your license application along with documentation supporting the real time stability of the product. Alternatively, you may submit a stability protocol for prior approval to be used in extension of dating as a Supplement to your license application.

We acknowledge the following commitments made in submissions to your license application dated April 15, June 2, August 10, August 11, August 17, and August 24, 1998:

1. to complete the validation study for final product shipping by fourth quarter, 1998. The container temperature mapping summary data for three shipping runs, a description of thermocouple calibration, and a schematic of the established load configuration(s) should be submitted to CBER by the fourth quarter of 1998.

2. to perform periodic evaluation of variances associated with potency testing of released lots, move towards a quantitative serotype-specific potency assay, and consider a two test format to control for unassigned errors in the development of future potency assays.

3. to perform stability testing according to your post-licensure stability testing plan.

4. to develop an improved container/closure system for your lyophilized vaccine product.

5. to perform post-marketing studies in at least 20,000 children as well as additional IND studies to examine safety in older infants and immune interference with other concurrently administered vaccines as outlined in the above submissions dated June 2, August 11, and August 24, 1998.

Changes in the manufacturing, testing, packaging or labeling of your Rotavirus Vaccine, Live, Oral, Tetravalent, or in the manufacturing facilities may require the submission of a Supplement to your license application for our review and written approval prior to implementation.

It is requested that adverse experience reports for Rotavirus Vaccine, Live, Oral, Tetravalent, be submitted in accordance with the adverse experience reporting requirements for licensed biological products (21 CFR 600.80) and that distribution reports be submitted as described (21 CFR 600.81). Since your product is categorized as a vaccine, these reports should be submitted to

the Vaccine Adverse Event Reporting System (VAERS) using the pre-addressed form VAERS-1.

Please submit three copies of all final printed labeling at the time of use and include part II of the label transmittal form with completed implementation information. In addition to these paper copies, we request that you submit an electronic version of the final labeling in Portable Document Format (PDF) (this is not an endorsement of any proprietary format but simply reflects the current technology available within CBER). Also, if you have not previously submitted a final draft package insert (8.5 x 11 inch, single-spaced page layout) in PDF, please do so as soon as possible. The PDF label files should be submitted on duplicate 3.5 inch PC-format floppies or CD-ROMs that are clearly labeled with the manufacturer and product name, submission date, label review number(s), Reference No., label type(s), and file name(s).

Final printed advertising and promotional labeling should be submitted at the time of initial dissemination accompanied by an FDA Form 2567. In addition, you may wish to submit draft copies of the proposed introductory advertising and promotional labeling with an FDA Form 2567 to the Center for Biologics Evaluation and Research, Advertising and Promotional Labeling Staff, HFM-202, 1401 Rockville Pike, Rockville, MD 20852-1448. 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.

It is requested that you acknowledge receipt of this Biologics License to the Director, Division of Vaccines and Related Products Applications, HFM-475.

Sincerely yours,

Steven A. Masiello
Acting Director
Office of Compliance
and Biologics Quality
Center for Biologics
Evaluation and Research

for

M. Carolyn Hardegree, M.D.
Director
Office of Vaccines
Research and Review
Center for Biologics
Evaluation and Research