

CENTER FOR DRUG EVALUATION AND RESEARCH

APPROVAL PACKAGE FOR:

**APPLICATION NUMBER
20-920**

Correspondence

MAR 26 1999

NDA 20-920

Scios Inc.
Attention: Mr. Michael A. Crockett
2450 Bayshore Parkway
Mountain View, CA 94043-1173

Dear Mr. Crockett:

Please refer to your new drug application (NDA) for Natrecor (nesiritide) Intravenous Infusion, 5.0 mg/vial.

In reviewing your submission of April 24, 1998, our Clinical Pharmacologist/Biopharmaceutist has raised a number of questions that require your attention. Our comments on your submission are detailed as part of this correspondence (see enclosure).

Sincerely yours,



Natalia A. Morgenstern
Chief, Project Management Staff
Division of Cardio-Renal Drug Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

Enclosure

March 25, 1999 Biopharmaceutics/Pharmacokinetics Review

cc:
Original NDA
HFD-110
HFD-110/D Willard
sb/3/26/99

GENERAL CORRESPONDENCE

MAR 17 1999

NDA 20-920

Scios Inc.
Attention: Mr. Michael A. Crockett
2450 Bayshore Parkway
Mountain View, CA 94043-1173

Dear Mr. Crockett:

Please refer to your new drug application (NDA) for Natrecor (nesiritide) Intravenous Infusion, 5.0 mg/vial.

In reviewing your submission of April 24, 1998, our Medical Officers and Statistician have raised a number of questions that require your attention. Our comments on your submission are detailed as part of this correspondence (see enclosure).

Sincerely yours,

/s/

Natalia A. Morgenstern
Chief, Project Management Staff
Division of Cardio-Renal Drug Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

Enclosures

March 3, 1999 Medical/Statistical Review
March 11, 1999 Clinical Pharmacology Review
March 11, 1999 Global Review

cc:

Original NDA
HFD-110

HFD-110/D Willard/3/15/99
sb/3/17/99

GENERAL CORRESPONDENCE

DF
DEC 4 1998

NDA 20-920

Scios Inc.
Attention: Mr. Michael A. Crockett
2450 Bayshore Parkway
Mountain View, CA 94043-1173

Dear Mr. Crockett:

Please refer to your new drug application (NDA) for Natrecor (nesiritide) Intravenous Infusion, 5.0 mg/vial.

In reviewing your submission of April 24, 1998, our Medical Officer has raised a number of questions that require your attention. Our comments on your submission are detailed as part of this correspondence (see enclosure).

Sincerely yours,

/S/

Natalia A. Morgenstern
Chief, Project Management Staff
Division of Cardio-Renal Drug Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

Enclosure
Draft Medical Review

cc:
Original NDA
HFD-110
HFD-110/D Willard
sb/12/4/98

GENERAL CORRESPONDENCE

OCT 30 1998

NDA 20-920

Scios Inc.
Attention: Mr. Michael A. Crockett
2450 Bayshore Parkway
Mountain View, CA 94043-1173

Dear Mr. Crockett:

Please refer to your new drug application (NDA) for Natrecor (nesiritide) Intravenous Infusion, 5.0 mg/vial.

In reviewing your submission of April 24, 1998, our Medical Officer and Statistician have raised a number of questions that require your attention. Our comments on your submission are detailed as part of this correspondence (see enclosure).

Sincerely yours,

/S/

Natalia A. Morgenstern
Chief, Project Management Staff
Division of Cardio-Renal Drug Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

Enclosure
Draft Medical/Statistical Review

cc:

~~Original NDA~~

HFD-110

HFD-110/D Willard

sb/10/29/98

GENERAL CORRESPONDENCE

D. Willard

AUG 17 1998

NDA 20-920

Scios Inc.
Attention: Mr. Michael A. Crockett
2450 Bayshore Parkway
Mountain View, CA 94043-1173

Dear Mr. Crockett:

Please refer to your new drug application (NDA) for Natrecor (nesiritide) Intravenous Infusion, 5.0 mg/vial.

In reviewing your submission of April 24, 1998, our Microbiologist has raised a number of questions that require your attention. Our concerns with your submission are detailed as part of this correspondence (see enclosure).

We would appreciate your written response.

Sincerely yours,

NS
Natalia A. Morgenstern
Chief, Project Management Staff
Division of Cardio-Renal Drug Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

Enclosure
8/13/98 Microbiology Review

cc:
Original NDA
HFD-110
HFD-110/DWillard
sb/8/14/98

GENERAL CORRESPONDENCE



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

NDA 20-920

Food and Drug Administration
Rockville MD 20857

Scios Inc.
Attention: Ms. Karen J. Harder
2450 Bayshore Parkway
Mountain View, CA 94043

APR 30 1998

Dear Ms. Harder:

We have received your new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for the following:

Name of Drug Product: Natrecor (nesiritide) Intravenous Infusion, 5.0 mg/vial

Therapeutic Classification: S

Date of Application: April 24, 1998

Date of Receipt: April 27, 1998

Our Reference Number: NDA 20-920

Unless we notify you within 60 days of the receipt date that the application is not sufficiently complete to permit a substantive review, this application will be filed under section 505(b) of the Act on June 26, 1998 in accordance with 21 CFR 314.101(a).

