

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: 020918

MICROBIOLOGY REVIEW(S)

**REVIEW FOR HFD-510
OFFICE OF NEW DRUG CHEMISTRY
MICROBIOLOGY STAFF HFD-805**

FEB 23 1998

**Microbiologist's Review #2 of NDA 20-918
Response to FDA Request of Information
February 23, 1998**

- A. 1. **APPLICATION NUMBER:** 20-918
- APPLICANT:** Novo Nordisk Pharmaceuticals Inc.
Suite 200
100 Overlook Center
Princeton, NJ 08540-7810
2. **PRODUCT NAMES:** GlucaGen (glucagon (rDNA))
3. **DOSAGE FORM AND ROUTE OF ADMINISTRATION:** Sterile powder for injection, 1 mg (1U) dosage in a 2 ml vial, accompanied by Sterile Water for reconstitution also in a 2 ml vial. GlucaGen is to be administered by SC, IM and IV injection.
4. **METHOD(S) OF STERILIZATION:** (b)(4)
- (b)(4)
5. **PHARMACOLOGICAL CATEGORY:** 1P, GlucaGen is indicated for the treatment of severe hypoglycemia which may occur in patients with diabetes treated with insulin. It is also used as a diagnostic aid to temporarily inhibit movement of the gastrointestinal tract.
- APPEARS THIS WAY ON ORIGINAL**
- B. 1. **DATE OF INITIAL SUBMISSION:** September 18, 1997
2. **AMENDMENT:** January 29, 1998, and February 17, 1998
3. **RELATED DOCUMENTS:** (b)(4)
4. **ASSIGNED FOR REVIEW:** February 10, 1998
5. **DATE OF CONSULT REQUEST:** February 3, 1998

APPEARS THIS WAY ON ORIGINAL

C. REMARKS:

The submission responds to questions presented to the Applicant as a result of Microbiologist's Review #1. (b)(4)

(b)(4)

D. CONCLUSIONS:

Satisfactory answers were submitted in response to Microbiology deficiencies. The submission is recommended for approval with respect to microbiology.

APPEARS THIS WAY ON ORIGINAL

/s/

2/23/98

**Brenda Uratani, Ph.D.
Review Microbiologist**

/s/

2/23/98

APPEARS THIS WAY ON ORIGINAL

cc:

**NDA 20-918
HFD-510/ Div. File
HFD-805/ Uratani
HFD-510/CSO/ Rhee
drafted by: Brenda Uratani, 2/23/98
R/D initialed by P. Cooney, 2/23/98**

**REVIEW FOR HFD-
OFFICE OF NEW DRUG CHEMISTRY
MICROBIOLOGY STAFF HFD-805**

DEC 19 1997

**Microbiologist's Review #1 of NDA 20-918
December 19, 1997**

A. 1. APPLICATION NUMBER: 20-918

APPLICANT: Novo Nordisk Pharmaceuticals Inc.
Suite 200
100 Overlook Center
Princeton, NJ 08540-7810

2. PRODUCT NAMES: GlucaGen (glucagon (rDNA))

3. DOSAGE FORM AND ROUTE OF ADMINISTRATION: Sterile powder for injection, 1 mg (1U) dosage in a 2 ml vial, accompanied by Sterile Water for reconstitution also in a 2 ml vial; GlucaGen is to be administered by SC, IM and IV injection.

4. METHOD(S) OF STERILIZATION: (b)(4)

(b)(4)

5. PHARMACOLOGICAL CATEGORY: 1P, GlucaGen is indicated for the treatment of severe hypoglycemia which may occur in patients with diabetes treated with insulin. It is also used as a diagnostic aid to temporarily inhibit movement of the gastrointestinal tract.

B. 1. DATE OF INITIAL SUBMISSION: September 18, 1997

2. AMENDMENT: none

3. RELATED DOCUMENTS: (b)(4)

4. ASSIGNED FOR REVIEW: October 20, 1997

5. DATE OF CONSULT REQUEST: October 15, 1997

C. REMARKS: ~~APPEARS THIS WAY ON ORIGINAL~~

Glucagon is a single-chain polypeptide containing 29 amino acid residues. The chemical structure of the glucagon in GlucaGen is identical to naturally occurring human

~~APPEARS THIS WAY ON ORIGINAL~~

glycagon and to glucagon extracted from beef and pork pancreas. GlucaGen [glycagon (rDNA)] is produced by expression of recombinant DNA in a *saccharomyces cerevisiae* vector. (b)(4)

(b)(4) The manufacturing of the drug product is performed at Novo Nordisk A/S, Gentofte

D. CONCLUSIONS:

The submission does not contain sufficient information to assure the sterility and safety of the drug product. (b)(4)

(b)(4)
The NDAs are, therefore, not recommended for approval as submitted. (b)(4)

(b)(4)

APPEARS THIS WAY ON ORIGINAL

(b)(4) 11/19/97

**Brenda Uratani, Ph.D.
Review Microbiologist**

(b)(4) 12/19/97

APPEARS THIS WAY ON ORIGINAL

cc:

**NDA 20-918
HFD-510/ Div. File
HFD-805/ Uratani
HFD-510/CSO/ Rhee
drafted by: Brenda Uratani, 12/19/97
R/D initialed by P. Cooney, 12/19/97**