DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 020563/S-191
NDA 205747/S-018

**SUPPLEMENT APPROVAL**

Eli Lilly and Company
Attention: Ingrid Hensley, Ph.D.
Advisor, Global Regulatory Affairs - U.S. Diabetes
Lilly Corporate Center,
Indianapolis, Indiana 46285

Dear Dr. Hensley:

Please refer to your Supplemental New Drug Applications (sNDAs) dated and received August 21, 2018, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Humalog (insulin lispro injection) U-100 and U-200.

These Prior Approval supplemental new drug applications, submitted in response to our letter dated June 22, 2018, provide for updates to the prescribing information (PI) and instructions for use (IFU) regarding the use of Humalog U-100 and U-200 by patients with visual impairment.

## APPROVAL & LABELING

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

- Revision dates updated to reflect the approval date of the supplements

## CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format using the FDA automated drug registration and listing system (eLIST), as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm. Content of labeling must be identical to the enclosed labeling (text for the Prescribing Information, Patient Package Insert, and Instructions for Use), with the addition of any labeling changes in pending "Changes Being Effected" (CBE) supplements, as well as annual reportable changes not included in the enclosed labeling.

Information on submitting SPL files using eList may be found in the guidance for industry titled "SPL Standard for Content of Labeling Technical Qs and As" at

http://www.fda.gov/downloads/DrugsGuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf.

The SPL will be accessible from publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications that include labeling changes for this NDA, including CBE supplements for which FDA has not yet issued an action letter, with the content of labeling [21 CFR 314.50(l)(1)(i)] in Microsoft Word format, that includes the changes approved in this supplemental application, as well as annual reportable changes. To facilitate review of your submission(s), provide a highlighted or marked-up copy that shows all changes, as well as a clean Microsoft Word version. The marked-up copy should provide appropriate annotations, including supplement number(s) and annual report date(s).

**REQUIRED PEDIATRIC ASSESSMENTS**

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients (which includes new salts and new fixed combinations), new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication in pediatric patients unless this requirement is waived, deferred, or inapplicable.

Because none of these criteria apply to your supplemental applications, you are exempt from this requirement.

**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 Callie Cappel-Lynch, Regulatory Project Manager, at (301) 796-8436.

Sincerely,

*{See appended electronic signature page}*

William Chong, M.D.
Deputy Director for Safety (Acting)
Division of Metabolism and Endocrinology Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

ENCLOSURES:

Content of Labeling

Prescribing Information
Patient Package Insert Humalog U-100 (previously approved March 13, 2015)
Patient Package Insert Humalog U-200 (previously approved May 26, 2015)
Instructions for Use U-100 KwikPen
Instructions for Use U-100 Junior KwikPen
Instructions for Use U-100 Vial (previously approved March 13, 2015)
Instructions for Use U-200 KwikPen

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**This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.**

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/s/

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WILLIAM H CHONG
11/01/2018