CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: 20-986/SE3-003

ADMINISTRATIVE DOCUMENTS

EXCLUSIVITY SUMMARY for NDA # 20-986 SUPPL # 003

Trade Name NovoLog®

Generic Name Insulin aspart (rDNA origin)

Applicant Name Novo Nordisk Pharmaceuticals, Inc. HFD-510

Approval Date _____

PART I: IS AN EXCLUSIVITY DETERMINATION NEEDED?

1. An exclusivity determination will be made for all original applications, but only for certain supplements. Complete Parts II and III of this Exclusivity Summary only if you answer "YES" to one or more of the following questions about the submission.

   a) Is it an original NDA? YES/___/ NO /_x_/

   b) Is it an effectiveness supplement? YES /_x_/ NO /___/

   If yes, what type(SE1, SE2, etc.)? SE3

   c) Did it require the review of clinical data other than to support a safety claim or change in labeling related to safety? (If it required review only of bioavailability or bioequivalence data, answer "NO.")

   YES /_x_/ NO /___/

   If your answer is "no" because you believe the study is a bioavailability study and, therefore, not eligible for exclusivity, EXPLAIN why it is a bioavailability study, including your reasons for disagreeing with any arguments made by the applicant that the study was not simply a bioavailability study.

   _____

   _____

   If it is a supplement requiring the review of clinical data but it is not an effectiveness supplement, describe the change or claim that is supported by the clinical data:

   _____

d) Did the applicant request exclusivity?

YES /___/ NO /_x_/

If the answer to (d) is "yes," how many years of exclusivity did the applicant request? ____

e) Has pediatric exclusivity been granted for this Active Moiety?

YES /___/ NO /_x_/

IF YOU HAVE ANSWERED "NO" TO ALL OF THE ABOVE QUESTIONS, GO DIRECTLY TO THE SIGNATURE BLOCKS ON Page 9.

2. Has a product with the same active ingredient(s), dosage form, strength, route of administration, and dosing schedule previously been approved by FDA for the same use? (Rx to OTC Switches should be answered No - Please indicate as such).

YES /___/ NO /_x_/

If yes, NDA # _____ Drug Name _____

IF THE ANSWER TO QUESTION 2 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON Page 9.

3. Is this drug product or indication a DESI upgrade?

YES /___/ NO /_x_/

IF THE ANSWER TO QUESTION 3 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON Page 9 (even if a study was required for the upgrade).

PART II: FIVE-YEAR EXCLUSIVITY FOR NEW CHEMICAL ENTITIES
(Answer either #1 or #2, as appropriate)

1. Single active ingredient product.

Has FDA previously approved under section 505 of the Act any drug product containing the same active moiety as the drug under consideration? Answer "yes" if the active moiety (including other esterified forms, salts, complexes, chelates or clathrates) has been previously approved, but this particular form of the active moiety, e.g., this particular ester or salt (including salts with hydrogen or coordination bonding) or other non-covalent derivative (such as a complex, chelate, or clathrate) has not been approved. Answer "no" if the compound requires metabolic conversion (other than deesterification of an esterified form of the drug) to produce an already approved active moiety.

YES /_x_/ NO /___/

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA # 20-986 NovoLog

NDA # _____ _____

NDA # _____ _____

2. Combination product.

If the product contains more than one active moiety (as defined in Part II, #1), has FDA previously approved an application under section 505 containing any one of the active moieties in the drug product? If, for example, the combination contains one never-before-approved active moiety and one previously approved active moiety, answer "yes." (An active moiety that is marketed under an OTC monograph, but that was never approved under an NDA, is considered not previously approved.)

YES /___/ NO /_x_/

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA # _____ _____

NDA # _____ _____

NDA # _____ _____

IF THE ANSWER TO QUESTION 1 OR 2 UNDER PART II IS "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON Page 9. IF "YES," GO TO PART III.

PART III: THREE-YEAR EXCLUSIVITY FOR NDA'S AND SUPPLEMENTS

To qualify for three years of exclusivity, an application or supplement must contain "reports of new clinical investigations (other than bioavailability studies) essential to the approval of the application and conducted or sponsored by the applicant." This section should be completed only if the answer to PART II, Question 1 or 2, was "yes."

