REVIEW FOR HFD-510
OFFICE OF NEW DRUG CHEMISTRY
MICROBIOLOGY STAFF
MICROBIOLOGIST'S REVIEW OF NDA 20-986
4 February 1999

A. 1. NDA 20-986 BI
APPLICANT: Novo Nordisk Pharmaceuticals, Inc.
Suite 200
100 Overlook Center
Princeton, NJ 08540-7810

2. PRODUCT NAME: Insulin Aspart (Insulin X-14) Injection (recombinant DNA origin)

3. DOSAGE FORM AND ROUTE OF ADMINISTRATION:
The product is a sterile injectable preparation for subcutaneous injection.

4. METHODS OF STERILIZATION:
The product is

5. PHARMACOLOGICAL CATEGORY and/or PRINCIPLE INDICATION:
The drug product is indicated in the treatment of diabetes mellitus.

B. 1. DATE OF INITIAL SUBMISSION: 16 September 1998

2. DATE OF AMENDMENT: 29 January 1999 (Subject of this Review)

3. RELATED DOCUMENTS: IND —— ; NDA 19-938; DMF ——
DMF —— ; DMF ——

4. ASSIGNED FOR REVIEW: 30 September 1998

C. REMARKS: The product will be manufactured by:

Novo Nordisk A/S
Novo Alle
DK-2880 Bagsvaerd
Denmark
The product is to be packaged in the following presentations:

10 mL vial

PenFill® 3 mL cartridge

Prefilled® 3 mL syringe

It is the applicant's intent to market only the 10mL vial, Penfill® 3mL cartridge, and Prefilled® 3mL syringe at the present time. Should Novo Nordisk decide the other presentations, labeling will be submitted to the Agency for review.

D. CONCLUSIONS: The application is recommended for approval on the basis of sterility assurance.

\[\text{signature}\]
Paul Stinavage, Ph.D.

\[\text{signature}\]
2/8/99

cc: Original NDA 20-986
HFD-510/J. Rhee/Div. File
HFD-805/Consult File/Stinavage

Drafted by: P. Stinavage, 4 February 1999
R/D initialed by P. Cooney

APPEARS THIS WAY ON ORIGINAL
TO (Division Office): Paul Stinavage, Ph.D., HFD-160
FROM: HFD-510 (Division of Metabolic and Endocrine Drug Products) Julie Rhee

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<td>DATE OF DOCUMENT: January 29, 1999</td>
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<td>Desired Completion Date: March 15, 1999</td>
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NAME OF DRUG: Insulin Aspart (insulin X-14 [rDNA])

NAME OF FIRM: Novo Nordisk

**REASON FOR REQUEST**

**I. GENERAL**

☐ NEW PROTOCOL
☐ PROGRESS REPORT
☐ NEW CORRESPONDENCE
☐ DRUG ADVERTISING
☐ ADVERSE REACTION REPORT
☐ MANUFACTURING CHANGE/ADDITION
☐ MEETING PLANNED BY

☐ NEW NDA REVIEW
☐ END OF PHASE II MEETING
☐ RESUBMISSION
☐ SAFETY/EFFICACY
☐ PAPER NDA
☐ CONTROL SUPPLEMENT

☐ RESPONSE TO DEFICIENCY LETTER
☐ FINAL PRINTED LABELING
☐ LABELING REVISION
☐ ORIGINAL NEW CORRESPONDENCE
☐ FORMULATIVE REVIEW
☐ OTHER (SPECIFY BELOW):

**II. BIOMETRICS**

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<th>STATISTICAL EVALUATION BRANCH</th>
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<td>☐ PROTOCOL REVIEW</td>
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**III. BIOPHARMACEUTICS**

☐ DEFICIENCY LETTER RESPONSE
☐ PROTOCOL-BIPHARMACEUTICS
☐ IN-VIVO WAIVER REQUEST

**IV. DRUG EXPERIENCE**

☐ PHASE IV SURVEILLANCE/EPIDEMIOLOGY PROTOCOL
☐ DRUG USE e.g. POPULATION EXPOSURE, ASSOCIATED DIAGNOSES
☐ CASE REPORTS OF SPECIFIC REACTIONS (List below)
☐ COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP

