

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

22-119

**ADMINISTRATIVE and CORRESPONDENCE
DOCUMENTS**

**PATENT INFORMATION SUBMITTED WITH THE
FILING OF AN NDA, AMENDMENT, OR SUPPLEMENT**
*For Each Patent That Claims a Drug Substance
(Active Ingredient), Drug Product (Formulation and
Composition) and/or Method of Use*

NDA NUMBER

22-119

NAME OF APPLICANT / NDA HOLDER

The Feinstein Institute for Medical Research

The following is provided in accordance with Section 505(b) and (c) of the Federal Food, Drug, and Cosmetic Act.

TRADE NAME (OR PROPOSED TRADE NAME)

Ammonia N 13 Injection

ACTIVE INGREDIENT(S)

Ammonia N 13 Injection

STRENGTH(S)

3.75-37.5mCi/mL

DOSAGE FORM

Intravenous injection

This patent declaration form is required to be submitted to the Food and Drug Administration (FDA) with an NDA application, amendment, or supplement as required by 21 CFR 314.53 at the address provided in 21 CFR 314.53(d)(4). Within thirty (30) days after approval of an NDA or supplement, or within thirty (30) days of issuance of a new patent, a new patent declaration must be submitted pursuant to 21 CFR 314.53(c)(2)(ii) with all of the required information based on the approved NDA or supplement. The information submitted in the declaration form submitted upon or after approval will be the only information relied upon by FDA for listing a patent in the Orange Book.

For hand-written or typewriter versions (only) of this report: If additional space is required for any narrative answer (i.e., one that does not require a "Yes" or "No" response), please attach an additional page referencing the question number.

FDA will not list patent information if you file an incomplete patent declaration or the patent declaration indicates the patent is not eligible for listing.

each patent submitted for the pending NDA, amendment, or supplement referenced above, you must submit all the information described below. If you are not submitting any patents for this pending NDA, amendment, or supplement, complete above section and sections 5 and 6.

1. GENERAL

a. United States Patent Number

N/A, CFR March 10, 2000. No Patent Exists.

b. Issue Date of Patent

c. Expiration Date of Patent

d. Name of Patent Owner

N/A This drug was in use for more than 20 years

Address (of Patent Owner)

City/State

ZIP Code

FAX Number (if available)

Telephone Number

E-Mail Address (if available)

e. Name of agent or representative who resides or maintains a place of business within the United States authorized to receive notice of patent certification under section 505(b)(3) and (j)(2)(B) of the Federal Food, Drug, and Cosmetic Act and 21 CFR 314.52 and 314.95 (if patent owner or NDA applicant/holder does not reside or have a place of business within the United States)

N/A

Address (of agent or representative named in 1.e.)

City/State

ZIP Code

FAX Number (if available)

Telephone Number

E-Mail Address (if available)

f. Is the patent referenced above a patent that has been submitted previously for the approved NDA or supplement referenced above?

Yes

No

g. If the patent referenced above has been submitted previously for listing, is the expiration date a new expiration date?

Yes

No

For the patent referenced above, provide the following information on the drug substance, drug product and/or method of use that is the subject of the pending NDA, amendment, or supplement.

Drug Substance (Active Ingredient)

Does the patent claim the drug substance that is the active ingredient in the drug product described in the pending NDA, amendment, or supplement? Yes No

2.2 Does the patent claim a drug substance that is a different polymorph of the active ingredient described in the pending NDA, amendment, or supplement? Yes No

2.3 If the answer to question 2.2 is "Yes," do you certify that, as of the date of this declaration, you have test data demonstrating that a drug product containing the polymorph will perform the same as the drug product described in the NDA? The type of test data required is described at 21 CFR 314.53(b). Yes No

2.4 Specify the polymorphic form(s) claimed by the patent for which you have the test results described in 2.3.
N/A

2.5 Does the patent claim only a metabolite of the active ingredient pending in the NDA or supplement? (Complete the information in section 4 below if the patent claims a pending method of using the pending drug product to administer the metabolite.) Yes No

2.6 Does the patent claim only an intermediate? Yes No

2.7 If the patent referenced in 2.1 is a product-by-process patent, is the product claimed in the patent novel? (An answer is required only if the patent is a product-by-process patent.) Yes No

Drug Product (Composition/Formulation)

Does the patent claim the drug product, as defined in 21 CFR 314.3, in the pending NDA, amendment, or supplement? Yes No

3.2 Does the patent claim only an intermediate? Yes No

3.3 If the patent referenced in 3.1 is a product-by-process patent, is the product claimed in the patent novel? (An answer is required only if the patent is a product-by-process patent.) Yes No

4. Method of Use

Sponsors must submit the information in section 4 separately for each patent claim claiming a method of using the pending drug product for which approval is being sought. For each method of use claim referenced, provide the following information:

4.1 Does the patent claim one or more methods of use for which approval is being sought in the pending NDA, amendment, or supplement? Yes No

4.2 Patent Claim Number (as listed in the patent) N/A	Does the patent claim referenced in 4.2 claim a pending method of use for which approval is being sought in the pending NDA, amendment, or supplement? <input type="checkbox"/> Yes <input type="checkbox"/> No
--	---

4.2a If the answer to 4.2 is "Yes," identify with specificity the use with reference to the proposed labeling for the drug product.	Use: (Submit indication or method of use information as identified specifically in the approved labeling.) N/A
---	---

5. No Relevant Patents

For this pending NDA, amendment, or supplement, there are no relevant patents that claim the drug substance (active ingredient), drug product (formulation or composition) or method(s) of use, for which the applicant is seeking approval and with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner of the patent engaged in manufacture, use, or sale of the drug product. Yes

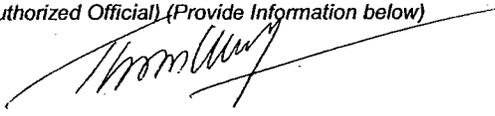
6. Declaration Certification

6.1 The undersigned declares that this is an accurate and complete submission of patent information for the NDA, amendment, or supplement pending under section 505 of the Federal Food, Drug, and Cosmetic Act. This time-sensitive patent information is submitted pursuant to 21 CFR 314.53. I attest that I am familiar with 21 CFR 314.53 and this submission complies with the requirements of the regulation. I verify under penalty of perjury that the foregoing is true and correct.

Warning: A willfully and knowingly false statement is a criminal offense under 18 U.S.C. 1001.

6.2 Authorized Signature of NDA Applicant/Holder or Patent Owner (Attorney, Agent, Representative or other Authorized Official) (Provide Information below)

Date Signed
10/16/2006



NOTE: Only an NDA applicant/holder may submit this declaration directly to the FDA. A patent owner who is not the NDA applicant/holder is authorized to sign the declaration but may not submit it directly to FDA. 21 CFR 314.53(c)(4) and (d)(4).

Check applicable box and provide information below.