1. Does the application contain reports of clinical investigations? (The Agency interprets "clinical investigations" to mean investigations conducted on humans other than bioavailability studies.) If the application contains clinical investigations only by virtue of a right of reference to clinical investigations in another application, answer "yes," then skip to question 3(a). If the answer to 3(a) is "yes" for any investigation referred to in another application, do not complete remainder of summary for that investigation.

YES /_x_/ NO /___/

IF "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON Page 9.

2. A clinical investigation is "essential to the approval" if the Agency could not have approved the application or supplement without relying on that investigation. Thus, the investigation is not essential to the approval if 1) no clinical investigation is necessary to support the supplement or application in light of previously approved applications (i.e., information other than clinical trials, such as bioavailability data, would be sufficient to provide a basis

for approval as an ANDA or 505(b)(2) application because of what is already known about a previously approved product), or 2) there are published reports of studies (other than those conducted or sponsored by the applicant) or other publicly available data that independently would have been sufficient to support approval of the application, without reference to the clinical investigation submitted in the application.

For the purposes of this section, studies comparing two products with the same ingredient(s) are considered to be bioavailability studies.

(a) In light of previously approved applications, is a clinical investigation (either conducted by the applicant or available from some other source, including the published literature) necessary to support approval of the application or supplement?

YES /_x_/ NO /___/

If "no," state the basis for your conclusion that a clinical trial is not necessary for approval **AND GO DIRECTLY TO SIGNATURE BLOCK ON Page 9:**

_____

_____

(b) Did the applicant submit a list of published studies relevant to the safety and effectiveness of this drug product and a statement that the publicly available data would not independently support approval of the application?

YES /___/ NO /_x_/

(1) If the answer to 2(b) is "yes," do you personally know of any reason to disagree with the applicant's conclusion? If not applicable, answer NO.

YES /___/ NO /_x_/

If yes, explain: _____

_____

(2) If the answer to 2(b) is "no," are you aware of published studies not conducted or sponsored by the applicant or other publicly available data that could independently demonstrate the safety and effectiveness of this drug product?

YES /___/ NO /_x_/

If yes, explain: _____

(c) If the answers to (b)(1) and (b)(2) were both "no," identify the clinical investigations submitted in the application that are essential to the approval:

Investigation #1, Study # ANA-2018

Investigation #2, Study # ANA-2024

Investigation #3, Study # ANA-2023

3. In addition to being essential, investigations must be "new" to support exclusivity. The agency interprets "new clinical investigation" to mean an investigation that 1) has not been relied on by the agency to demonstrate the effectiveness of a previously approved drug for any indication and 2) does not duplicate the results of another investigation that was relied on by the agency to demonstrate the effectiveness of a previously approved drug product, i.e., does not redemonstrate something the agency considers to have been demonstrated in an already approved application.

(a) For each investigation identified as "essential to the approval," has the investigation been relied on by the agency to demonstrate the effectiveness of a previously approved drug product? (If the investigation was relied on only to support the safety of a previously approved drug, answer "no.")

Investigation #1	YES /___/	NO /_x_/
Investigation #2	YES /___/	NO /_x_/
Investigation #3	YES /___/	NO /_x_/

If you have answered "yes" for one or more investigations, identify each such investigation and the NDA in which each was relied upon:

NDA # _____ Study # _____
NDA # _____ Study # _____
NDA # _____ Study # _____

(b) For each investigation identified as "essential to the approval," does the investigation duplicate the results of another investigation that was relied on by the agency to support the effectiveness of a previously approved drug product?

Investigation #1 YES /___/ NO /_x_/

Investigation #2 YES /___/ NO /_x_/

Investigation #3 YES /___/ NO /_x_/

If you have answered "yes" for one or more investigations, identify the NDA in which a similar investigation was relied on:

NDA # _____ Study # _____

NDA # _____ Study # _____

NDA # _____ Study # _____

(c) If the answers to 3(a) and 3(b) are no, identify each "new" investigation in the application or supplement that is essential to the approval (i.e., the investigations listed in #2(c), less any that are not "new"):

Investigation #_1_, Study # ANA-2018

Investigation #_2_, Study # ANA-2024

Investigation #_3_, Study # ANA-2023

4. To be eligible for exclusivity, a new investigation that is essential to approval must also have been conducted or sponsored by the applicant. An investigation was "conducted or sponsored by" the applicant if, before or during the conduct of the investigation, 1) the applicant was the sponsor of the IND named in the form FDA 1571 filed with the Agency, or 2) the applicant (or its predecessor in interest) provided substantial support for the study. Ordinarily, substantial support will mean providing 50 percent or more of the cost of the study.

