CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

76-092

MICROBIOLOGY REVIEW

OFFICE OF GENERIC DRUGS, HFD-640

Microbiology Review #1
September 24, 2001

A. 1. **ANDA** 76-092

APPLICANT Bioniche Pharma Group
383 Sovereign Road,
London, Ont., Canada

2. PRODUCT NAME: Ketamine Hydrochloride Injection USP

3. DOSAGE FORM AND ROUTE OF ADMINISTRATION: 50mg/mL (base) 10mL/vial Fill; I/V and I/M

4. METHOD(S) OF STERILIZATION: [redacted]

5. PHARMACOLOGICAL CATEGORY: Anesthetic

B. 1. DATE OF INITIAL SUBMISSION: March 8, 2001
Subject of this Review (Received March 12, 2001)

2. DATE OF AMENDMENT: None

3. RELATED DOCUMENTS: None

4. ASSIGNED FOR REVIEW: September 18, 2001

C. REMARKS: The subject drug product is manufactured by Bioniche Teoranta in Ireland for the applicant. The subject [redacted]

D. CONCLUSIONS: The submission is **not recommended** for approval on the basis of sterility assurance. Specific comments are provided in "E. Review Notes" and "Microbiology Comments to be Provided to the Applicant" found at the end of this review. The deficiencies represent major/minor amendment.

/S/ 10/4/01
Nrapendra Nath, Ph. D.

cc: Original **ANDA**
Duplicate ANDA
Division Copy
Field Copy
Drafted by N. Nath, HFD 600; V:\microrev\76-092.doc
Initialed by A. High/M. Fanning

/4. 10/10/01

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Microbiology Comments to be Provided to the Applicant

ANDA: 76-092 APPLICANT: Bioniche Pharma Group

DRUG PRODUCT: Ketamine Hydrochloride Injection USP, 50mg/mL

A. Microbiology Deficiencies:

1. You have stated that [redacted] stability studies for [redacted] formulations of the subject drug product (volume 1.2, page 472). Please describe who will conduct stability studies on 50mg/mL formulation.

2. Among the list of equipment used in production (volume 1.2, page 536) you mention [redacted] in addition to [redacted]. Please describe the function of [redacted] in the manufacture of the subject drug product and provide summary of its validation.

3. Validation of [redacted] testing of the subject drug product are contained in a report dated May 22, 2000 noting that the results were inconclusive (volume 1.2, page 312). Please explain the reason for providing results of an incomplete study and provide results of a full and conclusive study in support of the subject drug product.

4. You provide results of [redacted] inhibition/enhancement tests for [redacted] strength of the subject drug product (volume 1.2, page 315). Please provide [redacted] test results for 50mg/mL of the subject drug product.

B. In addition to responding to the deficiencies presented above, please note and acknowledge the following comments in your response:

The acceptance criteria for [redacted] of the subject drug product by [redacted] however, you should consider [redacted] to the acceptance criteria because [redacted]. Please comment.

Please clearly identify your amendment to this facsimile as RESPONSE TO MICROBIOLOGY DEFICIENCIES. The RESPONSE TO MICROBIOLOGY DEFICIENCIES should also be noted in your cover page/letter.

Sincerely yours,

/S/

Mary Fanning, M.D. Ph.D.
Associate Director of Medical Affairs
Office of Generic Drugs
Center for Drug Evaluation and Research

OFFICE OF GENERIC DRUGS, HFD-640

Microbiology Review #2
November 27, 2001

A. 1. **ANDA** 76-092

APPLICANT Bioniche Pharma Group
383 Sovereign Road,
London, Ont., Canada

2. PRODUCT NAME: Ketamine Hydrochloride Injection USP

3. DOSAGE FORM AND ROUTE OF ADMINISTRATION: 50mg/mL (base) 10mL/vial Fill; I/V and I/M

4. METHOD(S) OF STERILIZATION: [redacted]

5. PHARMACOLOGICAL CATEGORY: Anesthetic

B. 1. DATE OF INITIAL SUBMISSION: March 8, 2001
(Received March 12, 2001)

2. DATE OF AMENDMENT: November 6, 2001
Subject of this Review (Recd. November 7, 2001)

3. RELATED DOCUMENTS: None

4. ASSIGNED FOR REVIEW: November 27, 2001

C. REMARKS: The subject amendment provides for the response to the microbiology deficiency letter dated October 24,2001.

D. CONCLUSIONS: The submission is **recommended** for approval on the basis of sterility assurance. Specific comments are provided in "E. Review Notes".

/S/
Nrapendra Nath, Ph. D.
/S/
29/01

cc: Original **ANDA**
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Field Copy
Drafted by N. Nath, HFD 600; V:\microrev\76-092a1.doc
Initialed by L. Ensor

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Micro Particle

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