Under 21 CFR 314.102(c) of the new drug regulations you may request an informal conference with this Division (to be held approximately 90 days from the above receipt date) for a brief report on the status of the review but not on the application's ultimate approvability. Alternatively, you may choose to receive such a report by telephone. Should you wish a conference, a telephone report, or if you have any questions concerning this NDA, please contact:

Ms. Diana Willard
Regulatory Health Project Manager
(301) 594-5311

Please cite the NDA number listed above at the top of the first page of any communications concerning this application.

Sincerely yours,

/s/

Natalia A. Morgenstern
Chief, Project Management Staff
Division of Cardio-Renal Drug Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

DUPLICATE

scios

■ Scios Inc.
2450 Bayshore Parkway
Mountain View, CA 94043
415 966 1550 Tel
415 968 2438 Fax

05 March 1999

Raymond J. Lipicky, MD, Director
Division of Cardio-Renal Drug Products
Food and Drug Administration
Woodmont Office Center 2
Document Control Room 5002
1451 Rockville Pike
Rockville, Maryland 20852

**Reference: NDA 20-920 Amendment
Natreacor® (nesiritide) for Injection
Request for Exclusivity**

Dear Dr. Lipicky:

In accordance with 21 CFR 314.50 (j), Scios hereby claims exclusivity for Natreacor® (nesiritide) for Injection, which was filed with the Agency on 27 April 1998 and assigned NDA number 20-920.

Natreacor® is a new chemical entity whose active moiety has not been approved by the FDA in any other application submitted under section 505(b) of the act. Therefore, Scios claims 5 years exclusivity under 21 CFR 314.108 (b) (2).

NDA 20-920 contains "new clinical investigations" that are essential to the approval of Natreacor®. The new clinical investigations, filed in NDA 20-920, meet the definition set forth in 314.108 (a). In addition, a list of published studies or publicly available reports of clinical investigation were supplied in NDA 20-920 (NDA volume 75, pages 5-11).

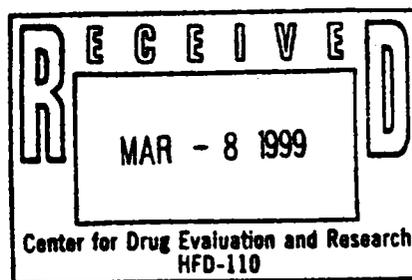
Scios sponsored all new clinical investigations conducted to support the approval of NDA 20-920. All new clinical investigations were conducted under IND [redacted] Scios was identified as the sponsor on the form FDA 1571.

Should the Agency have any questions regarding Scios' request for exclusivity, please do not hesitate to contact me at (650) 962-5970.

Sincerely,



Michael A. Crockett,
Associate Director
Regulatory Affairs



DUPLICATE



NDA 20-920

INFORMATION REQUEST LETTER

Scios Inc.
Attention: Michael A. Crockett
749 North Mary Avenue
Sunnyvale, CA 94085

Dear Mr. Crockett:

Please refer to your new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Natrecor (nesiritide) for Injection, 1.5 mg vial.

We also refer to your submissions dated January 9 and March 30, 2001.

We are reviewing the Chemistry section of your submissions and have the following comments and information requests. We need your prompt written response to continue our evaluation of your NDA:

Drug Product:

1. [

2. We will permit a 12-month expiration date for the 1.5-mg vial on the basis of the stability data provided. Please revise your stability protocol to include Bioassay testing at 12 time point as well as at 6 months.

3. Regarding Labeling:

The package insert should include a solubility statement for the drug substance in the DESCRIPTION section.

Both the vial and carton labels should read "Natrecor (nesiritide) for Injection" to conform to the Package Insert and comply with the USP <1>.

Please amend your application with respect to the above issues and submit a revised specifications for the drug product (by facsimile followed by hard copy) in a expeditious manner.

If you have any questions, call Quynh Nguyen, Regulatory Project Manager, at (301) 594-5311.