(a) For each investigation identified in response to question 3(c): if the investigation was carried out under an IND, was the applicant identified on the FDA 1571 as the sponsor?

Investigation #1	
IND # [redacted] YES /_x_/	NO /___/ Explain: _____
	_____
	_____
Investigation #2	
IND # [redacted] YES /_x_/	NO /___/ Explain: _____
	_____
	_____
Investigation #3	
IND # [redacted] YES /_x_/	NO /___/ Explain: _____
	_____

(b) For each investigation not carried out under an IND or for which the applicant was not identified as the sponsor, did the applicant certify that it or the applicant's predecessor in interest provided substantial support for the study?

Investigation #1	
YES /___/ Explain _____	NO /___/ Explain _____
_____	_____
_____	_____

Investigation #2	
YES /___/ Explain _____	NO /___/ Explain _____
_____	_____
_____	_____

(c) Notwithstanding an answer of "yes" to (a) or (b), are there other reasons to believe that the applicant should not be credited with having "conducted or sponsored" the study? (Purchased studies may not be used as the basis for exclusivity. However, if all rights to the drug are purchased (not just studies on the drug), the applicant may be considered to have sponsored or conducted the studies sponsored or conducted by its predecessor in interest.)

YES /___/ NO /_x_/

If yes, explain: _____

_____

_____

_____ _____

Signature of Preparer Date

Title: _____

_____ _____

Signature of Office or Division Director Date

cc:
Archival NDA
HFD- /Division File
HFD- /RPM

HFD-093/Mary Ann Holovac
HFD-104/PEDS/T.Crescenzi

Form OGD-011347
Revised 8/7/95; edited 8/8/95; revised 8/25/98, edited 3/6/00

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Printable Pediatric Page

Welcome to the Pediatric Page Printed Page. To produce your pediatric page, simply print this page (this paragraph will not print). However, most versions of Internet Explorer will print a header on each page (i.e., the name of the web site, etc.) To eliminate these when printing the Pediatric Page, go to 'File', then 'Page Setup', and clear the 'Header' and 'Footer' Boxes. (Cut and paste to a document [or write down] the contents of these boxes first if you want to restore the headers and footers afterwards.)

PEDIATRIC PAGE

NDA Number:	020986	**Trade Name:**	NOVOLOG
Supplement Number:	003	**Generic Name:**	INSULIN ASPART RECOMBINANT
Stamp date:	12/21/00	**Action Date:**	12/21/00
Supplement Type:	SE3		
COMIS Indication:	TREATMENT OF DIABETES MELLITUS		

Indication #1: NovoLog is indicated for the treatment of adult patients with diabetes mellitus, for the control of hyperglycemia. - Date Entered: 12/10/01

Status: Pediatric Ranges were specified.

Range #1	Status: Deferred Exp. Completion Date: 8/31/03	Edit this Range Delete this Range
Reason for Deferral:	Adult Studies Ready for Approval	
Range Values:	Minimum: 6 yr Maximum: 16 yr	
Comments:	Pediatric studies have not been conducted	

This page was printed on 12/10/01

Signature _____ Date _____

NDA 20-986 NovoLog® Debarment Statement		Date: December 20, 2000	Novo Nordisk

Debarment Statement

Novo Nordisk Pharmaceuticals Inc. hereby certifies that it did not and will not use in any capacity the services of any person debarred under Section 306 of the Federal Food, Drug and Cosmetic Act in connection with this submission.

Barry Reit, PhD
Vice President
Regulatory Affairs

APPEARS THIS WAY
ON ORIGINAL

MEMORANDUM

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
Food and Drug Administration
Center For Drug Evaluation and Research

DATE: December 21, 2001

FROM: David G. Orloff, M.D.
Director, Division of Metabolic and Endocrine Drug Products

TO: NDA 20-986/S-003

SUBJECT: NDA review issues and recommended action

Background
The development of Novolog (insulin aspart) for pumps included *in vitro* studies of insulin integrity and pump function consistent with the draft 1985 guidance from the Division on use of insulin in pumps. In addition, the sponsor conducted, at the request of the Division, three clinical studies of safety and effectiveness using two different pumps types (MiniMed 506, Disetronic H-tron plus V-100).

