NDA 20-986

Novo Nordisk Pharmaceuticals Inc.
Attention: Barry Reit, Ph.D.
Vice President, Regulatory Affairs
Suite 200
100 Overlook Center
Princeton, NJ 08540-7810

Dear Dr. Reit:

Please refer to your new drug application (NDA) dated September 15, 1998, received September 16, 1998, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for NovoLog (insulin aspart [rDNA origin] injection), 10 mL vials, NovoLog PenFill, 3 mL cartridges, and NovoLog Prefilled, 3 mL syringes.

We acknowledge receipt of your submissions dated December 6, 8, and 14, 1999, and April 24 and 28, May 18, 24, and 31, and June 7 (2), 2000. Your submission of December 6, 1999, constituted a complete response to our September 15, 1999, letter.

This new drug application provides for the use of NovoLog, NovoLog PenFill, and NovoLog Prefilled for the treatment of adult patients with diabetes mellitus, for the control of hyperglycemia.

We have completed the review of this application, as amended, and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the agreed-upon labeling text with the minor editorial revisions listed below. Accordingly, the application is approved effective on the date of this letter.

1. The established name should be made more prominent in relation to the tradename. Per 21 CFR 201.10(g)(2), the prominence of the generic name should be similar to the prominence of the tradename, taking into account such factors as type font and contrast.

2. During today's telephone conversations with Ms. Julie Rhee of the Division of Metabolic and Endocrine Drug Products, Mr. Robert Fischer of your office agreed to include the generic name whenever the tradename is mentioned on carton labels of the vial, PenFill 3 mL cartridge, and Prefilled 3 mL syringe and to make the revisions indicated on the enclosed patient package inserts.

The final printed labeling (FPL) must include the minor editorial revisions indicated above and on the enclosed patient package inserts but otherwise be identical to the submitted draft labeling (package insert submitted June 7, 2000, patient package inserts submitted June 7, 2000, immediate container and carton labels for PenFill 3mL cartridges and Prefilled 3 mL syringes submitted August 20, 1999, and immediate container and carton labels for 10 mL vials submitted August 26, 1999). These revisions are terms of the NDA approval. Marketing the product with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

Please submit 20 copies of the FPL as soon as it is available, in no case more than 30 days after it is printed. Please individually mount ten of the copies on heavy-weight paper or similar material. For administrative purposes, this submission should be designated "FPL for approved NDA 20-986." Approval of this submission by FDA is not required before the labeling is used.

As specified in our September 15, 1999, letter, we remind you of your Phase 4 commitments to perform studies on the pharmacokinetics/pharmacodynamics of insulin aspart in the following special populations. These commitments, along with the completion dates agreed upon during the May 26, 2000, telephone conversation between Mr. Robert Fischer of your office and Ms. Julie Rhee of the Division of Metabolic and Endocrine Drug Products, are listed below.

1. Renally-impaired patients:

Protocol Submission:	December 24, 1999
Study Start:	March 2000
Final Report Submission:	No later than September 2000

2. Hepatically-impaired patients:

Protocol Submission:	December 24, 1999
Study Start:	March 2000
Final Report Submission:	No later than September 2000

3. Obese versus non-obese patients:

Protocol Submission:	December 24, 1999
Study Start:	March 2000
Final Report Submission:	No later than September 2000

Final reports should be submitted to this NDA and a copy of the cover letter sent to the appropriate IND. In addition, under 21 CFR 314.81(b)(2)(vii), we request that you include a status summary of each commitment in your annual report to this NDA. The status summary should include the number of patients entered in each study, expected completion and submission dates, and any changes in plans since the last annual report. For administrative purposes, all submissions, including labeling supplements, relating to these Phase 4 commitments should be prominently labeled **"Phase 4 Commitments."**

Validation of the regulatory methods has not been completed. At the present time, it is the policy of the Center not to withhold approval because the methods are being validated. Nevertheless, we expect your continued cooperation to resolve any problems that may be identified.

Be advised that, as of April 1, 1999, all applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred (63 *FR* 66632). We note that you have not fulfilled the requirements of 21 CFR 314.55. We are deferring submission of your pediatric studies until December 31, 2002. However, in the interim, please submit your pediatric drug development plans within 120 days from the date of this letter unless you believe a waiver is appropriate. Within approximately 120 days of receipt of your pediatric drug development plan, we will review your plan and notify you of its adequacy.

If you believe that this drug qualifies for a waiver of the pediatric study requirement, you should submit a request for a waiver with supporting information and documentation in accordance with the provisions of 21 CFR 314.55 within 60 days from the date of this letter. We will notify you within 120 days of receipt of your response whether a waiver is granted. If a waiver is not granted, we will ask you to submit your pediatric drug development plans within 120 days from the date of denial of the waiver.

Pediatric studies conducted under the terms of section 505A of the Federal Food, Drug, and Cosmetic Act may result in additional marketing exclusivity for certain products (pediatric exclusivity). You should refer to the *Guidance for Industry on Qualifying for Pediatric Exclusivity* (available on our web site at www.fda.gov/cder/pediatric) for details. We note that a Written Request for studies of insulin aspart in pediatric patients with diabetes mellites was issued on December 14, 1999. Satisfaction of the requirements in 21 CFR 314.55 alone may not qualify you for pediatric exclusivity. FDA does not necessarily ask a sponsor to complete the same scope of studies to qualify for pediatric exclusivity as it does to fulfill the requirements of the pediatric rule.

In addition, please submit three copies of the introductory promotional materials that you propose to use for this product. All proposed materials should be submitted in draft or mock-up form, not final print. Please send one copy to the Division of Metabolic and Endocrine Drug Products and two copies of both the promotional materials and the package insert directly to:

Division of Drug Marketing, Advertising, and Communications, HFD-40
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857

Please submit one market package of each drug product when it is available.

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, call Julie Rhee, Regulatory Project Manager, (301) 827-6424.

Sincerely,

John K. Jenkins, M.D.
Director
Office of Drug Evaluation II
Center for Drug Evaluation and Research

Enclosures: Patient package inserts for vial, PenFill, and Prefilled.