NDA 20-563/S-010, S-011, S-012, and S-013

Eli Lilly and Company
Attention: Gregory G. Enas, Ph.D.
Director, U.S. Regulatory Affairs
Lilly Corporate Center
Indianapolis, IN 46285

Dear Dr. Enas:

Please refer to your supplemental new drug applications dated August 31, 1998, received August 31, 1998, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Humalog (insulin lispro [rDNA origin] injection).

We acknowledge receipt of your submissions dated September 3, October 1, November 11, and December 16, 1999, and February 29 and March 17 and 28, 2000. Your submission of October 1, 1999, constituted a complete response to our August 31, 1999, action letter.

These supplemental new drug applications provide for the use of Humalog for the following changes to the package insert:

S-010:
(1) Addition of postprandial dosing (WARNINGS , DOSAGE AND ADMINISTRATION),
(2) Addition of the use of Humalog with a sterile diluent (DOSAGE AND ADMINISTRATION),
(3) Revised "Renal Impairment" subsection (CLINICAL PHARMACOLOGY),
(4) Revised "Hepatic Impairment" subsection (CLINICAL PHARMACOLOGY),
(5) Clarification of "*Mixing of Insulins*" subsection (PRECAUTIONS), and
(6) Addition of a precaution for patients taking drugs sensitive to serum potassium level (PRECAUTIONS).

S-011: Use in pediatric patients (PRECAUTIONS).

S-012: New indication for combination therapy with sulfonylurea agents in patients with Type 2 diabetes (INDICATIONS AND USAGE).

S-013: Use in geriatric patients (PRECAUTIONS).

We have completed the review of these supplemental applications, as amended, and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the agreed upon labeling text. Accordingly, these supplemental applications are approved effective on the date of this letter.

The final printed labeling (FPL) must be identical to the submitted draft labeling (package insert [circular PA 6662-BB AMP] submitted March 28, 2000, patient package inserts [circular PA 6601-A AMP for vial] [circular PA 9082-B FSAMP for 1.5 mL cartridge] submitted November 11, 1999, and sterile diluent vial label and carton dated August 31, 1998) including the following minor change to which your representative agreed as noted below:

Patient package insert for 1.5 mL cartridge (circular PA 9082-B FSAMP):

Delete “s” after “insulin” in line 8, “WARNINGS” section and line 10, “Description” section.

Please submit 20 copies of the FPL as soon as it is available, in no case more than 30 days after it is printed. Please individually mount ten of the copies on heavy-weight paper or similar material. For administrative purposes, these submissions should be designated "FPL for approved supplement NDA 20-563/S-010, S-011, S-012, and S-013." Approval of these submissions by FDA is not required before the labeling is used.

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). We note that you have fulfilled the pediatric study requirements.

If a letter communicating important information about this drug product (i.e., a "Dear Health Care Practitioner" letter) is issued to physicians and others responsible for patient care, we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH, HF-2
FDA
5600 Fishers Lane
Rockville, MD 20857

Please submit one market package of the drug product when it is available.

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

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

Sincerely,

John K. Jenkins, M.D.
Acting Director
Division of Metabolic
and Endocrine Drug Products, HFD-510
Office of Drug Evaluation II
Center for Drug Evaluation and Research