DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 20-100/S-021

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 June 24, 2003, received June 25, 2003, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Humulin 50/50 (50% human insulin isophane suspension and 50% human insulin injection, [rDNA origin]).

We acknowledge receipt of your submissions dated October 2 and 22, 2003.

This supplemental new drug application provides for(b)(4)----------at the Lilly facility in Fegersheim, France, as an additional manufacturing site for Humulin N/R Mixture 50/50 Vials, HI-1510.

We have completed the review of this application, 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, this application is approved effective on the date of this letter.

The final printed labeling (FPL) must be identical to the enclosed labeling (text for the patient package insert, immediate container, and carton labels).

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 20-100/S-021." Approval of this submission by FDA is not required before the labeling is used.

We remind you that you must submit patent information on form FDA 3542, *Patent Information Submitted Upon and After Approval of an NDA or Supplement*, within 30 days of the date of this letter as required by 21 CFR 314.53(c)(2)(ii) and 314.53(d)(2) at the address provided by 21 CFR 314.53(d)(4). The form may be obtained at http://www.fda.gov/opacom/morechoices/fdaforms/cder.html. To expedite review of this patent declaration form, we request you submit an additional copy of the form to this application and to the Center for Drug Evaluation and Research "Orange Book" staff at

Food and Drug Administration
Office of Generic Drugs, HFD-610
Orange Book Staff
7500 Standish Place
Metro Park North II
Rockville, MD 20855-2773

In addition, submit three copies of the introductory promotional materials that you propose to use for this product. Submit all proposed materials in draft or mock-up form, not final print. Send one copy to this division and two copies of both the promotional materials and the package insert directly to:

Division of Drug Marketing, Advertising, and Communications, HFD-42
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857

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
Food and Drug Administration
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).

Approval of this supplemental new drug application (S-021) supercedes labeling supplement 011 (submitted August 20, 1998, and received August 20, 1998), and supplement 013 (submitted April 12, 2001, and received April 13, 2001), and our approvable letter dated March 19, 2002, which requested revised labeling.

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 (A2.0 NL 4590 AMP)
2. Carton label (A1.0 NL 3890 AMS)
3. Vial label (A1.0 NL 4060 AMX)