DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 20-563/S-075; NDA 21-017/S-040; NDA 21-018/S-034

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 October 5, 2006, under section 505(b) of the Federal Food, Drug, and Cosmetic Act for the products described below.

NDA	Supplement	Drug Product Name
20-563	S-075	Humalog (insulin lispro injection [rDNA origin])
21-017	S-040	Humalog Mix75/25 (75% insulin lispro protamine suspension/25% insulin lispro injection [rDNA origin])
21-018	S-034	Humalog Mix50/50 (50% insulin lispro protamine suspension/50% insulin lispro injection [rDNA origin])

We acknowledge receipt of your amendments dated April 30, July 17 and 25, and August 22 and 27, 2007.

Your submissions dated April 30, 2007, received May 2, 2007, constituted a complete response to our February 11, 2007, action letter.

These supplemental new drug applications provide for the addition of disposable (prefilled) insulin injector pens: Humalog® KwikPen™, Humalog Mix75/25® KwikPen™, and Humalog Mix50/50® KwikPen™.

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 agreed-upon labeling text and with the minor agreed-upon, editorial revision listed below.

1. Cartons: To the back panel of each carton, add the website address "www.humalog.com" immediately following the phone number.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, please submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format as described at http://www.fda.gov/oc/datacouncil/spl.html that is identical to the enclosed labeling (text for the

package inserts submitted August 22, 2007, text for the patient package inserts submitted August 22, 2007, and the text for the KwikPen User Manual submitted April 30, 2007). Upon receipt, we will transmit that labeling to the National Library of Medicine for public dissemination. For administrative purposes, please designate this submission, "**SPL for approved NDA 20-563/S-075, NDA 21-017/S-040, NDA 21-018/S-034**."

CARTON AND IMMEDIATE CONTAINER LABELS

Submit final printed carton and container labels that are identical to the immediate container labels submitted July 17, 2007, and the carton labels submitted August 22, 2007, except with the addition of "www.humalog.com" to the back panel of the cartons as described in your August 27, 2007, submission, 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 20-563/S-075 and S-064; NDA 21-017/S-040 and S-029; NDA 21-018/S-034 and 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 July 25, 2007, agreement to review and submit to FDA incoming reports of medication errors or pharmaceutical product complaints received by Lilly for the KwikPen product line along with the new start/switch data. We request that medication error reports or pharmaceutical product complaints relating to the Global Color Differentiation System labels be submitted 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

Enclosures:
NDA 20-563/S-075 PI
NDA 20-563/S-075 PPI
NDA 21-017/S-040 PI
NDA 21-017/S-040 PPI
NDA 21-018/S-034 PI
NDA 21-018/S-034 PPI
KwikPen User Manual

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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