NDA Applicant/Holder

NDA Applicant's/Holder's Attorney, Agent (Representative) or other Authorized Official

Patent Owner

Patent Owner's Attorney, Agent (Representative) or Other Authorized Official

Name

Dr. Thomas Chaly, Ph.D, FAIC

Address

The Feinstein Institute for Medical Research
Chief, Radiochemistry,
Cyclotron/Radiochemistry,
North Shore/LIJ Health System, 350 Community Drive,

City/State

Manhasset, New York

ZIP Code

11030

Telephone Number

516-562-1042

FAX Number (if available)

516-562-1041

E-Mail Address (if available)

tchaly@nshs.edu

The public reporting burden for this collection of information has been estimated to average 9 hours per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:

Food and Drug Administration
CDER (HFD-007)
5600 Fishers Lane
Rockville, MD 20857

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.

EXCLUSIVITY SUMMARY

NDA # 22-119

SUPPL #

HFD # 160

Trade Name [None requested by Sponsor.]

Generic Name Ammonia N 13 Injection

Applicant Name Feinstein Institute for Medical Research

Approval Date, If Known

PART I IS AN EXCLUSIVITY DETERMINATION NEEDED?

1. An exclusivity determination will be made for all original applications, and all efficacy supplements. Complete PARTS II and III of this Exclusivity Summary only if you answer "yes" to one or more of the following questions about the submission.

a) Is it a 505(b)(1), 505(b)(2) or efficacy supplement?

YES NO

If yes, what type? Specify 505(b)(1), 505(b)(2), SE1, SE2, SE3, SE4, SE5, SE6, SE7, SE8

505(b)(2)

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:

d) Did the applicant request exclusivity?

YES NO

If the answer to (d) is "yes," how many years of exclusivity did the applicant request?

e) Has pediatric exclusivity been granted for this Active Moiety?

YES NO

If the answer to the above question in YES, is this approval a result of the studies submitted in response to the Pediatric Written Request?

IF YOU HAVE ANSWERED "NO" TO ALL OF THE ABOVE QUESTIONS, GO DIRECTLY TO THE SIGNATURE BLOCKS AT THE END OF THIS DOCUMENT.

2. Is this drug product or indication a DESI upgrade?

YES NO

IF THE ANSWER TO QUESTION 2 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8 (even if a study was required for the upgrade).

PART II FIVE-YEAR EXCLUSIVITY FOR NEW CHEMICAL ENTITIES

(Answer either #1 or #2 as appropriate)

1. Single active ingredient product.

Has FDA previously approved under section 505 of the Act any drug product containing the same active moiety as the drug under consideration? Answer "yes" if the active moiety (including other esterified forms, salts, complexes, chelates or clathrates) has been previously approved, but this particular form of the active moiety, e.g., this particular ester or salt (including salts with hydrogen or coordination bonding) or other non-covalent derivative (such as a complex, chelate, or clathrate) has not been approved. Answer "no" if the compound requires metabolic conversion (other than deesterification of an esterified form of the drug) to produce an already approved active moiety.

YES NO

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

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. (Caution: The questions in part II of the summary should only be answered "NO" for original approvals of new molecular entities.)

IF "YES," GO TO PART III.

PART III THREE-YEAR EXCLUSIVITY FOR NDAs 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.

- a) For each investigation identified as "essential to the approval," has the investigation been relied on by the agency to demonstrate the effectiveness of a previously approved drug product? (If the investigation was relied on only to support the safety of a previously approved drug, answer "no.")

Investigation #1 YES NO

Investigation #2 YES NO

If you have answered "yes" for one or more investigations, identify each such investigation and the NDA in which each was relied upon:

- b) For each investigation identified as "essential to the approval", does the investigation duplicate the results of another investigation that was relied on by the agency to support the effectiveness of a previously approved drug product?

Investigation #1 YES NO

Investigation #2 YES NO

If you have answered "yes" for one or more investigation, identify the NDA in which a similar investigation was relied on:

c) If the answers to 3(a) and 3(b) are no, identify each "new" investigation in the application or supplement that is essential to the approval (i.e., the investigations listed in #2(c), less any that are not "new"):

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 ! NO
Explain: ! 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:

Name of person completing form: Thuy Nguyen, M.P.H.

Title: Regulatory Health Project Manager, Division of Medical Imaging and Hematology Products

Date: July 5, 2007

Name of Office/Division Director signing form: Rafel Dwaine Rieves, M.D.

Title: Acting Division Director, Division of Medical Imaging and Hematology Products

Form OGD-011347; Revised 05/10/2004; formatted 2/15/05

**This is a representation of an electronic record that was signed electronically and
this page is the manifestation of the electronic signature.**

/s/

Rafel Rieves

7/18/2007 03:53:35 PM

PEDIATRIC PAGE

(Complete for all filed original applications and efficacy supplements)

NDA#: 22-119

HFD-160

Stamp Date: October 25, 2006

PDUFA Goal Date: August 24, 2007

Trade and generic names/dosage form: Ammonia N 13 Injection (Ammonia in 0.9% Sodium Chloride solution)

Applicant: Feinstein Institute for Medical Research

Therapeutic Class: 1S

Does this application provide for new active ingredient(s), new indication(s), new dosage form, new dosing regimen, or new route of administration? *

YES. Please proceed to the next question.

* SE5, SE6, and SE7 submissions may also trigger PREA. If there are questions, please contact the Rosemary Addy or Grace Carmouze.

Indication(s) previously approved (please complete this section for supplements only): N/A

Each indication covered by current application under review must have pediatric studies: *Completed, Deferred, and/or Waived.*

Number of indications for this application(s): 1

Indication #1: Ammonia N 13 Injection is indicated for PET imaging of the myocardium under rest or pharmacologic stress conditions to evaluate myocardial perfusion in patients with suspected or existing coronary artery disease.

Is this an orphan indication?

NO. Please proceed to the next question.

Is there a full waiver for this indication?

YES. Please proceed to Section A.

Please proceed to Section B, Section C, and/or Section D and complete as necessary.

Section A: Fully Waived Studies

Reason(s) for full waiver:

- Products in this class for this indication have been studied/labeled for pediatric population
- Disease/condition does not exist in children
- Too few children with disease to study
- There are safety concerns
- Other: The safety and effectiveness of Ammonia N 13 Injection have been established in pediatric patients on the basis of clinical studies in adults, known metabolism of ammonia, and radiation dosimetry in the pediatric population.

If studies are fully waived, then pediatric information is complete for this indication. If there is another indication, please see Attachment A. Otherwise, this Pediatric Page is complete and should be entered into DFS.

Section B: Partially Waived Studies

Age/weight range being partially waived (fill in applicable criteria below):

Min _____ kg _____ mo. _____ yr. _____ Tanner Stage _____
Max _____ kg _____ mo. _____ yr. _____ Tanner Stage _____

Reason(s) for partial waiver:

- Products in this class for this indication have been studied/labeled for pediatric population
- Disease/condition does not exist in children
- Too few children with disease to study
- There are safety concerns
- Adult studies ready for approval
- Formulation needed
- Other: _____

If studies are deferred, proceed to Section C. If studies are completed, proceed to Section D. Otherwise, this Pediatric Page is complete and should be entered into DFS.

