

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: 021012

ADMINISTRATIVE/CORRESPONDENCE DOCUMENTS

June 25, 1999

Mr. James Moore
Division of Medical Imaging and Radiopharmaceutical Drug Products (HFD-160)
Center for Drug Evaluation and Research
Food & Drug Administration
Parklawn Building, Room 18B-08
5600 Fishers Lane
Rockville, MD 20857

RE: NDA 21-012
NeoTect™
Kit for the Preparation of Technetium Tc 99m Depreotide Injection

Dear Mr. Moore:

Please refer to your fax dated June 23, 1999 requesting that we recommit to various CMC issues regarding NeoTect. Please refer also to your fax dated May 30, 1999, our responses dated June 4, 1999, and our telephone conference call with the agency on June 21, 1999.

The comments and commitments listed in your June 23rd fax are discussed in the enclosed material. We are committing to specification levels which were previously discussed or submitted in the correspondence identified in the above paragraph. These specifications differ somewhat (i.e., there is no decimal place) from those contained in your most recent fax.

Please contact me if you have any questions regarding this submission.

Sincerely,



J. Kris Piper
Vice President
Clinical and Regulatory Affairs

JKP/slb

enclosure

TO: Sally Loewkes, M.D.
Team Leader, Clinical Medical Imaging Group

DATE: 30 JUN 99

FROM: Raymond J. Farkas, M.S. /S/
Nuclear Pharmacist, FDA, HFD-160

SUBJECT: Amendment: Changes to draft package insert for NDA 21,012
Drug Name: NeoTect (kit for the preparation of Tc 99m Depreotide Injection)

SPONSOR: Diatide, Inc.

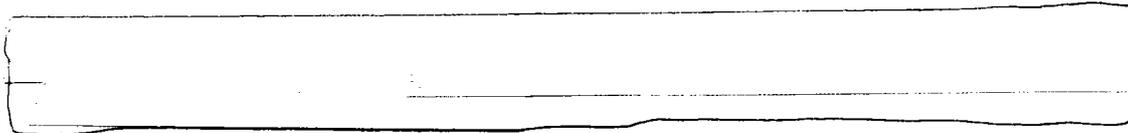
Dosage and Administration – pg. 19/38

For imaging, NeoTect is administered as a peripheral intravenous injection at a single dose of (approximately) up to 50 ug of peptide radiolabeled with 15 to 20 mCi technetium 99m.

Reason: The kit contains 50 ug of peptide and if up to 50 mCi of Tc 99m can be added and a dose of 15 to 20 mCi Tc99m can contain as little as 15 to 20 ug of peptide which is not approximately 50 ug.

Cautionary Notes: pg. 22-23/41

Encapsulate Cautionary Notes 1 and 2 into reading:



Reason: It may not be necessary to dilute a generator eluate to not exceed 50 mCi Tc 99m/mL. A generator eluate may often have a radioactive concentration of less than 50 mCi Tc99m/mL. If, in fact, it does exceed 50 mCi/mL the practice would of necessity require proper dilution with Sodium Chloride Injection, U.S.P.

If the above cautionary note changes are adopted there would be an obvious need for the changing of the numbers in the cautionary notes and the reference to the cautionary notes found in the 3rd step of the INSTRUCTIONS FOR THE PREPARATION OF TECHNETIUM 99m DEPREOTIDE.

Recommendation:

Consider the above changes to the package insert.

cc: Moore
Harapanhalli

Item 13 PATENT INFORMATION [21 U.S.C. 355 (b) and (c)]

The required information on patents is presented below.

<u>Patent Number</u>	<u>Expiration Date</u>	<u>Type of Patent</u>
US 5,443,815	8/22/2022	Drug product
US 5,185,433	4/9/2010	Drug
US 5,066,716	12/13/2008	Drug

000016

Diatide, Inc. CONFIDENTIAL

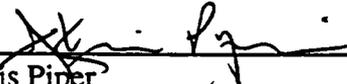
Item 14 PATENT INFORMATION [21 U.S.C. 355 (b) (2) and (j) (2) (A)]

Diatide, Inc. certifies that Patent Nos. 5,443,815, 5,185,433, and 5,066,716 will not be infringed by the manufacture, use or sale of Kit for the Preparation of Technetium Tc 99m Depreotide Injection for which this application is submitted.