Clinical
Efficacy and safety
The clinical studies are discussed in Dr. Koller's review. There were two studies in type 1 DM and one in type 2 DM. Study 018 in type 1 DM was an open-label, parallel group study with HbA1c at 6 weeks as the primary endpoint comparing Velosulin (currently the only approved insulin for pumps) to NovoLog, both in pumps (N=20 on NovoLog). Study 024, also in type 1, was a 16-week trial comparing Velosulin and NovoLog and Humalog (lispro), all in pumps (N=59 on NovoLog). Finally, study 023 was a 16-weeek study in type 2 DM comparing the efficacy and safety of NovoLog in pumps to NovoLog by repeat injection (in regimens that included intermediate or long-acting insulins-- N=66 on NovoLog in pumps).

The efficacy results are discussed in labeling to the extent that the levels of glycemic control across the treatment groups in each individual trial were essentially equivalent, as were the rates of hypoglycemia. There were no cases of ketoacidosis in the type 1 trials or non-ketotic hyperosmolar state in the type 2 study. In the comparision of NovoLog by injection to NovoLog by pumps in type 1 DM, the reduction in HbA1c from baseline was about 0.5 percentage units in each treatment group.

No new safety issues related to the use of NovoLog were raised in this application.

Labeling
Because of the absence of any differences in efficacy across the treatment groups in the pump studies, the decision was made not to include a tabular summary of those data in the label, but rather to include a statement to that effect in the text.

The Indications and Usage states that NovoLog may be infused subcutaneously by pumps and refers the reader to other sections where the specific recommended pumps and infusion sets are listed.

Dr. Koller devoted considerable time in addressing the Warning and Precautions sections with regard to use of NovoLog in pumps, with particular emphasis on the importance of vigilance with regard to pump malfunction because of the risk of rapid deterioration to ketoacidosis in type 1 DM due to the very small reservoir of insulin in the skin when administered by continuous infusion and the short duration of action of NovoLog. In addition, emphasis is placed on the need to change cartridges/syringes and infusion sets every two days and to take care with the temperature exposures not only of NovoLog in unopened cartridges/syringes and vials, but also in the pump under conditions of actual use.

The Patient Package Insert has likewise been extensively modified to address use of NovoLog in pumps.

Biopharmaceutics
No new data.

Pharmacology/Toxicology
No new data.

Chemistry/ Microbiology
The chemistry section included in-use stability data using two pumps: MiniMed 506 and Disetronic H-TRON plus V-100. Stability was satisfactory and supports use in the two pumps with replacement of cartridges/syringes and infusion sets every 2 days. With regard to preservatives, of note, for the MiniMed, after 7 days, the concentration of metacresol was slightly below the shelf-life limit. The concentration of phenol was at the shelf-life limit. This loss was felt due to evaporation. The insulin appeared stable over 7 days.

In the Disetronic pump, there was likewise a decline in metacresol concentrations, though it remained above the shelf-life limit at 7 days. Phenol concentrations were stable. The insulin was stable for 7 days.

A categorical exclusion from the environmental assessment was claimed by the sponsor and accepted by the Agency.

DSI/Data Integrity
The clinical audit of l [redacted] site was satisfactory. He enrolled 25 subjects in study 023 and 27 subjects in protocol 024. The classification was NAI.

Financial disclosure
The financial disclosure information is in order. The sponsor has certified that no investigator received outcome payments, that no investigator disclosed a proprietary interest in the product or

an equity interest in the company, and that no investigator was the recipient of significant payments of other sorts.

OPDRA/nomenclature
No issues. Approved product.

Recommendation
Final labeling has been negotiated. Adequate information has been provided to establish that NovoLog is safe and effective for use in pumps according to the label. This supplement may be approved. There are no Phase 4 commitments.