**V. SCIENTIFIC INVESTIGATIONS**

☐ CLINICAL

**COMMENTS/SPECIAL INSTRUCTIONS:**

Paul, this is Novo's response to your earlier requests. For your information, a copy of the fax that was sent to Novo is attached. Thank you.

cc Original NDA 20-986
HFD-510/Div. Files

**NATURE OF REQUESTER:** /S/

**METHOD OF DELIVERY (Check one):**
☐ MAIL
☐ HAND

**SIGNATURE OF DELIVERER:** /S/ 2-3-99

**SIGNATURE OF RECEIVER:** /S/ 2-3-99
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OFFICE OF NEW DRUG CHEMISTRY
MICROBIOLOGY STAFF
MICROBIOLOGIST'S REVIEW OF NDA 20-986
4 January 1999

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B. 1. DATE OF INITIAL SUBMISSION: 16 September 1998

2. DATE OF AMENDMENT: (none)

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D. CONCLUSIONS: The application is approvable pending resolution of microbiology concerns.

4 January 1999

Paul Stinavage, Ph.D.

cc: Original NDA 20-986
    HFD-510/J. Rhee/Div. File
    HFD-805/Consult File/Stinavage

Drafted by: P. Stinavage, 4 January 1999
R/D initialed by P. Cooney
**REQUEST FOR CONSULTATION**

**TO:** Division/Office  
HFD-805 Microbiology  
Peter Coury

**FROM:** HFD-510 Drug Products

**DATE:** September 23, 1993  
**IND NO.:** 20-916  
**NDA NO.:**

**TYPE OF DOCUMENT:**  
**DATE OF DOCUMENT:** Sept 16, 1998

**NAME OF DRUG:** Insulin Aspen  
**PRIORITY CONSIDERATION:** X-14  
**CLASSIFICATION OF DRUG:** Standard

**NAME OF FIRM:** Novo Nordisk Pharmaceuticals

**DESIRED COMPLETION DATE:** July 30, 1999

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**REASON FOR REQUEST**

**I. GENERAL**

- NEW PROTOCOL
- PROGRESS REPORT
- NEW CORRESPONDENCE
- DRUG ADVERTISING
- ADVERSE REACTION REPORT
- MANUFACTURING CHANGE/ADDITION
- MEETING PLANNED BY

- PRE-ND A MEETING
- END OF PHASE II MEETING
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- PAPER NDA
- CONTROL SUPPLEMENT

- RESPONSE TO DEFICIENCY LETTER
- FINAL PRINTED LABELING
- LABELING REVISION
- ORIGINAL NEW CORRESPONDENCE
- FORMULATIVE REVIEW
- OTHER (SPECIFY BELOW)

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**III. BIOPHARMACEUTICS**

- DISSOLUTION
- BIOAVAILABILITY STUDIES
- PHASE IV STUDIES

| DEFICIENCY LETTER RESPONSE |
| PROTOCOL-BIOPHARMACEUTICS  |
| IN-VIVO WAIVER REQUEST     |

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**IV. DRUG EXPERIENCE**

- PHASE IV SURVEILLANCE/EPIDEMIOLOGY PROTOCOL
- DRUG USE e.g. POPULATION EXPOSURE, ASSOCIATED DIAGNOSES
- CASE REPORTS OF SPECIFIC REACTIONS (List below)
- COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP

- REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY
- SUMMARY OF ADVERSE EXPERIENCE
- POISON RISK ANALYSIS

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**V. SCIENTIFIC INVESTIGATIONS**

- CLINICAL

**COMMENTS/SPECIAL INSTRUCTIONS:**

(Paper Message 7-624)

[Initials and Signature]

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**SIGNATURE OF REQUESTER:**

(IS)/Julie Rhed

**METHOD OF DELIVERY:**

- EMAIL

**SIGNATURE OF DELIVERER:**

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**NATURE OF RECIPIENT:**

(IS)