Diatide, Inc. will comply with the requirements under 21 CFR 314.52 (a) with respect to providing notice to the owner of each patent or their representative.

To the best of Diatide's knowledge all patents which pertain to the drug, drug product or method of use for the product which is the subject of this application are either assigned to Diatide or have been licensed to Diatide by the patent holder.

On behalf of Diatide, Inc. I certify that the above statement is accurate and correct.



J. Kris Piper
Senior Director Regulatory Affairs
Diatide, Inc.

15 Jun 98
Date

000017

Diatide, Inc. CONFIDENTIAL

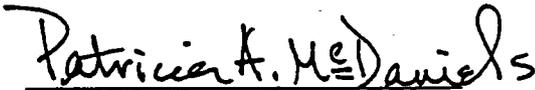
**Declaration and Submission of Patent Information Pursuant to 21 U.S.C. sec. 355(b) and
21 C.F.R. sec. 314.53 (c) for NDA Directed to Kit for the Preparation of Technetium Tc
99m Depreotide**

Patent Number	Expiration Date	Type of Patent	Name of Patent Owner
US 5,443,815	8/22/2012	Drug Product	Assigned to: Diatide, Inc., Londonderry, NH USA 03053
US 5,185,433	4/9/2010	Drug	Assigned to: Centocor, Inc., Malvern, PA Licensed to Diatide, Inc., Londonderry, NH USA 03053
US 5,066,716	12/13/2008	Drug	Assigned to: United States of America as represented by the Secretary of the Department of Health and Human Services Licensed to Diatide, Inc., Londonderry, NH USA 03053

The undersigned declares that U.S. Pat. Nos. 5,443,815; 5,185,433; and 5,066,716 cover the formulation, composition, and/or method of use of Kit for the Preparation of Technetium Tc 99m Depreotide. This product is the subject of this application for which approval is being sought.

DIATIDE, INC.

Date: 4/16/98

By: 
Patricia A. McDaniels
Patent Counsel

NeoTect, Kit for the Preparation of Technetium Tc 99m Depreotide

Applicant Name Diatie, Inc.

HFD # 160

Approval Date If Known _____

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 question about the submission.

a) Is it an original NDA?

YES / / NO / ___ /

b) Is it an effectiveness supplement?

YES / ___ / NO / /

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

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 / / 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:

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

NDA# _____

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 8. 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 / ___ / NO / ___ /

IF "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8.

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.

(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 / ___ / 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 8:

(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 / ___ /

(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 /___/

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 /___/

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:

Studies comparing two products with the same ingredient(s) are considered to be bioavailability studies for the purpose of this section.

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.

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 # ____ YES / __ / ! NO / __ / Explain: _____
! _____

Investigation #2 !

IND # ____ YES / __ / ! 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 /___/

If yes, explain: _____

/S/
Signature Date
Title: Consumer Safety Officer

/S/ du 7/30/99
Chief, Regulatory Project Management Staff

/S/
Signature of Office/ Date
Division Director

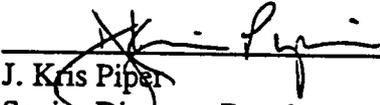
APPEARS THIS WAY
ON ORIGINAL

cc: Original NDA 21-012
Division File HFD-160
HFD-93 Mary Ann Holovac

Item 16 DEBARRMENT CERTIFICATE [FD&C Act 306 (k) (1)]

In accordance with Section 306 (k) of the Food, Drug and Cosmetic Act, Diatide, Inc. certifies that it did not and will not use in any capacity the services of any person debarred under Subsection (a) or (b) of Section 306 of the Act in connection with this application.

On behalf of Diatide, Inc. I certify that the above statement is accurate and correct.