Section C: Deferred Studies

Age/weight range being deferred (fill in applicable criteria below):

Min _____ kg _____ mo. _____ yr. _____ Tanner Stage _____
Max _____ kg _____ mo. _____ yr. _____ Tanner Stage _____

Reason(s) for deferral:

- Products in this class for this indication have been studied/labeled for pediatric population
- Disease/condition does not exist in children
- Too few children with disease to study
- There are safety concerns
- Adult studies ready for approval
- Formulation needed
- Other: _____

Date studies are due (mm/dd/yy): _____

If studies are completed, proceed to Section D. Otherwise, this Pediatric Page is complete and should be entered into DFS.

Section D: Completed Studies

Age/weight range of completed studies (fill in applicable criteria below):

Min _____ kg _____ mo. _____ yr. _____ Tanner Stage _____
Max _____ kg _____ mo. _____ yr. _____ Tanner Stage _____

Comments:

If there are additional indications, please proceed to Attachment A. Otherwise, this Pediatric Page is complete and should be entered into DFS.

NDA 22-119: Ammonia N 13 Injection
Page 3

The Pediatric Page was completed by:

{See appended electronic signature page}

Thuy Nguyen, M.P.H.
Regulatory Health Project Manager

**FOR QUESTIONS ON COMPLETING THIS FORM CONTACT THE PEDIATRIC AND MATERNAL HEALTH
STAFF at 301-796-0700**

(Revised: 10/10/2006)

Attachment A

(This attachment is to be completed for those applications with multiple indications only.)

Indication #2: _____

Is this an orphan indication?

- Yes. PREA does not apply. Skip to signature block.
- No. Please proceed to the next question.

Is there a full waiver for this indication (check one)?

- Yes: Please proceed to Section A.
- No: Please check all that apply: ___ Partial Waiver ___ Deferred ___ Completed
NOTE: More than one may apply
Please proceed to Section B, Section C, and/or Section D and complete as necessary.

Section A: Fully Waived Studies

Reason(s) for full waiver:

- Products in this class for this indication have been studied/labeled for pediatric population
- Disease/condition does not exist in children
- Too few children with disease to study
- There are safety concerns
- Other: _____

If studies are fully waived, then pediatric information is complete for this indication. If there is another indication, please see Attachment A. Otherwise, this Pediatric Page is complete and should be entered into DFS.

Section B: Partially Waived Studies

Age/weight range being partially waived (fill in applicable criteria below)::

Min _____ kg _____ mo. _____ yr. _____ Tanner Stage _____
Max _____ kg _____ mo. _____ yr. _____ Tanner Stage _____

Reason(s) for partial waiver:

- Products in this class for this indication have been studied/labeled for pediatric population
- Disease/condition does not exist in children
- Too few children with disease to study
- There are safety concerns
- Adult studies ready for approval
- Formulation needed
- Other: _____

If studies are deferred, proceed to Section C. If studies are completed, proceed to Section D. Otherwise, this Pediatric Page is

complete and should be entered into DFS.

Section C: Deferred Studies

Age/weight range being deferred (fill in applicable criteria below)::

Min _____ kg _____ mo. _____ yr. _____ Tanner Stage _____
Max _____ kg _____ mo. _____ yr. _____ Tanner Stage _____

Reason(s) for deferral:

- Products in this class for this indication have been studied/labeled for pediatric population
- Disease/condition does not exist in children
- Too few children with disease to study
- There are safety concerns
- Adult studies ready for approval
- Formulation needed
- Other: _____

Date studies are due (mm/dd/yy): _____

If studies are completed, proceed to Section D. Otherwise, this Pediatric Page is complete and should be entered into DFS.

Section D: Completed Studies

Age/weight range of completed studies (fill in applicable criteria below):

Min _____ kg _____ mo. _____ yr. _____ Tanner Stage _____
Max _____ kg _____ mo. _____ yr. _____ Tanner Stage _____

Comments:

If there are additional indications, please copy the fields above and complete pediatric information as directed. If there are no other indications, this Pediatric Page is complete and should be entered into DFS.

This page was completed by:

{See appended electronic signature page}

Regulatory Project Manager

FOR QUESTIONS ON COMPLETING THIS FORM CONTACT THE PEDIATRIC AND MATERNAL HEALTH STAFF at 301-796-0700

(Revised: 10/10/2006)

**This is a representation of an electronic record that was signed electronically and
this page is the manifestation of the electronic signature.**

/s/

Thuy Nguyen

5/10/2007 01:41:30 PM

THOMAS CHALY, Ph.D., FAIC

Chief, Radiochemistry
Cyclotron/Radiochemistry Facility

DEBARMENT CERTIFICATION

DATE: October 16, 2006

TO: Dr. George Mills, M.D, M.B.A.
FDA-Center for Drug Evaluation and Research
Division of Medical Imaging and Hematology products
ATTN: Central Document Room
5901-B Ammendale Road
Beltsville, MD 20705-1266

FROM: Thomas Chaly, PhD, FAIC
Chief of Radiochemistry
The Feinstein Institute for Medical Research
Cyclotron/Radiochemistry
North Shore-LIJ Health System
350 Community Drive
Manhasset, New York 11030



As of June 1, 1992, based on the Federal Act 306(a) or (b) and Act 21 U.S.C. 355a(a) or (b), the applicant submitting a NDA has to provide a Debarment Certification stating that the applicant did not and will not use the service (in any capacity) of any person debarred. Therefore my statement is given below:

I, Dr. Thomas Chaly, on behalf of The Feinstein Institute For Medical Research, certify that I did not and will not use the service, in any capacity, of any person debarred under Section 306 of the Federal Food, Drug, and Cosmetic Act in connection with the NDA application for Ammonia N 13 Injection.

**CERTIFICATION: FINANCIAL INTERESTS AND
ARRANGEMENTS OF CLINICAL INVESTIGATORS**

TO BE COMPLETED BY APPLICANT

With respect to all covered clinical studies (or specific clinical studies listed below (if appropriate)) submitted in support of this application, I certify to one of the statements below as appropriate. I understand that this certification is made in compliance with 21 CFR part 54 and that for the purposes of this statement, a clinical investigator includes the spouse and each dependent child of the investigator as defined in 21 CFR 54.2(d).

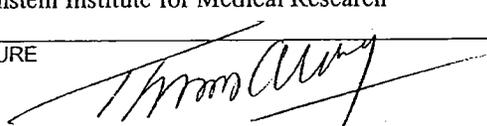
Please mark the applicable checkbox.

- (1) As the sponsor of the submitted studies, I certify that I have not entered into any financial arrangement with the listed clinical investigators (enter names of clinical investigators below or attach list of names to this form) whereby the value of compensation to the investigator could be affected by the outcome of the study as defined in 21 CFR 54.2(a). I also certify that each listed clinical investigator required to disclose to the sponsor whether the investigator had a proprietary interest in this product or a significant equity in the sponsor as defined in 21 CFR 54.2(b) did not disclose any such interests. I further certify that no listed investigator was the recipient of significant payments of other sorts as defined in 21 CFR 54.2(f).

