DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-017/S-006 and S-015

Eli Lilly and Company
Attention: Jeffrey L. Winn, D.D.S., R.Ph.
Senior Regulatory Research Scientist
U.S. Regulatory Affairs
Lilly Corporate Center
Indianapolis, IN 46285

Dear Dr. Winn:

Please refer to your supplemental new drug application dated October 2, 2002, received October 3, 2002 (for S-006), and dated October 22, 2003, received October 23, 2003 (for S-015), submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Humalog® Mix 75/25(75% insulin lispro protamine suspension and 25% insulin lispro injection, [rDNA origin]).

We acknowledge receipt of your submissions dated March 25, April 11, and July 16 and 25, 2003, for S-006. Your submission of July 16, 2003, constituted a complete response to our March 31, 2003, action letter for S-006.

We acknowledge receipt of your submission dated February 19 and April 8, 2004, for S-015.

These "Changes Being Effected" supplements provide for the following labeling changes to the (1) INFORMATION FOR THE PATIENT 3 ML DISPOSABLE INSULIN DELIVERY DEVICE (for Humalog Mix 75/25 Pen), and (2) Humalog Mix 75/25 Pen User Manual, and Humalog Mix 75/25 Pen carton label:

Supplement 006: Revisions to emphasize the need to prime the Pen before each injection.

Supplement 015: Safety labeling changes.

We completed our review of these applications, as amended. These applications are approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text.

The final printed labeling (FPL) must be identical to the enclosed labeling (text for the patient package insert, Humalog Mix 75/25 Pen User Manual, and Humalog Mix 75/25 Pen carton label).

Please submit the FPL electronically according to the guidance for industry titled Providing Regulatory Submissions in Electronic Format – NDA. Alternatively, you may submit 20 paper copies of the FPL as soon as it is available, in no case more than 30 days after it is printed. Please individually mount 15 of the copies on heavy-weight paper or similar material. For administrative purposes, this submission should be designated "FPL for approved supplement NDA 21-017/S-006 and S-015." Approval of this submission by FDA is not required before the labeling is used.

If you issue a letter communicating important information about this drug product (i.e., a "Dear Health Care Professional" letter), we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH, HFD-410
FDA
5600 Fishers Lane
Rockville, MD 20857

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, call Julie Rhee, Regulatory Project Manager, at (301) 827-6424.

Sincerely,

{See appended electronic signature page}

David G. Orloff, M.D.
Director
Division of Metabolic
and Endocrine Drug Products, HFD-510
Office of Drug Evaluation II
Center for Drug Evaluation and Research

Enclosures:
1. INFORMATION FOR THE PATIENT (5.01 PA 9235 FSAMP)
2. Humalog Mix 75/25 Pen User Manual (5.01 PA 9115 FSAMP)
3. Carton label for Humalog Mix 75/25 Pen (SH 8933 FSAMS)

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

/s/

David Orloff

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