J. Kris Piper
Senior Director, Regulatory Affairs
Diatide, Inc.

15 Jun 98
Date

000019

Diatide, Inc. CONFIDENTIAL

MAY 21 1999

RECORD OF TELEPHONE CONVERSATION/MEETING	Date: 05/20/99 (1:32 PM)
<p>The review of responses from Diatide required some additional information on the [redacted] assayed by [redacted]. I called Kris Piper and left him a message that the question was faxed to him as an information request. Attached is a copy of the question sent to Diatide.</p> <p style="text-align: center;">APPEARS THIS WAY ON ORIGINAL</p> <p style="text-align: center;">[redacted] /S/</p> <hr/> <p>Name: Ravi S. Harapanhalli HFD-160 Review chemist</p>	<p>NDA# 21012</p> <p>Telecon/Meeting initiated by:</p> <p><input type="radio"/> Applicant/Sponsor <input checked="" type="radio"/> FDA</p> <p>By: Ravi S Harapanhalli</p> <p>Product Name: Tc 99m Depreotide</p> <p>Firm Name: Diatide, Inc.</p> <p>Name and Title of Person with whom conversation was held: Kris Piper Sr. Director Regulatory Affairs</p> <p>Phone: (603) 437-8970</p>

cc : Orig. NDA 21012
HFD-160/NDA21012-Division File
HFD-160/Harapanhalli
R/D Init. by: Leutzinger

[redacted] /S/ 5/21/99

RECORD OF TELEPHONE CONVERSATION/MEETING	DATE 4/23/99, 11:30 am		
<p>I called Mr. Piper at 11:00 am and left a voicemail message that I needed to speak with him regarding the Company's response to the approvable letter.</p> <p>Mr. Piper returned my call while I was out of my office. I called him back at 11:17 am and asked him if he had the submission dated 1/21/99 in front of him so that I could walk through my concerns point by point. He did not have this submission and went to retrieve it and told me he would call me back.</p> <p>Kris Piper called at 11:30am. I discussed with him the need for clarification and further information in regards to the responses submitted on 1/21/99.</p> <p>1.) Referring to page 022 of the submission under section " B" - I requested that the Sponsor clarify the number of patients who had biopsy prior to enrollment. I told Kris that using the submission 8/26/99, I found 33 violators for Study 34A and 63 violators for Study 34B. These numbers do not agree with the text of the NDA.</p> <p>2.) Referring to page 023 under section " 2" - I requested clarification of the histopathology for two patients 8-06, 10-6 for study A and one patient 5-26 for study B. I referred him to Table 16.2.10.3 of the original NDA that shows that histopathology exists for these three patients. I requested verification of their histopathology results.</p> <p>3.) Referring to page 024 under section " b" . I requested the Sponsor do an analysis on those patients that had SPN by both x-ray and CT. For example if a patient had SPN on chest x-ray but was not confirmed by CT, then this patient's data should not be factored into the analysis.</p> <p>I asked Kris if these requests were clear and he said yes. I told him to call if he had any questions. T-con end 11:39am.</p>	NDA NUMBER 21012		
	IND NUMBER		
	TELECON/MEETING T-con		
	INITIATED BY APPLICANT/SPONSOR XFDA	MADE XBY TELEPHONE IN PERSON	
	PRODUCT NAME NeoTect		
	FIRM NAME Diatide		
	NAME AND TITLE OF PERSON WITH WHOM CONVERSATION WAS HELD J. Kris Piper Senior Director Regulatory Affairs and Quality Assurance		
TELEPHONE (603) 437-8970			
SIGNATURE 4/23/99	DIVISION HFD-160		



DEPARTMENT OF HEALTH & HUMAN SERVICES

Ernie Dell
8-8-99
Public Health Service

Food and Drug Administration
Rockville MD 20857

FEB 23 1999

NDA 21-012

Diatide, Inc.
9 Delta Drive
Londonderry, NH 03053

Attention: J. Kris Piper
Senior Director Regulatory Affairs

Dear Mr. Piper:

We acknowledge receipt on February 8, 1999, of your February 5, 1999, resubmission to your new drug application (NDA) for NeoTect™ (Kit for the Preparation of Technetium Tc 99m Depreotide Injection).

