



NDA 20-563/S-091
NDA 21-017/S-053
NDA 21-018/S-049
NDA 18-781/S-108
NDA 19-717/S-087

SUPPLEMENT APPROVAL

Eli Lilly and Company
Attn: 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 January 18, 2008, received January 18, 2008, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for the following products:

NDA #	Supplement #	Tradename	Established Name
20-563	S-091	Humalog	insulin lispro (rDNA origin) injection
21-017	S-053	Humalog Mix 75/25	75% insulin lispro protamine suspension and 25% insulin lispro injection, (rDNA origin)
21-018	S-049	Humalog Mix 50/50	50% insulin lispro protamine suspension and 50% insulin lispro injection, (rDNA origin)
18-781	S-108	Humulin N	human insulin (rDNA origin) isophane suspension
19-717	S-087	Humulin 70/30	70% human insulin isophane suspension and 30% human insulin injection, (rDNA origin)

We acknowledge receipt of your submissions dated July 22 and August 11, 2008.

The August 11, 2008, submission constituted a complete response to our July 16, 2008, action letter.

These supplemental new drug applications provide for the Rear Cartridge Capture (RCC) modification to the existing Humalog/Humulin prefilled Pen product line.

We have completed our review of this application, as amended. It is approved, effective on the date of this letter, for use as recommended in the enclosed agreed-upon labeling text.

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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, patient package inserts, and User Manuals submitted on August 11, 2008. Upon receipt, we will transmit that version to the National Library of Medicine for public dissemination. For administrative purposes, please designate these submissions “**SPL for approved NDA 20-563/S-091, NDA 21-017/S-053, NDA 21-018/S-049, NDA 18-781/S-108, NDA 19-717/S-087**” respectively.

CARTON AND IMMEDIATE CONTAINER LABELS

Submit final printed carton and container labels that are identical to the enclosed carton and immediate container labels submitted on January 18, 2008, 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 these submissions “**Final Printed Carton and Container Labels for approved NDA 20-563/S-091, NDA 21-017/S-053, NDA 21-018/S-049, NDA 18-781/S-108, NDA 19-717/S-087**” respectively. 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 product misbranded and an unapproved new drug.

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 insert(s) 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

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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 this drug product (i.e., a “Dear Health Care Professional” letter), we request that you submit an electronic copy of the letter to both this NDA and to the following address:

MedWatch
Food and Drug Administration
Suite 12B05
5600 Fishers Lane
Rockville, MD 20857

If you have any questions, call Rachel Hartford, Regulatory Project Manager, at (301) 796-0331.

Sincerely,

{See appended electronic signature page}

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

Enclosures:

Humulin N - Patient Package Insert, Pen Carton, and Immediate Container
Humulin 70/30 - Patient Package Insert, Pen Carton, and Immediate Container
Humalog - Package Insert, Pen Carton, and Immediate Container
Humalog 75/25 - Package Insert, Pen Carton, and Immediate Container
Humalog 50/50 - Package Insert, Pen Carton, and Immediate Container
Prefilled Insulin Delivery Device 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/

Eric Colman
3/16/2009 12:49:48 PM
Eric Colman for Mary Parks