APPEARS THIS WAY
ON ORIGINAL

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

David Orloff
12/21/01 05:17:55 PM
MEDICAL OFFICER

APPEARS THIS WA
ON ORIGINAL

APPEARS THIS WAY
ON ORIGINAL

RECORD OF TELEPHONE CONVERSATION/MEETING	**Date:** December 10, 2001
Re: 12/20/00 submission (S-003) Since immediate container and carton labels were not included in the 12/20/00 submission (S-003), I called Dr. Tan and asked her if there are any changes to immediate container and carton labels. Dr. Tan responded that she does not believe there are any changes to the immediate container and carton labels but is going to check and will get back to me. --- **Name: Julie Rhee**	**NDA#:** 20-986/S-003 **Telecon/Meeting initiated by:** FDA **By:** Telephone **Product Name:** NovoLog **Firm Name:** Novo Nordisk **Name and Title of Person with whom conversation was held:** Elizabeth Tan, Ph.D. Regulatory Affairs **Phone:** (609) 987-5940

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
Food and Drug Administration

Form Approved: OMB No. 0910-0396
Expiration Date: 3/31/02

CERTIFICATION: FINANCIAL INTERESTS AND ARRANGEMENTS OF CLINICAL INVESTIGATORS

TO BE COMPLETED BY APPLICANT

With respect to all covered clinical studies (or specific clinical studies listed below (if appropriate)) submitted in support of this application, I certify to one of the statements below as appropriate. I understand that this certification is made in compliance with 21 CFR part 54 and that for the purposes of this statement, a clinical investigator includes the spouse and each dependent child of the investigator as defined in 21 CFR 54.2(d).

Please mark the applicable checkbox.

(1) As the sponsor of the submitted studies, I certify that I have not entered into any financial arrangement with the listed clinical investigators (enter names of clinical investigators below or attach list of names to this form) whereby the value of compensation to the investigator could be affected by the outcome of the study as defined in 21 CFR 54.2(a). I also certify that each listed clinical investigator required to disclose to the sponsor whether the investigator had a proprietary interest in this product or a significant equity in the sponsor as defined in 21 CFR 54.2(b) did not disclose any such interests. I further certify that no listed investigator was the recipient of significant payments of other sorts as defined in 21 CFR 54.2(f).

Clinical Investigators		
	See attached list	

(2) As the applicant who is submitting a study or studies sponsored by a firm or party other than the applicant, I certify that based on information obtained from the sponsor or from participating clinical investigators, the listed clinical investigators (attach list of names to this form) did not participate in any financial arrangement with the sponsor of a covered study whereby the value of compensation to the investigator for conducting the study could be affected by the outcome of the study (as defined in 21 CFR 54.2(a)); had no proprietary interest in this product or significant equity interest in the sponsor of the covered study (as defined in 21 CFR 54.2(b)); and was not the recipient of significant payments of other sorts (as defined in 21 CFR 54.2(f)).

(3) As the applicant who is submitting a study or studies sponsored by a firm or party other than the applicant, I certify that I have acted with due diligence to obtain from the listed clinical investigators (attach list of names) or from the sponsor the information required under 54.4 and it was not possible to do so. The reason why this information could not be obtained is attached.

NAME	TITLE
Barry Reit	Vice President, Regulatory Affairs
FIRM/ORGANIZATION: Novo Nordisk Pharmaceuticals, Inc.	
SIGNATURE	DATE: 12/19/00

Paperwork Reduction Act Statement

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number. Public reporting burden for this collection of information is estimated to average 1 hour per response, including time for reviewing instructions, searching existing data sources, gathering and maintaining the necessary data, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information to the address to the right:

Department of Health and Human Services
Food and Drug Administration
5600 Fishers Lane, Room 14C-03
Rockville, MD 20857

FORM FDA 3454 (3/99)

Redacted 3

pages of trade

secret and/or

confidential

commercial

information

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

Form Approved: OMB No. 0910-0297
Expiration Date: 04-30-01

USER FEE COVER SHEET

See Instructions on Reverse Side Before Completing This Form

1. APPLICANT'S NAME AND ADDRESS

Novo Nordisk Pharmaceuticals, Inc.
100 College Road West
Princeton, New Jersey 08540

2. TELEPHONE NUMBER *(Include Area Code)*

(609) 987-5822

3. PRODUCT NAME

NovoLog
Insulin aspart (rDNA)

4. DOES THIS APPLICATION REQUIRE CLINICAL DATA FOR APPROVAL? IF YOUR RESPONSE IS "NO" AND THIS IS FOR A SUPPLEMENT, STOP HERE AND SIGN THIS FORM. Yes

IF RESPONSE IS 'YES', CHECK THE APPROPRIATE RESPONSE BELOW:

☒ THE REQUIRED CLINICAL DATA ARE CONTAINED IN THE APPLICATION.