We acknowledge receipt of your submissions dated January 21, and 28, 1999.

This resubmission contains additional CMC information submitted in response to our December 16, 1998, action letter. Your submission of January 28, 1999, contains additional CMC information, and your submission of January 21, 1999, contains additional Clinical and Statistical, Pharmacology/Toxicology, Human Biopharmaceutics, and Microbiology information.

Even though we informed you in our February 12, 1999, letter that this was a class 1 response, we have reevaluated the situation. After further evaluation, we consider this a class 2 response to our action letter due to the large amount of the CMC issues and the complexity of the Clinical and Statistical issues. Therefore, the user fee goal date is August 8, 1999. We apologize for the inconvenience.

If you have any questions, contact Catalina Ferre-Hockensmith, Consumer Safety Officer, at (301) 827-7510.

Sincerely,

ISP
2/18/99

Robert K. Leedham, Jr.
Chief, Project Management Staff
Division of Medical Imaging and Radiopharmaceutical
Drug Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research



Food and Drug Administration
Rockville MD 20857

NDA 21-012

FEB 12 1999

Diatide, Inc.
9 Delta Drive
Londonderry, NH 03053

Attention: J. Kris Piper
Senior Director Regulatory Affairs

Dear Mr. Piper:

We acknowledge receipt on February 8, 1999, of your February 5, 1999, resubmission to your new drug application (NDA) for NeoTect™ (Kit for the Preparation of Technetium Tc 99m Depreotide Injection).

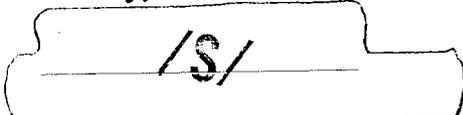
We acknowledge receipt of your submissions dated January 21, and 28, 1999.

This resubmission contains additional CMC information submitted in response to our December 16, 1998, action letter. Your submission of January 28, 1999, contains additional CMC information, and your submission of January 21, 1999, contains additional Clinical and Statistical, Pharmacology/Toxicology, Human Biopharmaceutics, and Microbiology information.

We consider this a complete class 1 response to our action letter. Therefore, the primary user fee goal date is April 8, 1999 and the secondary user fee goal date is June 8, 1999.

If you have any questions, contact Catalina Ferre-Hockensmith, Consumer Safety Officer, at (301) 827-7510.

Sincerely,

 2/18/99

Robert K. Leedham, Jr.
Chief, Project Management Staff
Division of Medical Imaging and Radiopharmaceutical
Drug Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

MEMORANDUM OF TELECON

DATE: September 18, 1998

APPLICATION NUMBER: NDA 21-012; NeoTect (Kit for the Preparation of Tc99m Depreotide)

BETWEEN:

Name: J. Kris Piper, Senior Director, Regulatory Affairs
Phone: 309-672-4190
Representing: Diatide, Inc

AND

Name: Kim Colangelo
Division of Medical Imaging and Radiopharmaceutical Drug Products, HFD-160

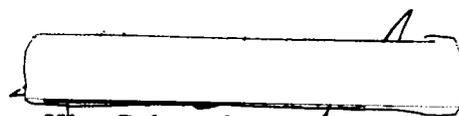
SUBJECT: Medical Imaging Drugs Advisory Committee Meeting

Mr. Piper contacted me to inquire if the Division had reached a decision regarding whether to take this application to a Medical Imaging Drugs Advisory Committee (MIDAC) Meeting.

I informed Mr. Piper that the Division had decided not to take this application to MIDAC at this time because of concerns with the application which include the following:

- ◆ problems and limitations with the submitted pharmacokinetic database,
- ◆ chemistry, manufacturing and controls issues,
- ◆ possible sample size limitations, and
- ◆ verification problems with the data provided (specifically regarding inconsistencies in data tables reported in multiple sections, and between paper and electronic data).