Clinical Investigators	N/A	N/A
	N/A	N/A
	N/A	N/A

- (2) As the applicant who is submitting a study or studies sponsored by a firm or party other than the applicant, I certify that based on information obtained from the sponsor or from participating clinical investigators, the listed clinical investigators (attach list of names to this form) did not participate in any financial arrangement with the sponsor of a covered study whereby the value of compensation to the investigator for conducting the study could be affected by the outcome of the study (as defined in 21 CFR 54.2(a)); had no proprietary interest in this product or significant equity interest in the sponsor of the covered study (as defined in 21 CFR 54.2(b)); and was not the recipient of significant payments of other sorts (as defined in 21 CFR 54.2(f)).

- (3) As the applicant who is submitting a study or studies sponsored by a firm or party other than the applicant, I certify that I have acted with due diligence to obtain from the listed clinical investigators (attach list of names) or from the sponsor the information required under 54.4 and it was not possible to do so. The reason why this information could not be obtained is attached.

NAME Dr. Thomas Chaly, Ph.D, FAIC	TITLE Chief, Radiochemistry
FIRM / ORGANIZATION The Feinstein Institute for Medical Research	
SIGNATURE 	DATE 10/16/06

Paperwork Reduction Act Statement

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number. Public reporting burden for this collection of information is estimated to average 1 hour per response, including time for reviewing instructions, searching existing data sources, gathering and maintaining the necessary data, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information to the address to the right:

Department of Health and Human Services
Food and Drug Administration
5600 Fishers Lane, Room 14C-03
Rockville, MD 20857

DISCLOSURE: FINANCIAL INTERESTS AND ARRANGEMENTS OF CLINICAL INVESTIGATORS

TO BE COMPLETED BY APPLICANT

The following information concerning N/A See Explanation attached, who par-
Name of clinical investigator
ticipated as a clinical investigator in the submitted study N/A
Name of
N/A, is submitted in accordance with 21 CFR part
clinical study

54. The named individual has participated in financial arrangements or holds financial interests that are required to be disclosed as follows:

Please mark the applicable checkboxes.

- any financial arrangement entered into between the sponsor of the covered study and the clinical investigator involved in the conduct of the covered study, whereby the value of the compensation to the clinical investigator for conducting the study could be influenced by the outcome of the study;
- any significant payments of other sorts made on or after February 2, 1999 from the sponsor of the covered study such as a grant to fund ongoing research, compensation in the form of equipment, retainer for ongoing consultation, or honoraria;
- any proprietary interest in the product tested in the covered study held by the clinical investigator;
- any significant equity interest as defined in 21 CFR 54.2(b), held by the clinical investigator in the sponsor of the covered study.

Details of the individual's disclosable financial arrangements and interests are attached, along with a description of steps taken to minimize the potential bias of clinical study results by any of the disclosed arrangements or interests.

NAME Dr. Thomas Chaly, Ph.D, FAIC	TITLE Chief, Radiochemistry
FIRM / ORGANIZATION The Feinstein Institute for Medical Research	
SIGNATURE	DATE 10/16/06

Paperwork Reduction Act Statement

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number. Public reporting burden for this collection of information is estimated to average 4 hours per response, including time for reviewing instructions, searching existing data sources, gathering and maintaining the necessary data, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information to:

Department of Health and Human Services
Food and Drug Administration
5600 Fishers Lane, Room 14-72
Rockville, MD 20857

DIVISION OF MEDICAL IMAGING AND HEMATOLOGY PRODUCTS

**REGULATORY HEALTH PROJECT MANAGER PHYSICIAN LABELING RULE (PLR)
LABELING REVIEW**

Application Number: NDA 22-119
Name of Drug: [N-13] Ammonia Injection
Applicant: The Feinstein Institute for Medical Research
Labeling Review Date: July 3, 2007

MATERIAL REVIEWED:

Submission Date of Revised Structure Product Labeling (SPL): June 28, 2007
Receipt Date: June 29, 2007
Original Submission Date of Structure Product Labeling (SPL): October 16, 2006
Receipt Date: October 25, 2006
Date of Previous PM Labeling Review: March 23, 2007
Type of Labeling Reviewed: WORD/SPL

REVIEW SUMMARY & RECOMMENDATIONS

The Sponsor's revised labeling dated 06\28\07, reflects the Division's labeling recommendations dated 06\20\07, and is deemed adequate and acceptable for a regulatory action.

See - DFS Electronic Signatory
Thuy Nguyen, M.P.H.
Regulatory Health Project Manager, DMIHP

**This is a representation of an electronic record that was signed electronically and
this page is the manifestation of the electronic signature.**

/s/

Thuy Nguyen
7/18/2007 08:39:56 AM
CSO

Thuy Nguyen
7/18/2007 08:40:21 AM
CSO



Division of Medical Imaging and
Hematology Products
Office of Oncology Drug Products
Center for Drug Evaluation and Research
U.S. Food and Drug Administration

FACSIMILE TRANSMITTAL SHEET

DATE: JUNE 14, 2007

TO: DR. THOMAS CHALY	FROM: Thuy Nguyen, M.P.H. Regulatory Health Project Manager
COMPANY: Feinstein Institute for Medical Research	Division of Division of Medical Imaging and Hematology Products
FAX Number: (516) 562-1041	Fax Number: (301) 796-9849
PHONE Number: (516) 562-1042	Phone Number: (301) 796-2050
SUBJECT: NDA 22-119: Ammonia [N-13] Injection	

TOTAL NO. OF PAGES (including cover): 2

COMMENTS: Please find attached the Division's CHEMISTRY comments regarding NDA 22-119: Ammonia [N-13], serial #000, submission dated October 16, 2006.

Please provide an official response to the NDA in *triplicate* hard copies along with an electronic copy (on CD-Rom) by Thursday, June 21, 2007.

If you have any questions, please feel free to contact me. Thank you.

THIS DOCUMENT IS INTENDED ONLY FOR THE USE OF THE PARTY TO WHOM IT IS ADDRESSED AND MAY CONTAIN INFORMATION THAT IS PRIVILEGED, CONFIDENTIAL, AND PROTECTED FROM DISCLOSURE UNDER APPLICABLE LAW.

If you are not the addressee, or a person authorized to deliver this document to the addressee, you are hereby notified that any review, disclosure, dissemination, copying, or other action based on the content of this communication is not authorized. If you have received this document in error, please notify us immediately by telephone at (301) 796-2050. Thank you.

