



NDA 021017/S-082

**SUPPLEMENT APPROVAL**

Eli Lilly and Company  
Attention: Christopher L. Jordan, BS, RAC  
Consultant, Global Regulatory Affairs –U.S.  
Lilly Corporate Center  
Indianapolis, IN 46285

Dear Mr. Jordan:

Please refer to your Supplemental New Drug Application (sNDA) dated and received March 23, 2012, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Humalog Mix 75/25 (75% insulin lispro protamine suspension and 25% insulin lispro, rDNA origin), injection, 100 U/mL.

We acknowledge receipt of your amendment dated December 17, 2012.

This “Prior Approval” supplemental new drug application proposes extensive revisions to the KwikPen Instructions for Use.

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

**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(1)] 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 package insert, patient package insert and KwikPen 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 includes 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 MS Word format, that includes the changes approved in this supplemental application, as well as annual reportable changes and annotate each change. To facilitate review of your submission, 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, 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(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable.

Because none of these criteria apply to your application, 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, please contact Mehreen Hai, Ph.D., Regulatory Project Manager, at (301) 796-5073.

Sincerely,

*{See appended electronic signature page}*

Mary Parks, M.D.  
Director  
Division of Metabolism & Endocrinology Products  
Center for Drug Evaluation and Research  
Food and Drug Administration

### **ENCLOSURES:**

Humalog Mix 75/25 Package Insert (previously approved on March 16, 2009)  
Humalog Mix 75/25 Patient Package Insert (previously approved on September 6, 2007)  
Humalog Mix 75/25 KwikPen Instructions for Use

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**This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.**  
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/s/  
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MARY H PARKS  
01/30/2013