I informed Mr. Piper that reviews were ongoing, therefore additional details would be premature at this time. I committed to keeping Mr. Piper informed on these issues as the reviews were completed, and to discuss these concerns with Diatide prior to taking an action.



Kim Colangelo
Consumer Safety Officer

cc: Original NDA 21-012

HFD-160/Div. File

HFD-160/Colangelo/Love/Jones/Loewke/Leutzingner/Harapanhalli/Meyers/Bailey

HFD-870/Lee/Choi

HFD-720/Mucci

TELECON

Sep 18 1998

Diatide, Inc.
9 Delta Drive
Londonderry, NH 03053

Attention: J. Kris Piper
Senior Director, Regulatory Affairs

Dear Mr. Piper:

Please refer to your pending June 15, 1998 new drug application submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for NeoTect (kit for the preparation of Technetium Tc99m Depreotide) Injection.

We also refer to your submission dated July 21, 1998.

We are reviewing the Clinical and Statistical section(s) of your submission and have the following comments and information requests:

- I. The SAS data diskette submitted contained errors and omissions as follows:
 - A. The CT scan Blinded Read data for variables such as LHC1, RLLC1, etc. contain data that are identical to the P829 Blinded Read data (variables LHP1, RLLP1, etc.) This duplication error extends to the data calculated from the above variable (e.g., the data for AGR11C1 are equal to the data for AGR11P1).
 - B. The date variables for the CT scan, X-ray, and biopsy dates are missing.
 - C. If data for X-ray variables (e.g., detection, diagnosis, and location of the abnormality in the lung) are available, this data should be submitted.

Either a corrected complete SAS data set (diskette) or corrected information restricted to the items above should be submitted.

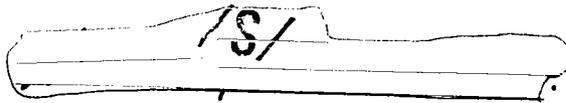
- II. The electronic images submitted are not accessible. The following error message is displayed when access to the images is attempted: "Sorry, an error occurred: Processing board is not installed. ID: 14". Appropriate personnel (e.g., Information Technologist) should provide guidance either in written format, verbally, or in person to allow access to the images.

We would appreciate your prompt written response so we can continue our evaluation of your NDA.

These comments are being provided to you prior to completion of our review of the application to give you preliminary notice of issues that have been identified. Per the user fee reauthorization agreements, these comments do not reflect a final decision on the information reviewed and should not be construed to do so. These comments are preliminary and are subject to change as the review of your application is finalized. In addition, we may identify other information that must be provided prior to approval of this application. If you choose to respond to the issues raised in this letter during this review cycle, depending on the timing of your response, as per the user fee reauthorization agreements, we may or may not be able to consider your response prior to taking an action on your application during this review cycle.

If you have any questions, contact Kim Colangelo at (301) 443-3500.

Sincerely,



9/18/98

Robert K. Leedham, Jr.
Chief, Project Management Staff
Division of Medical Imaging and Radiopharmaceutical
Drug Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

MEMORANDUM OF TELECON

DATE: July 8, 1998

APPLICATION NUMBER: NDA 21-012; Technetium Tc99m Depreotide

BETWEEN:

Name: J. Kris Piper, Senior Director, Regulatory Affairs
Phone: 603-437-8970
Representing: Diatide, Inc.

AND

Name: Kim Colangelo
Division of Medical Imaging and Radiopharmaceutical Drug Products, HFD-160

SUBJECT: Information requested by Division

Mr. Piper contacted me to inform the Division that all of the information requested by the Division would be submitted either today or tomorrow with the exception of the scatter plots. Instructions on accessing the SAS data sets would be provided.

I requested clarification on the following issues:

1. The principal statistical analyses are done with respect to the "Main Presenting Lesion". It is not clear as to how this lesion was defined. Clarification is needed as to how this lesion was selected (what diagnostic modalities were used), and when in the course of the protocol was it designated as the "Main Presenting Lesion" (i.e., at the time of enrollment or at the time of biopsy).
2. Did the surgeon in any way contribute to the designation of the "Main Presenting Lesion"? If so, how? A clear description is needed of the criteria used to determine what would be biopsied and what if any, diagnostic tests led to that conclusion.
3. Did the Investigator Read of the Tc99m P829 images contribute to the definition/designation of the "Main Presenting Lesion" or the designation as to what would be biopsied?