Sincerely,

{See appended electronic signature page}

Kasturi Srinivasachar, Ph.D.
Chemistry Team Leader, DNDC I for the
Division of Cardio-Renal Drug Products, (HFD-110)
DNDC I, Office of New Drug Chemistry
Center for Drug Evaluation and Research

**APPEARS THIS WAY
ON ORIGINAL**

**DIVISION OF CARDIO-RENAL DRUG PRODUCTS
FOOD AND DRUG ADMINISTRATION**



US Mail address:
FDA/CDER/HFD-110
5600 Fishers Lane
Rockville, MD 20857

Woodmont II
1451 Rockville Pike
Rockville, MD 20852

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Transmitted to FAX Number: (408) 616-8598

Attention: Ms. Klara Dickinson

Company Name: Scios Inc.

Phone: (408) 616-8591

Subject: Chemistry comments

Date: May 11, 2001

Pages including this sheet: 2

From: Quynh Nguyen, Pharm.D.
Phone: (301) 594-5311
Fax: (301) 594-5494

Hello, Klara,

Please find attached chemistry comments from Dr. Komanduri for NDA 20-920/Natreacor. The information on the drug substance and bioassay test was submitted in the major amendment dated January 9, 2001. If you have any questions, please feel free to contact me at the above numbers.

Thanks,
Quynh

PLEASE LET ME KNOW YOU RECEIVED THIS. THANKS!

NDA 20-920
Natreacor (nesiritide) for Injection

The following comments are in reference to the drug substance:

1. _____ s.
2. Considering the stability data presented on all the three batches at both the storage conditions, the specification limit set for the drug substance assay test _____
Therefore it is recommended _____
3. Please provide the container-closure system used in the drug substance stability study. Alternately, indicate whether the same system presented in the original NDA has been employed.

The following comment is in reference to the bioassay test:

1. _____

**APPEARS THIS WAY
ON ORIGINAL**

**DIVISION OF CARDIO-RENAL DRUG PRODUCTS
FOOD AND DRUG ADMINISTRATION**



US Mail address:
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Transmitted to FAX Number: (408) 616-8598

Attention: Ms. Klara A. Dickinson

Company Name: Scios Inc.

Phone: (408) 616-8591

Subject: Clinical questions from Dr. Karkowsky

Date: February 21, 2001

Pages including this sheet: 2

From: Quynh Nguyen, Pharm.D.

Phone: (301) 594-5311

Fax: (301) 594-5494

PLEASE LET ME KNOW YOU RECEIVED THIS. THANKS!



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration
Rockville MD 20857

NDA 20-920

Scios Inc.
Attention: Mr. Michael A. Crockett
820 West Maude Avenue
Sunnyvale, CA 94085

Dear Mr. Crockett:

We acknowledge receipt on January 10, 2001 of your January 9, 2001 resubmission to your new drug application for Natrecor (nesiritide) Injection.

We consider this resubmission a complete response to our April 27, 1999 not-approvable letter. The new user fee goal date is July 10, 2001.

If you have any questions, please contact:

Quynh Nguyen, Pharm.D.
Regulatory Health Project Manager
(301) 594-5311

Sincerely yours,

Natalia A. Morgenstern
Chief, Project Management Staff
Division of Cardio-Renal Drug Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

DUPLICATE

scios

■ Scios Inc.
2450 Bayshore Parkway
Mountain View, CA 94043
415 966 1550 Tel
415 968 2438 Fax

05 March 1999

Raymond J. Lipicky, MD, Director
Division of Cardio-Renal Drug Products
Food and Drug Administration
Woodmont Office Center 2
Document Control Room 5002
1451 Rockville Pike
Rockville, Maryland 20852

**Reference: NDA 20-920 Amendment
Natrecor® (nesiritide) for Injection
Request for Exclusivity**

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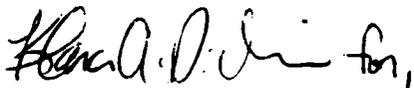
Natrecor® is a new chemical entity whose active moiety has not been approved by the FDA in any other application submitted under section 505(b) of the act. Therefore, Scios claims 5 years exclusivity under 21 CFR 314.108 (b) (2).

NDA 20-920 contains "new clinical investigations" that are essential to the approval of Natrecor®. The new clinical investigations, filed in NDA 20-920, meet the definition set forth in 314.108 (a). In addition, a list of published studies or publicly available reports of clinical investigation were supplied in NDA 20-920 (NDA volume 75, pages 5-11).

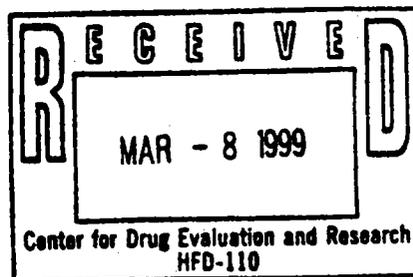
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Should the Agency have any questions regarding Scios' request for exclusivity, please do not hesitate to contact me at (650) 962-5970.

Sincerely,



Michael A. Crockett,
Associate Director
Regulatory Affairs



DUPLICATE