☐ THE REQUIRED CLINICAL DATA ARE SUBMITTED BY REFERENCE TO ____ (APPLICATION NO. CONTAINING THE DATA).

5. USER FEE I.D. NUMBER

4077

6. LICENSE NUMBER / NDA NUMBER

20-986

7. IS THIS APPLICATION COVERED BY ANY OF THE FOLLOWING USER FEE EXCLUSIONS? IF SO, CHECK THE APPLICABLE EXCLUSION.

☐ A LARGE VOLUME PARENTERAL DRUG PRODUCT APPROVED UNDER SECTION 505 OF THE FEDERAL FOOD, DRUG, AND COSMETIC ACT BEFORE 9/1/92 *(Self Explanatory)*

☐ A 505(b)(2) APPLICATION THAT DOES NOT REQUIRE A FEE *(See Item 7, reverse side before checking box.)*

☐ THE APPLICATION QUALIFIES FOR THE ORPHAN EXCEPTION UNDER SECTION 736(a)(1)(E) of the Federal Food, Drug, and Cosmetic Act *(See Item 7, reverse side before checking box.)*

☐ THE APPLICATION IS A PEDIATRIC SUPPLEMENT THAT QUALIFIES FOR THE EXCEPTION UNDER SECTION 736(a)(1)(F) of the Federal Food, Drug, and Cosmetic Act *(See Item 7, reverse side before checking box.)*

☐ THE APPLICATION IS SUBMITTED BY A STATE OR FEDERAL GOVERNMENT ENTITY FOR A DRUG THAT IS NOT DISTRIBUTED COMMERCIALLY *(Self Explanatory)*

FOR BIOLOGICAL PRODUCTS ONLY

☐ WHOLE BLOOD OR BLOOD COMPONENT FOR TRANSFUSION

☐ A CRUDE ALLERGENIC EXTRACT PRODUCT

☐ AN APPLICATION FOR A BIOLOGICAL PRODUCT FOR FURTHER MANUFACTURING USE ONLY

☐ AN "IN VITRO" DIAGNOSTIC BIOLOGICAL PRODUCT LICENSED UNDER SECTION 351 OF THE PHS ACT

☐ BOVINE BLOOD PRODUCT FOR TOPICAL APPLICATION LICENSED BEFORE 9/1/92

8. HAS A WAIVER OF AN APPLICATION FEE BEEN GRANTED FOR THIS APPLICATION?

☐ YES ☒ NO *(See reverse side if answered YES)*

A completed form must be signed and accompany each new drug or biologic product application and each new supplement. If payment is sent by U.S. mail or courier, please include a copy of this completed form with payment.

Public reporting burden for this collection of information is estimated to average 30 minutes per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:

DHHS, Reports Clearance Officer
Paperwork Reduction Project (0910-0297)
Hubert H. Humphrey Building, Room 531-H
200 Independence Avenue, S.W.
Washington, DC 20201

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number

Please **DO NOT RETURN** this form to this address.

SIGNATURE OF AUTHORIZED COMPANY REPRESENTATIVE	TITLE	DATE
Barry Reit, Ph.D.	Vice President, Regulatory Affairs	December 20, 2000

FORM FDA 3397 (5/98)

NDA/EFFICACY SUPPLEMENT ACTION PACKAGE CHECKLIST

NDA 20-986 /SE 3 - 003

Drug NovoLog (insulin aspart [rDNA origin] injection) Applicant Novo Nordisk

RPM Julie Rhee Phone 827-6424

x505(b)(1)
☐505(b)(2) Reference listed drug

☐Fast Track ☐Rolling Review Review priority: x S ☐P

Pivotal IND: [redacted]

Application classifications:
Chem Class 3031500
Other (e.g., orphan, OTC) Rx

PDUFA Goal Dates:
Primary: Oct 21, 2001
Secondary: Dec 21, 2001

Arrange package in the following order:

Indicate N/A (not applicable), X (completed), or add a comment.