Mr. Piper committed to responding to these questions by the end of the week (July 10, 1998).

/s/

Kim Colangelo
Consumer Safety Officer

cc: Original NDA 21-012
HFD-160/Div. File
HFD-160/Kim Colangelo
TELECON

MEMORANDUM OF TELECON

DATE: July 7, 1998

APPLICATION NUMBER: NDA 21-012; Technetium Tc99m Depreotide

BETWEEN:

Name: J. Kris Piper, Senior Director, Regulatory Affairs
Phone: 603-437-8970
Representing: Diatide, Inc.

AND

Name: Kim Colangelo
Division of Medical Imaging and Radiopharmaceutical Drug Products, HFD-160

SUBJECT: Safety Data Tabulations

I contacted Mr. Piper to request that the safety data tabulations by patient requested on July 2, 1998, be submitted in the same format as the tables provided for the abnormal laboratory values, and be done for all patients in Phases 1 to 3.



Kim Colangelo
Consumer Safety Officer

cc: Original NDA 21-012
HFD-160/Div. File
HFD-160/Kim Colangelo

TELECON

APPEARS THIS WAY
ON ORIGINAL

7/10/1998/Colangelo

MEMORANDUM OF TELECON

DATE: July 6, 1998

APPLICATION NUMBER: NDA 21-012; Technetium Tc99m Depreotide

BETWEEN:

Name: J. Kris Piper, Senior Director, Regulatory Affairs
Phone: 603-437-8970
Representing: Diatide, Inc.

AND

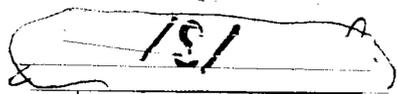
Name: Kim Colangelo
Division of Medical Imaging and Radiopharmaceutical Drug Products, HFD-160

SUBJECT: SAS Data Sets

I informed Mr. Piper that we had not been able to access the SAS data sets as provided, and requested that they be provided separately on diskettes, or alternatively that instructions for accessing the data sets be provided. I clarified that the SAS data sets should include the following:

1. All information for each patient should be provided in one row.
2. Columns should include exhaustive categories for safety and efficacy (e.g., demographics, adverse events, blinded read information, histopathology, etc.).
3. All columns should be defined in text provided either on paper or diskette.

Mr. Piper agreed to investigate this matter and to either forward instructions for the data sets, or provide an estimated time for submission of new diskettes.



Kim Colangelo
Consumer Safety Officer

cc: Original NDA 21-012
HFD-160/Div. File
HFD-160/Kim Colangelo

TELECON

AUG - 5 1998

MEMORANDUM OF TELECON

DATE: July 2, 1998

APPLICATION NUMBER: NDA 21-012; Technetium Tc99m Depreotide

BETWEEN:

Name: J. Kris Piper, Senior Director, Regulatory Affairs
Phone: 603-437-8970
Representing: Diatide, Inc.

AND

Name: Kim Colangelo
Division of Medical Imaging and Radiopharmaceutical Drug Products, HFD-160

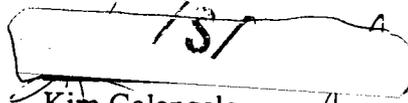
SUBJECT: Filing of NDA 21-012

I contacted Mr. Piper to inform him that the Depreotide application would be classified as a Priority review, but that the following information was needed to consider the application complete for filing:

1. References for the data tables which list the data source (i.e., the patient data listings [not summary tables] which the tables are based on).
2. Efficacy analysis and ISE tables provided for the majority read should also be provided for each individual blinded reader. These tables will be needed for all Phase 3 studies; however, please submit the pivotal studies first in the interest of time.
3. Dose of peptide for each patient (only mean data was provided).
4. Scatter plots are needed for the safety data as requested at the April 30, 1998, pre-NDA meeting.
5. A summary of the amendments for the Phase 1, 2, and non-pivotal Phase 3 studies as requested at the April 30, 1998, pre-NDA meeting. We acknowledge that this information has been provided for the pivotal Phase 3 studies.
6. Additional information is needed regarding the nature of the problems in the uncorrected database, and how they were corrected.
7. Safety data tables presented by patient (listing all timepoints), in the same manner as submitted for the patients with abnormal laboratory values, instead of by timepoint as submitted. Reference ranges should be provided as a footnote on the tables, or at a minimum, provided in a separate table (footnotes are preferred).
8. Indices for volumes 1.1 and 1.27 which include the titles of the clinical studies with the study number (as provided in the Nonclinical Pharmacology and Toxicology sections).
9. Any efficacy data and analyses available for the dose ranging study (#829-20) performed with the previously studied formulation.

NDA 21-012
page 2

In addition, I told Mr. Piper that the SAS data sets had not been verified. I told Mr. Piper I would inform him if there were concerns regarding these within the next few days.


Kim Colangelo
Consumer Safety Officer

cc: Original NDA 21-012
HFD-160/Div. File
HFD-160/Kim Colangelo

TELECON

**APPEARS THIS WAY
ON ORIGINAL**

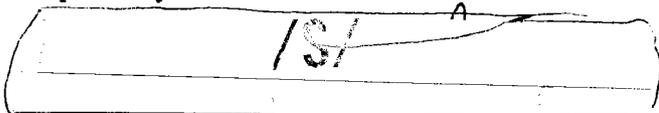
MEMORANDUM OF T-CON BETWEEN FDA AND DIATIDE ON JULY 28, 1999

On July 28, 1999, Robert K. Leedham, Chief Project Manager, Thuy Nguyen, Project Manager, and Tia M. Harper-Velazquez, Project Manager, FDA spoke to Mr. Kris Piper, Vice President, Clinical and Regulatory Affairs, Diatide, Inc by telephone and discussed Phase IV Commitments, pediatric page, safety data, and exclusivity issues.

POINTS:

- 1) Phase 4 commitments: FDA to fax sponsor list of phase IV commitments for review and response.
- 2) Pediatric page: Sponsor will fax request for a waiver.
- 3) Safety data: Per sponsor, no new studies have been done since the original submission, therefore no additional safety data is needed.
- 4) Exclusivity: Sponsor stated that since the product had a patent that exclusivity was not needed.

Prepared by:



Tia Harper-Velazquez, Regulatory Project Manager



Thuy Nguyen, Regulatory Project Manager



Robert K. Leedham, Jr.
Chief, Regulatory Project Management Staff

PEDIATRIC PAGE

(Complete for all original application and all efficacy supplements)

NDA/BLA Number: <u>21012</u>	Trade Name:	<u>KIT FOR THE PREP TECHNETIUM TC 99M</u>
Supplement Number:	Generic Name:	<u>DEPRE</u>
Supplement Type:	Dosage Form:	<u>FIJ</u>
Regulatory Action: <u>PN</u>	Proposed Indication:	<u>Scintigraphic imaging of malignant tumors in the lung.</u>

IS THERE PEDIATRIC CONTENT IN THIS SUBMISSION? NO

What are the INTENDED Pediatric Age Groups for this submission?

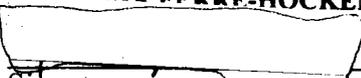
NeoNates (0-30 Days) Children (25 Months-12 years)
 Infants (1-24 Months) Adolescents (13-16 Years)

Label Status -
Formulation Status -
Studies Needed -
Study Status -

Are there any Pediatric Phase 4 Commitments in the Action Letter for the Original Submission? NO

COMMENTS: See ATTACHED

This Page was completed based on information from a PROJECT MANAGER/CONSUMER SAFETY OFFICER, CATALINA FERRE-HOCKENSMITH



 Signature

 Date 11/6/98

APPEARS THIS WAY
ON ORIGINAL