1 Page(s) Withheld

 Trade Secret / Confidential

 X Draft Labeling

 Deliberative Process

Withheld Track Number: Administrative- 1

ACTION PACKAGE CHECKLIST

Application Information		
NDA # 22-119		
Established Name: Ammonia N 13 Injection		Applicant: Feinstein Institute for Medical Research
RPM: Thuy Nguyen, M.P.H.	Division: 160 - DMIHP	Phone #: (301) 796-2050
NDA Application Type: 505(b)(2)	<p>505(b)(2) NDAs and 505(b)(2) NDA supplements: Listed drug(s) referred to in 505(b)(2) application (NDA #(s), Drug name(s)):</p> <p>See tab for FR Notice –March 10, 2000 (enclosed)</p> <p>Provide a brief explanation of how this product is different from the listed drug. See FR Notice – March 10, 2000</p> <p>X: If no listed drug, check here and explain: See FR Notice – March 10, 2000.</p> <p>Review and confirm the information previously provided in Appendix B to the Regulatory Filing Review. Use this Checklist to update any information (including patent certification information) that is no longer correct.</p> <p>X Confirmed Date: 06/04/07</p>	
❖ User Fee Goal Date	August 24, 2007	
❖ Action Goal Date (if different)	August 23, 2007	
❖ Actions		
• Proposed action	APPROVAL	
• Previous actions (<i>specify type and date for each action taken</i>)	None	
❖ Advertising (<i>approvals only</i>) Note: If accelerated approval (21 CFR 314.510/601.41), advertising must have been submitted and reviewed (<i>indicate dates of reviews</i>)	Requested in AP letter	

Application Characteristics	
Review priority:	Standard
Chemical classification (new NDAs only):	IS
NDAs, BLAs and Supplements: <input type="checkbox"/> Fast Track <input type="checkbox"/> Rolling Review <input type="checkbox"/> CMA Pilot 1 <input type="checkbox"/> CMA Pilot 2 <input type="checkbox"/> Orphan drug designation	
NDAs: Subpart H <input type="checkbox"/> Accelerated approval (21 CFR 314.510) <input type="checkbox"/> Restricted distribution (21 CFR 314.520) Subpart I <input type="checkbox"/> Approval based on animal studies	BLAs: Subpart E <input type="checkbox"/> Accelerated approval (21 CFR 601.41) <input type="checkbox"/> Restricted distribution (21 CFR 601.42) Subpart H <input type="checkbox"/> Approval based on animal studies
NDAs and NDA Supplements: <input type="checkbox"/> OTC drug	
Other:	
Other comments:	
Application Integrity Policy (AIP)	
<ul style="list-style-type: none"> Applicant is on the AIP 	NO
<ul style="list-style-type: none"> This application is on the AIP <ul style="list-style-type: none"> Exception for review (<i>file Center Director's memo in Administrative Documents section</i>) OC clearance for approval (<i>file communication in Administrative Documents section</i>) 	NO <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Yes <input type="checkbox"/> Not an AP action
❖ Public communications (approvals only)	
<ul style="list-style-type: none"> Office of Executive Programs (OEP) liaison has been notified of action 	N/A
<ul style="list-style-type: none"> Press Office notified of action 	N/A
<ul style="list-style-type: none"> Indicate what types (if any) of information dissemination are anticipated 	<input checked="" type="checkbox"/> None <input type="checkbox"/> FDA Press Release <input type="checkbox"/> FDA Talk Paper <input type="checkbox"/> CDER Q&As <input type="checkbox"/> Other

Page 3: NDA 22-119: Ammonia N 13 Injection

Exclusivity	
<ul style="list-style-type: none"> • NDAs: Exclusivity Summary (approvals only) (<i>file Summary in Administrative Documents section</i>) 	X – July 18, 2007
<ul style="list-style-type: none"> • Is approval of this application blocked by any type of exclusivity? <ul style="list-style-type: none"> • NDAs/BLAs: Is there existing orphan drug exclusivity for the “same” drug or biologic for the proposed indication(s)? <i>Refer to 21 CFR 316.3(b)(13) for the definition of “same drug” for an orphan drug (i.e., active moiety). This definition is NOT the same as that used for NDA chemical classification.</i> • NDAs: Is there remaining 5-year exclusivity that would bar effective approval of a 505(b)(2) application? <i>(Note that, even if exclusivity remains, the application may be tentatively approved if it is otherwise ready for approval.)</i> • NDAs: Is there remaining 3-year exclusivity that would bar effective approval of a 505(b)(2) application? <i>(Note that, even if exclusivity remains, the application may be tentatively approved if it is otherwise ready for approval.)</i> • NDAs: Is there remaining 6-month pediatric exclusivity that would bar effective approval of a 505(b)(2) application? <i>(Note that, even if exclusivity remains, the application may be tentatively approved if it is otherwise ready for approval.)</i> 	<p>NO</p> <p>NO</p> <p>NO If yes, NDA # and date exclusivity expires:</p> <p>NO If yes, NDA # and date exclusivity expires:</p> <p>NO If yes, NDA # and date exclusivity expires:</p>
Patent Information (NDAs and NDA supplements only)	
<ul style="list-style-type: none"> • Patent Information: Verify that form FDA-3542a was submitted for patents that claim the drug for which approval is sought. If the drug is an old antibiotic, skip the Patent Certification questions. 	Verified
<ul style="list-style-type: none"> • Patent Certification [505(b)(2) applications]: Verify that a certification was submitted for each patent for the listed drug(s) in the Orange Book and identify the type of certification submitted for each patent. • [505(b)(2) applications] If the application includes a paragraph III certification, it cannot be approved until the date that the patent to which the certification pertains expires (but may be tentatively approved if it is otherwise ready for approval). 	<p>N/A</p> <p>N/A</p>
<ul style="list-style-type: none"> • [505(b)(2) applications] For each paragraph IV certification, verify that the applicant notified the NDA holder and patent owner(s) of its certification that the patent(s) is invalid, unenforceable, or will not be infringed (review documentation of notification by applicant and documentation of receipt of notice by patent owner and NDA holder). <i>(If the application does not include any paragraph IV certifications, mark “N/A” and skip to the next section below (Summary Reviews)).</i> • [505(b)(2) applications] For each paragraph IV certification, based on the questions below, determine whether a 30-month stay of approval is in effect due to patent infringement litigation. <p>Answer the following questions for each paragraph IV certification:</p> <p>(1) Have 45 days passed since the patent owner’s receipt of the applicant’s notice of certification?</p>	<p>N/A (no paragraph IV certification)</p> <p><input type="checkbox"/> Yes <input type="checkbox"/> No</p>

(Note: The date that the patent owner received the applicant's notice of certification can be determined by checking the application. The applicant is required to amend its 505(b)(2) application to include documentation of this date (e.g., copy of return receipt or letter from recipient acknowledging its receipt of the notice) (see 21 CFR 314.52(e)).

If "Yes," skip to question (4) below. If "No," continue with question (2).

- (2) Has the patent owner (or NDA holder, if it is an exclusive patent licensee) submitted a written waiver of its right to file a legal action for patent infringement after receiving the applicant's notice of certification, as provided for by 21 CFR 314.107(f)(3)?

Yes No

If "Yes," there is no stay of approval based on this certification. Analyze the next paragraph IV certification in the application, if any. If there are no other paragraph IV certifications, skip to the next section below (Summary Reviews).

If "No," continue with question (3).

- (3) Has the patent owner, its representative, or the exclusive patent licensee filed a lawsuit for patent infringement against the applicant?

Yes No

(Note: This can be determined by confirming whether the Division has received a written notice from the (b)(2) applicant (or the patent owner or its representative) stating that a legal action was filed within 45 days of receipt of its notice of certification. The applicant is required to notify the Division in writing whenever an action has been filed within this 45-day period (see 21 CFR 314.107(f)(2)).

If "No," the patent owner (or NDA holder, if it is an exclusive patent licensee) has until the expiration of the 45-day period described in question (1) to waive its right to bring a patent infringement action or to bring such an action. After the 45-day period expires, continue with question (4) below.

