CENTER FOR DRUG EVALUATION AND RESEARCH

APPROVAL PACKAGE FOR:

APPLICATION NUMBER
20-920

Microbiology Review(s)
REVIEW TO HFD-110
OFFICE OF NEW DRUG CHEMISTRY
MICROBIOLOGY STAFF/HFD-805
MICROBIOLOGY REVIEW #4 OF NDA

14 February 2001

A. 1. NDA: 20-920/AZ
2. TYPE OF SUPPLEMENT: N/A
3. SUPPLEMENT PROVIDES FOR: N/A
4. APPLICANT/SPONSOR: Scios, Inc.
   820 West Maude Ave
   Sunnyvale, CA 94085
5. MANUFACTURING SITE:
6. DRUG PRODUCT NAME:
   Proprietary: Natrecor®
   Nonproprietary: nesiritide
   Drug Priority Classification:
7. DOSAGE FORM, ROUTE OF ADMINISTRATION AND
   STRENGTH/POTENCY: Lyophilized powder, 1.5 mg in a 5 mL vial, for
   IV Infusion
8. METHOD(S) OF STERILIZATION:
9. PHARMACOLOGICAL CATEGORY: Anti-Arrhythmic

B. 1. DOCUMENT/LETTER DATE: April 24, 1998
2. RECEIPT DATE: January 10, 2001
3. CONSULT DATE: January 11, 2001
4. DATE OF AMENDMENT: January 9, 2001
5. ASSIGNED FOR REVIEW: January 22, 2001
6. SUPPORTING/RELATED DOCUMENTS: Previous Microbiology
   reviews of 20-920 dated 8/12/98; 12/1/98; and 3/25/99.

C. REMARKS: The original NDA was recommended for approval from a product
   quality microbiology standpoint (3/25/99). This amendment covers changes made
   to the manufacturing process since that recommendation.
D. CONCLUSIONS: This submission is recommended for approval on the basis of product quality microbiology.

\[\text{Signature}\]

Bryan S. Riley, Ph.D.
Microbiology Reviewer

cc.: Original NDA 20-920
HFD 110/Division File
HFD 110/Project Manager
HFD 110/Other
HFD 805/Consult File
HFD 805/ B. Riley

Drafted by: Bryan Riley, Ph.D.
R/D initialed by: Peter Cooney, Ph.D.
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REVIEW FOR HFD-110
OFFICE OF NEW DRUG CHEMISTRY
MICROBIOLOGY STAFF HFD-805

Microbiologist’s Review #3 of NDA 20-920/BC
March 25, 1999

A. 1. APPLICATION NUMBER: 20-920/BC

APPLICANT: Scios Inc.
2450 Bayshore Parkway
Mountain View, CA 94043

2. PRODUCT NAMES: Natrecor (nesiritide) for Injection; recombinant human B-type natriuretic peptide (hBNP).

3. DOSAGE FORM AND ROUTE OF ADMINISTRATION: 5 mg/vial (lyophilized powder) for single use; it contains no preservative. Natrecor is reconstituted with 5% Dextrose for Injection, or sterile WFI or 0.9% sodium chloride for Injection prior to intravenous administration.

4. METHOD(S) OF STERILIZATION: [ ]

5. PHARMACOLOGICAL CATEGORY: Natrecor is indicated for the short term intravenous therapy of congestive heart failure (CHF).

B. 1. DATE OF INITIAL SUBMISSION: April 24, 1998

2. AMENDMENT: October 2, 1998 and March 11, 1999

3. RELATED DOCUMENTS:

4. ASSIGNED FOR REVIEW: March 22, 1999

5. DATE OF CONSULT REQUEST: March 16, 1999

C. REMARKS:

The amendment provides for responses to “List of Microbiology Comments and Deficiencies” in Microbiologist’s Review #2.
D. CONCLUSIONS:

The submission is recommended for approval for issues concerning microbiology.

