DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 18-780/S-094; NDA 18-781/S-088; NDA 19-717/S-068; NDA 20-100/S-031
NDA 20-563/S-064; NDA 21-017/S-029; NDA 21-018/S-023

Eli Lilly and Company
Attention: Gregory Enas, PhD
Director, US Regulatory Affairs
Lilly Corporate Center
Indianapolis, IN 46285

SUPPLEMENT APPROVAL

Dear Dr. Enas:

Please refer to your supplemental new drug applications submitted August 17, 2005, received August 19, 2005, under section 505(b) of the Federal Food, Drug, and Cosmetic Act for the products described below.

NDA	Supple-ment	Drug Product Name
18-780	S-094	Humulin R (insulin human injection, USP [rDNA origin])
18-781	S-088	Humulin N NPH (human insulin isophane suspension [rNDA origin])
19-717	S-068	Humulin 70/30 (70% human insulin isophane suspension/30% insulin human injection, rDNA origin)
20-100	S-031	Humulin 50/50 (50% human insulin isophane suspension/50% insulin human injection, rDNA origin)
20-563	S-064	Humalog (insulin lispro injection [rDNA origin])
21-017	S-029	Humalog Mix75/25 (75% insulin lispro protamine suspension/25% insulin lispro injection [rDNA origin])
21-018	S-023	Humalog Mix50/50 (50% insulin lispro protamine suspension/50% insulin lispro injection [rDNA origin])

We acknowledge receipt of your amendments dated February 15, July 10, and August 21, 2007. (We also refer to submissions dated August 22 and 27, 2007, to NDA 20-563/S-075; NDA 21-017/S-040; and NDA 21-018/S-034 with color differentiation carton and container labeling for KwikPens approved September 6, 2007.)

Your submissions dated February 15, 2007, received February 16 2007, constituted a complete response to our February 16, 2006, action letter.

These supplemental new drug applications provide for the implementation of a color differentiation plan (Global Color Differentiation System [GCDS]) for the carton and container labels for the products listed above.

We have completed our review of these applications, as amended. They are approved, effective on the date of this letter, for use as recommended in the submitted labeling text and with the minor agreed-upon revision listed below.

1. Remove the red color from the alert information (in an oval pattern) on the principle display panel of the Humalog Pen, Humalog Mix75/25 Pen, and Humalog Mix50/50 Pen cartons and replace it with an alternative presentation that uses black text on white background as agreed in your September 7, 2007, secure email.

CARTON AND IMMEDIATE CONTAINER LABELS

Submit final printed carton and container labels that are identical to the carton and immediate container labels **for 10 mL Vials for all seven NDAs; for Humulin N Pens, Humulin 70/30 Pens, Humalog Pens, Humalog Mix75/25 Pens, and Humalog Mix50/50 Pens, and 3 mL Humalog cartridges** submitted July 10, 2007, except with the revision listed above, as soon as they are available, but no more than 30 days after they are printed. Please submit these labels electronically according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format – Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications (October 2005).* Alternatively, you may submit 12 paper copies, with 6 of the copies individually mounted on heavy-weight paper or similar material. For administrative purposes, designate this submission "**Final Printed Carton and Container Labels for approved NDA 18-780/S-094; NDA 18-781/S-088; NDA 19-717/S-068; NDA 20-100/S-031; NDA 20-563/S-064; NDA 21-017/S-029; NDA 21-018/S-023**." Approval of this submission by FDA is not required before the labeling is used.

Marketing the products with FPL that is not identical to the approved labeling text may render the products misbranded and unapproved new drugs.

We remind you of your September 7, 2007, agreement (via secure email) to review and submit to FDA medication error reports and pharmaceutical product complaints relating to the Global Color Differentiation System labels on a quarterly basis for one year and semi-annually thereafter.

We also wish to remind you to ensure that the established name is at least one half the size of the proprietary name on all carton and container labels.

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit, in triplicate, a cover letter requesting advisory comments, the proposed materials in draft or mock-up form with annotated references, and the package inserts to:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Drug Marketing, Advertising, and Communications
5901-B Ammendale Road
Beltsville, MD 20705-1266

As required under 21 CFR 314.81(b)(3)(i), you must submit final promotional materials, and the package insert(s), at the time of initial dissemination or publication, accompanied by a Form FDA 2253. For instruction on completing the Form FDA 2253, see page 2 of the Form. For more

information about submission of promotional materials to the Division of Drug Marketing, Advertising, and Communications (DDMAC), see www.fda.gov/cder/ddmac.

LETTERS TO HEALTH CARE PROFESSIONALS

If you issue a letter communicating important safety related information about these drug products (i.e., a "Dear Health Care Professional" letter), we request that you submit an electronic copy of the letters to both the NDAs and to the following address:

MedWatch
Food and Drug Administration
HFD-001, Suite 5100
5515 Security Lane
Rockville, MD 20852

REPORTING REQUIREMENTS

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 Enid Galliers, Chief, Project Management Staff, at 301-796-1211.

Sincerely,

{See appended electronic signature page}

Mary H. Parks, M.D.
Director
Division of Metabolism and Endocrinology Products (DMEP)
Office of Drug Evaluation II
Center for Drug Evaluation and Research

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

/s/

Mary Parks

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