- (4) Did the patent owner (or NDA holder, if it is an exclusive patent licensee) submit a written waiver of its right to file a legal action for patent infringement within the 45-day period described in question (1), as provided for by 21 CFR 314.107(f)(3)?

Yes No

If "Yes," there is no stay of approval based on this certification. Analyze the next paragraph IV certification in the application, if any. If there are no other paragraph IV certifications, skip to the next section below (Summary Reviews).

If "No," continue with question (5).

- (5) Did the patent owner, its representative, or the exclusive patent licensee bring suit against the (b)(2) applicant for patent infringement within 45 days of the patent owner's receipt of the applicant's notice of certification?

Yes No

(Note: This can be determined by confirming whether the Division has received a written notice from the (b)(2) applicant (or the patent owner or its representative) stating that a legal action was filed within 45 days of receipt of its notice of certification. The applicant is required to notify the Division in writing whenever an action has been filed within this 45-day period (see 21 CFR 314.107(f)(2)). If no written notice appears in the NDA file, confirm with the applicant whether a lawsuit was commenced within the 45-day period).

Page 5: NDA 22-119: Ammonia N 13 Injection

<p><i>If "No," there is no stay of approval based on this certification. Analyze the next paragraph IV certification in the application, if any. If there are no other paragraph IV certifications, skip to the next section below (Summary Reviews).</i></p> <p><i>If "Yes," a stay of approval may be in effect. To determine if a 30-month stay is in effect, consult with the Director, Division of Regulatory Policy II, Office of Regulatory Policy (HFD-007) and attach a summary of the response.</i></p>	
Summary Reviews	
<p>❖ Summary Reviews (e.g., Office Director, Division Director) (indicate date for each review)</p>	<p>X – July 20, 2007 (DMIHP) X – August 15, 2007 (OODP)</p>
<p>❖ BLA approvals only: Licensing Action Recommendation Memo (LARM) (indicate date)</p>	<p>N/A</p>
Labeling	
❖ Package Insert	
<ul style="list-style-type: none"> • Most recent division-proposed labeling (only if generated after latest applicant submission of labeling) 	<p>X</p>
<ul style="list-style-type: none"> • Most recent applicant-proposed labeling (only if subsequent division labeling does not show applicant version) 	<p>N/A</p>
<ul style="list-style-type: none"> • Original applicant-proposed labeling 	<p>X</p>
<ul style="list-style-type: none"> • Other relevant labeling (e.g., most recent 3 in class, class labeling), if applicable 	<p>N/A</p>
Patient Package Insert	
<ul style="list-style-type: none"> • Most-recent division-proposed labeling (only if generated after latest applicant submission of labeling) 	<p>N/A</p>
<ul style="list-style-type: none"> • Most recent applicant-proposed labeling (only if subsequent division labeling does not show applicant version) 	<p>N/A</p>
<ul style="list-style-type: none"> • Original applicant-proposed labeling 	<p>N/A</p>
<ul style="list-style-type: none"> • Other relevant labeling (e.g., most recent 3 in class, class labeling), if applicable 	<p>N/A</p>
❖ Medication Guide	
<ul style="list-style-type: none"> • Most recent division-proposed labeling (only if generated after latest applicant submission of labeling) 	<p>N/A</p>
<ul style="list-style-type: none"> • Most recent applicant-proposed labeling (only if subsequent division labeling does not show applicant version) 	<p>N/A</p>
<ul style="list-style-type: none"> • Original applicant-proposed labeling 	<p>N/A</p>
<ul style="list-style-type: none"> • Other relevant labeling (e.g., most recent 3 in class, class labeling) 	<p>N/A</p>
❖ Labels (full color carton and immediate-container labels)	
<ul style="list-style-type: none"> • Most-recent division-proposed labels (only if generated after latest applicant submission) 	<p>See CMC Review</p>
<ul style="list-style-type: none"> • Most recent applicant-proposed labeling 	<p>X</p>
<p>❖ Labeling reviews and minutes of any labeling meetings (indicate dates of reviews and meetings)</p>	<p>X DMETS – March 5, 2007 X DDMAC – March 5, 2007 X SEALD – May 24, 2007 X PM Review – April 13, 2007 X Memos of Mtgs - Jan-Jun 2007</p>

Administrative Documents

❖ Administrative Reviews (RPM Filing Review/Memo of Filing Meeting; ADRA) <i>(indicate date of each review)</i>	X – December 7, 2006
❖ NDA and NDA supplement approvals only: Exclusivity Summary <i>(signed by Division Director)</i>	Included
❖ AIP-related documents <ul style="list-style-type: none"> Center Director's Exception for Review memo If AP: OC clearance for approval 	N/A
❖ Pediatric Page (all actions)	Included
❖ Debarment certification (original applications only): verified that qualifying language was not used in certification and that certifications from foreign applicants are cosigned by U.S. agent. <i>(Include certification.)</i>	Verified, statement is acceptable
❖ Postmarketing Commitment Studies	None
<ul style="list-style-type: none"> Outgoing Agency request for post-marketing commitments <i>(if located elsewhere in package, state where located)</i> Incoming submission documenting commitment 	
❖ Outgoing correspondence (letters including previous action letters, emails, faxes, telecons)	X
❖ Internal memoranda, telecons, email, etc.	X
❖ Minutes of Meetings	
<ul style="list-style-type: none"> Pre-Approval Safety Conference <i>(indicate date; approvals only)</i> Pre-NDA/BLA meeting <i>(indicate date)</i> EOP2 meeting <i>(indicate date)</i> Other (e.g., EOP2a, CMC pilot programs) 	N/A
❖ Advisory Committee Meeting	No AC meeting
<ul style="list-style-type: none"> Date of Meeting 48-hour alert or minutes, if available 	
❖ Federal Register Notices, DESI documents, NAS/NRC reports (if applicable)	March 10, 2000 (enclosed)
CMC/Product Quality Information	
❖ CMC/Product review(s) <i>(indicate date for each review)</i>	X – June 27, 2007
❖ Reviews by other disciplines/divisions/Centers requested by CMC/product reviewer <i>(indicate date for each review)</i>	None
❖ BLAs: Product subject to lot release (APs only)	N/A
❖ Environmental Assessment (check one) (original and supplemental applications)	
<ul style="list-style-type: none"> <input type="checkbox"/> Categorical Exclusion <i>(indicate review date)(all original applications and all efficacy supplements that could increase the patient population)</i> <input type="checkbox"/> Review & FONSI <i>(indicate date of review)</i> <input type="checkbox"/> Review & Environmental Impact Statement <i>(indicate date of each review)</i> 	X - June 27, 2007
	X - June 27, 2007
	X - June 27, 2007
❖ NDA: Microbiology reviews (sterility & apyrogenicity) <i>(indicate date of each review)</i>	X – March 23, 2007
❖ Facilities Review/Inspection	<input type="checkbox"/> Not a parenteral product
❖ NDA: Facilities inspections (include EER printout)	Date Completed: April 30, 2007 Acceptable

