DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 18-780/S-067 and S-078

Eli Lilly and Company
Attention: Jeffrey 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 applications dated December 1, 2000, received December 4, 2000 (for S-067), and dated September 24, 2002, received September 24, 2002 (for S-078), submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Humulin R (human insulin injection, USP, [rDNA origin]).

We acknowledge receipt of your submissions dated February 7, 2003, for S-067 and January 28, 2003, for S-078.

Your submission of February 7, 2003, constituted a complete response to our April 15, 2002, action letter for S-067. In addition, your submission of January 28, 2003, constituted a complete response to our January 24, 2003, action letter for S-078. These supplements provide for the following changes:

Supplement 067: Submitted as a "Changes Being Effected" supplemental new drug application provide for (1) an additional language for the "good control message" in the DIABETES section and (2) removal of the pictorial graphic of the insulin carton and vial in the *Identification* section of the labeling.

Supplement 078: Submitted as a prior approval supplemental new drug application provides for an additional manufacturing site (b)(4)----------for Humulin R Vials, HI-210, in Fegersheim, France.

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 package insert, 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 ten of the copies on heavy-weight paper or similar material. For administrative purposes, this submission

should be designated "FPL for approved supplement NDA 18-780/S-067, S-078." Approval of this submission by FDA is not required before the labeling is used.

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, HF-2
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 (for 10 mL vial)
2. Immediate container label (for 10 mL vial)
3. Carton label (for 10 mL vial)

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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