GENERAL INFORMATION:

- User Fee Information: x User Fee Paid
  ☐ User Fee Waiver (attach waiver notification letter)
  ☐ User Fee Exemption

- Action Letter..... xAP ☐ AE ☐NA

- Labeling & Labels
  FDA revised labeling and reviews..... x
  Original proposed labeling (package insert, patient package insert) x
  Other labeling in class (most recent 3) or class labeling..... x
  Has DDMAC reviewed the labeling? ..... x Yes (include review) ☐ No
  Immediate container and carton labels ..... N/A
  Nomenclature review ..... N/A

- Application Integrity Policy (AIP) ☐ Applicant is on the AIP. This application ☐ is x is not on the AIP.
  Exception for review (Center Director's memo)..... _____
  OC Clearance for approval..... _____

Continued ⇨

- Status of advertising (if AP action) ☐ Reviewed (for Subpart H – attach review) — x Materials requested in AP letter

- Post-marketing Commitments — N/A
  - Agency request for Phase 4 Commitments.....
  - Copy of Applicant's commitments .....

- Was Press Office notified of action (for approval action only)?..... — ☐ Yes x No
  - Copy of Press Release or Talk Paper.....

- Patent
  - Information [505(b)(1)] .....
  - Patent Certification [505(b)(2)].....
  - Copy of notification to patent holder [21 CFR 314.50 (i)(4)].....

- Exclusivity Summary ..... — x

- Debarment Statement ..... — x

- Financial Disclosure
  - No disclosable information ..... — x
  - Disclosable information – indicate where review is located .....

- Correspondence/Memoranda/Faxes .....

- Minutes of Meetings ..... — N/A
  - Date of EOP2 Meeting _____
  - Date of pre NDA Meeting _____
  - Date of pre-AP Safety Conference _____

- Advisory Committee Meeting ..... — N/A
  - Date of Meeting .....
  - Questions considered by the committee .....
  - Minutes or 48-hour alert or pertinent section of transcript .....

- Federal Register Notices, DESI documents ..... — N/A

CLINICAL INFORMATION: — **Indicate N/A (not applicable), X (completed), or add a comment.**

- Summary memoranda (e.g., Office Director's memo, Division Director's memo, Group Leader's memo) ..... — pending

- Clinical review(s) and memoranda ..... — pending

Continued ⇨

- Safety Update review(s) ..... N/A

- Pediatric Information
  ☐ Waiver/partial waiver (Indicate location of rationale for waiver) x Deferred
  Pediatric Page..... _____
  ☐ Pediatric Exclusivity requested? ☐ Denied x Granted ☐ Not Applicable

- Statistical review(s) and memoranda ..... N/A

- Biopharmaceutical review(s) and memoranda..... N/A

- Abuse Liability review(s) ..... N/A
  Recommendation for scheduling ..... _____

- Microbiology (efficacy) review(s) and memoranda ..... N/A

- DSI Audits x
  x Clinical studies ☐ bioequivalence studies ..... _____

CMC INFORMATION: **Indicate N/A (not applicable), X (completed), or add a comment.**

- CMC review(s) and memoranda x

- Statistics review(s) and memoranda regarding dissolution and/or stability ..... N/A

- DMF review(s) ..... N/A

- Environmental Assessment review/FONSI/Categorical exemption x

- Micro (validation of sterilization) review(s) and memoranda ..... N/A

- Facilities Inspection (include EES report)
  Date completed _____ ..... ☐ Acceptable ☐ Not Acceptable

- Methods Validation ..... ☐ Completed ☐ Not Completed

PRECLINICAL PHARM/TOX INFORMATION: **Indicate N/A (not applicable), X (completed), or add a comment.**

- Pharm/Tox review(s) and memoranda ..... N/A

- Memo from DSI regarding GLP inspection (if any) ..... N/A

Continued ⇨

- Statistical review(s) of carcinogenicity studies ..... N/A
- CAC/ECAC report ..... N/A

APPEARS THIS WAY
ON ORIGINAL

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