Page 7: NDA 22-119: Ammonia N 13 Injection

❖ BLAs: Facility-Related Documents <ul style="list-style-type: none"> • Facility review (<i>indicate date(s)</i>) • Compliance Status Check (approvals only, both original and supplemental applications) (<i>indicate date completed, must be within 60 days prior to AP</i>) 	N/A
❖ NDAs: Methods Validation	Completed
Nonclinical Information	
❖ Pharm/tox review(s), including referenced IND reviews (<i>indicate date for each review</i>)	X – August 1, 2007
❖ Review(s) by other disciplines/divisions/Centers requested by P/T reviewer (<i>indicate date for each review</i>)	N/A
❖ Statistical review(s) of carcinogenicity studies (<i>indicate date for each review</i>)	N/A
❖ ECAC/CAC report/memo of meeting	N/A
❖ Nonclinical inspection review Summary (DSI)	N/A
Clinical Information	
❖ Clinical review(s) (<i>indicate date for each review</i>)	X – May 25, 2007
❖ Financial Disclosure reviews(s) or location/date if addressed in another review	X – May 25, 2007 – See Clinical Review
❖ Clinical consult reviews from other review disciplines/divisions/Centers (<i>indicate date of each review</i>)	None
❖ Microbiology (efficacy) reviews(s) (<i>indicate date of each review</i>)	Not needed
❖ Safety Update review(s) (<i>indicate location/date if incorporated into another review</i>)	X – May 25, 2007 – See Clinical Review
❖ Risk Management Plan review(s) (including those by OSE) (<i>indicate location/date if incorporated into another review</i>)	N/A
❖ Controlled Substance Staff review(s) and recommendation for scheduling (<i>indicate date of each review</i>)	Not needed
❖ DSI Inspection Review Summary(ies) (<i>include copies of DSI letters to investigators</i>)	N/A
• Clinical Studies	
• Bioequivalence Studies	
• Clin Pharm Studies	
❖ Statistical Review(s) (<i>indicate date for each review</i>)	N/A
❖ Clinical Pharmacology review(s) (<i>indicate date for each review</i>)	N/A

MEMORANDUM

To: Thuy Nguyen
Division of Medical Imaging and Hematology Products

From: Iris Masucci, PharmD, BCPS
Division of Drug Marketing, Advertising, and Communications
for the Study Endpoints and Label Development (SEALD) Team, OND

Date: May 22, 2007

Re: Comments on draft labeling for Ammonia N 13 solution
NDA 22-119

We have reviewed the proposed label for Ammonia N 13 (received 5/17/07) and offer the following comments. These comments are based on Title 21 of the Code of Federal Regulations (201.56 and 201.57), the preamble to the Final Rule, labeling Guidances, and FDA recommendations to provide for labeling quality and consistency across review divisions. We recognize that final labeling decisions rest with the review division after a full review of the submitted data.

GENERAL COMMENTS

- Please revise all cross-references in the FPI to the preferred formatting for PLR labels (e.g., “[see Warnings and Precautions (5.2)]”). Note that the cross-reference should name the main section heading, but use the appropriate subsection number in parentheses.
- For ease of reading, we suggest adding an extra hard return between paragraphs of text in the Full Prescribing Information (FPI).

HIGHLIGHTS

- “Ammonia N 13 Injection (Ammonia in 0.9% Sodium Chloride solution)”

We recommend that all the lettering of the established name (in parentheses) be all lower case, as is usually done.

- Please be sure that the “Initial U.S. Approval” date is filled in upon approval of this product.

Indications and Usage

5 Page(s) Withheld

 Trade Secret / Confidential

X Draft Labeling

 Deliberative Process

Withheld Track Number: Administrative-2

**This is a representation of an electronic record that was signed electronically and
this page is the manifestation of the electronic signature.**

/s/

Iris Masucci
5/24/2007 03:58:35 PM
DDMAC REVIEWER

Laurie Burke
5/24/2007 06:05:28 PM
INTERDISCIPLINARY



Division of Medical Imaging and
Hematology Products
Office of Oncology Drug Products
Center for Drug Evaluation and Research
U.S. Food and Drug Administration

FACSIMILE TRANSMITTAL SHEET

DATE: MARCH 5, 2007

TO: DR. THOMAS CHALY	FROM: Thuy Nguyen, M.P.H. Regulatory Health Project Manager
COMPANY: Feinstein Institute for Medical Research	Division of Division of Medical Imaging and Hematology Products
FAX Number: (516) 562-1041	Fax Number: (301) 796-9849
PHONE Number: (516) 562-1042	Phone Number: (301) 796-2050
SUBJECT: NDA 22-119: Ammonia [N-13] Injection	

TOTAL NO. OF PAGES (including cover): 2

COMMENTS: Please find attached the Division's MICROBIOLOGY comments regarding NDA 22-119: Ammonia [N-13], serial #000, submission dated October 16, 2006.

Please provide an official response to the NDA in *triplicate* hard copies by Monday, March 26, 2007.

If you have any questions, please feel free to contact me. Thank you.

THIS DOCUMENT IS INTENDED ONLY FOR THE USE OF THE PARTY TO WHOM IT IS ADDRESSED AND MAY CONTAIN INFORMATION THAT IS PRIVILEGED, CONFIDENTIAL, AND PROTECTED FROM DISCLOSURE UNDER APPLICABLE LAW.

If you are not the addressee, or a person authorized to deliver this document to the addressee, you are hereby notified that any review, disclosure, dissemination, copying, or other action based on the content of this communication is not authorized. If you have received this document in error, please notify us immediately by telephone at (301) 796-2050. Thank you.

MICROBIOLOGY COMMENTS TO THE SPONSOR

NDA 22-119: [N-13] Ammonia

March 5, 2007

We refer to your NDA 22-119, Serial No. 000, submission dated October 16, 2006.

We have reviewed the submission and have the following information requests.

Please provide a response to the NDA, in *triplicate* hard copies by Monday, March 26, 2007.

1. _____, should simulate the manufacturing process as closely as possible including all production steps in the _____.

In addition, SOP NH3V011 should address in more detail the actions taken following a _____.

_____ An investigation should be initiated to identify the cause of the _____.

_____ and appropriate actions taken _____.

CONSULTATION RESPONSE

**Division of Medication Errors and Technical Support
Office of Surveillance and Epidemiology
WO 22, Mailstop 4447, HFD-420
Center for Drug Evaluation and Research**

DATE RECEIVED: December 5, 2006

**DESIRED COMPLETION
DATE:** March 1, 2007

OSE REVIEW #: 2006-863

TO: Rafel Rieves, MD Acting Director
Division of Medical Imaging and Hematology Products
HFD-160

THROUGH: Linda Kim-Jung, PharmD, Team Leader
Denise Toyer, PharmD, Deputy Director
Carol Holquist, RPh, Director
Division of Medication Errors and Technical Support
HFD-420

FROM: Walter L. Fava, R.Ph., Safety Evaluator
Division of Medication Errors and Technical Support
HFD-420

PRODUCT NAME: Ammonia [N-13] Injection USP

NDA: 22-119

NDA SPONSOR: Feinstein Institute

RECOMMENDATIONS:

DMETS recommends implementation of the label and labeling revisions outlined in Section II of this review.

DMETS would appreciate feedback of the final outcome of this consult. We would be willing to meet with the Division for further discussion, if needed. If you have further questions or need clarification, please contact Sam Chan, Project Manager at (301) 796-2283.