Brenda Uratani, Ph.D.
Review Microbiologist

cc:

NDA 20-920/BC
HFD-110/ Div. File
HFD-805/ Uratani
HFD-110/ Willard
drafted by: Brenda Uratani, 3/25/99
R/D initialed by P. Cooney, 3/25/99
REVIEW FOR HFD-110
OFFICE OF NEW DRUG CHEMISTRY
MICROBIOLOGY STAFF HFD-805

Microbiologist's Review #1 of NDA 20-920
August 12, 1998

A. 1. APPLICATION NUMBER: 20-920

APPLICANT: Scios Inc.
2450 Bayshore Parkway
Mountain View, CA 94043

2. PRODUCT NAMES: Natrecor (nesiritide) for Injection; recombinant human B-type natriuretic peptide (hBNP).

3. DOSAGE FORM AND ROUTE OF ADMINISTRATION: 5 mg/vial (lyophilized powder) for single use; it contains no preservative. Natrecor is reconstituted with 5% Dextrose for Injection, or sterile WFI or 0.9% sodium chloride for Injection prior to intravenous administration.

4. METHOD(S) OF STERILIZATION:

5. PHARMACOLOGICAL CATEGORY: Natrecor is indicated for the short term intravenous therapy of congestive heart failure (CHF).

B. 1. DATE OF INITIAL SUBMISSION: April 24, 1998

2. AMENDMENT:

3. RELATED DOCUMENTS:

4. ASSIGNED FOR REVIEW: May 1, 1998

5. DATE OF CONSULT REQUEST: June 10, 1998

C. REMARKS:

Human B-type natriuretic peptide (hBNP), a 32-amino acid peptide, is produced as a fusion protein in Escherichia coli. The fermentation and manufacture of the drug substance are performed in The manufacture of the drug product is conducted at

1
D. CONCLUSIONS:

The submission is approvable pending on resolution on container-closure integrity issue. Specific comments are provided in "Review Notes" and in the "List of Microbiology Deficiencies and Comments".

/\S/ 8/12/98
Brenda Uratani, Ph.D.
Review Microbiologist

\_{\text{JMK}} 8/12/98

cc:

NDA 20-920
HFD-110/ Div. File
HFD-805/ Uratani
HFD-110/ Willard
drafted by: Brenda Uratani, 8/12/98
R/D initialed by P. Cooney, 8/12/98
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REVIEW FOR HFD-110
OFFICE OF NEW DRUG CHEMISTRY
MICROBIOLOGY STAFF HFD-805

Microbiologist’s Review #2 of NDA 20-920/BI
December 1, 1998

A. 1. APPLICATION NUMBER: 20-920/BI

APPLICANT: Scios Inc.
2450 Bayshore Parkway
Mountain View, CA 94043

2. PRODUCT NAMES: Natrecor (nesiritide) for Injection; recombinant human B-type natriuretic peptide (hBNP).

3. DOSAGE FORM AND ROUTE OF ADMINISTRATION: 5 mg/vial (lyophilized powder) for single use; it contains no preservative. Natrecor is reconstituted with 5% Dextrose for Injection, or sterile WFI or 0.9% sodium chloride for Injection prior to intravenous administration.

4. METHOD(S) OF STERILIZATION: 

5. PHARMACOLOGICAL CATEGORY: Natrecor is indicated for the short term intravenous therapy of congestive heart failure (CHF).

B. 1. DATE OF INITIAL SUBMISSION: April 24, 1998

2. AMENDMENT: October 2, 1998

3. RELATED DOCUMENTS:

4. ASSIGNED FOR REVIEW: October 26, 1998

5. DATE OF CONSULT REQUEST: October 5, 1998

C. REMARKS:

The amendment provides for responses to “List of Microbiology Comments and Deficiencies” in Microbiologist’s Review #1.
D. CONCLUSIONS:

The response to Microbiology deficiency is not satisfactory. The submission is approvable pending on resolution on container-closure integrity issue. Specific comments are provided in "Review Notes" and in the "List of Microbiology Deficiencies and Comments".

Brenda Uratani, Ph.D.
Review Microbiologist

cc:
NDA 20-920 /BI
HFD-110/ Div. File
HFD-805/ Uratani
HFD-110/ Willard
drafted by: Brenda Uratani, 12/1/98
R/D initialed by P. Cooney, 12/1/98
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