**Division of Medication Errors and Technical Support
Office of Surveillance and Epidemiology
WO 22, Mailstop 4447, HFD-420
Center for Drug Evaluation and Research**

LABEL AND LABELING REVIEW

Date of Review: January 10, 2007
Drug Name: Ammonia [N-13] Injection
NDA #: 22-119
NDA Holder: Feinstein Institute
Project: OSE Review # 2006-863

I. INTRODUCTION

This consult was written in response to a request from the Division of Medical Imaging and Hematology Products (HFD-160) for a review of the container labels, carton and insert labeling of Ammonia [N-13] Injection. A proposed trade name was not submitted for review and comment at this time.

PRODUCT INFORMATION

Ammonia [N-13] Injection is a positron emitting radiopharmaceutical agent containing radioactive [¹³N] ammonia. It is used for diagnostic purposes in conjunction with positron emission tomography (PET) imaging. Ammonia N-13 Injection is indicated for PET imaging of the myocardium at rest or under pharmacologic stress conditions, to evaluate myocardial perfusion in patients with suspected or existing coronary artery disease. The product has a range of radioactivity _____ (3.75 mCi/mL to 37.5 mCi/mL). The actual concentration is measured using a _____ prior to patient administration. The recommended intravenous dose for both resting and stress imaging studies is 10-20 mCi Ammonia [N-13]. Doses are administered through a catheter into a large vein. Due to its short half-life (9.96 minutes), and its short expiration time (30 minutes after the end of synthesis), Ammonia [N-13] is _____ for immediately delivery to the PET scanner. Ammonia [N-13] is supplied in 20 mL multiple dose glass vials. To prevent radiation exposure, the 20 mL multiple dose glass vials are shielded in labeled, lead pig containers.

II. LABELING, PACKAGING, AND SAFETY RELATED ISSUES

In review of the container label (container closure system and lead pig container) and the package insert labeling for Ammonia [N-13] Injection USP, DMETS has focused on safety issues relating to possible medication errors. DMETS has the following recommendations:

A. General Comments

1. Copies of the labels and labeling were provided in black and white, and may not represent the true color of the labels and labeling. Therefore, DMETS cannot assess if there are any safety concerns due to the colors utilized on the labels and labeling. Please forward copies of the

2 Page(s) Withheld

 Trade Secret / Confidential

X Draft Labeling

 Deliberative Process

Withheld Track Number: Administrative-3

**This is a representation of an electronic record that was signed electronically and
this page is the manifestation of the electronic signature.**

/s/

Walter Fava
3/5/2007 08:05:45 AM
DRUG SAFETY OFFICE REVIEWER

Linda Kim-Jung
3/5/2007 08:14:37 AM
DRUG SAFETY OFFICE REVIEWER

Carol Holquist
3/5/2007 09:05:36 AM
DRUG SAFETY OFFICE REVIEWER

FOOD AND DRUG ADMINISTRATION
Center for Drug Evaluation and Research
Division of Drug Marketing, Advertising, and Communications

MEMORANDUM

****PRE-DECISIONAL AGENCY MEMO****

Date: March 3, 2007

To: Thuy Nguyen, Project Manager
Division of Medical Imaging and Hematology Drug Products

From: Sean K. Bradley, Regulatory Review Officer
Division of Drug Marketing, Advertising, and Communications

Subject: NDA 22-119
Ammonia [N 13] Injection, Diagnostic-For Intravenous Administration
Proposed Product Labeling

The Division of Drug Marketing, Advertising, and Communications (DDMAC) has reviewed the proposed product labeling for Ammonia N 13 Injection and have the following comments. The proposed label was compared to the labels of previously approved products Myoview and FDG F 18. Additional information was also taken from the Federal Register/Vol. 65, No. 48/March 10, 2000.

1. DESCRIPTION

Regarding Table 1 Principle Radiation Emission Data for Nitrogen N 13; are these actual or mean values for **% Per Disintegration and Energy**?

Should the paragraph after Table 1 be headed by the subsection title, "**External Radiation**" as in the FDG F 18 and Myoview labeling?

2. CLINICAL PHARMACOLOGY

General

"Ammonia N 13 Injection is a radiolabeled analog of ammonia that is ~~is~~ distributed to all organs of the body after intravenous administration."

3 Page(s) Withheld

 Trade Secret / Confidential

X Draft Labeling

 Deliberative Process

Withheld Track Number: Administrative-4

**This is a representation of an electronic record that was signed electronically and
this page is the manifestation of the electronic signature.**

/s/

Sean Bradley
3/5/2007 10:05:28 AM
DDMAC REVIEWER

4 Page(s) Withheld

 Trade Secret / Confidential

X Draft Labeling

 Deliberative Process

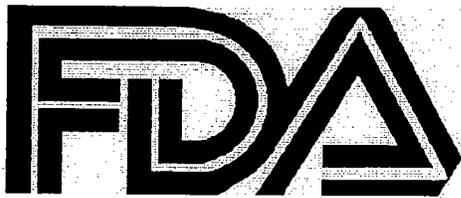
Withheld Track Number: Administrative-5

**This is a representation of an electronic record that was signed electronically and
this page is the manifestation of the electronic signature.**

/s/

Thuy Nguyen
4/5/2007 02:28:22 PM
CSO

Kyong Kang
4/13/2007 08:42:08 AM
CSO



Division of Medical Imaging and
Hematology Products
Office of Oncology Drug Products
Center for Drug Evaluation and Research
U.S. Food and Drug Administration

FACSIMILE TRANSMITTAL SHEET

DATE: FEBRUARY 22, 2007

TO: DR. THOMAS CHALY	FROM: Thuy Nguyen, M.P.H. Regulatory Health Project Manager
COMPANY: Feinstein Institute for Medical Research	Division of Division of Medical Imaging and Hematology Products
FAX Number: (516) 562-1041	Fax Number: (301) 796-9849
PHONE Number: (516) 562-1042	Phone Number: (301) 796-2050

SUBJECT: NDA 22-119: Ammonia [N-13] Injection

TOTAL NO. OF PAGES (including cover): 2

COMMENTS: Please find attached the Division's CLINICAL comments regarding
NDA 22-119: Ammonia [N-13], serial #000, submission dated October 16, 2006.

Please provide an official response to the NDA in *triplicate* hard copies along with a
electronic copy on CD-Rom, by Wednesday, March 14, 2007, and mail it to the
FDA: Central Doc Room: 5901-B Ammendale Rd, Beltsville, MD 20705-1266.

Please also mail one hard copy of the response along with an electronic copy on CD-Rom, to
me at the following address: T.Nguyen, FDA, Div of Medical Imaging and Hematology
Products, 10903 New Hampshire Ave, White Oak Bldg #22, Room #2315, Silver Spring, MD
20993.

If you have any questions, please feel free to contact me. Thank you.

THIS DOCUMENT IS INTENDED ONLY FOR THE USE OF THE PARTY TO WHOM IT IS ADDRESSED
AND MAY CONTAIN INFORMATION THAT IS PRIVILEGED, CONFIDENTIAL, AND PROTECTED
FROM DISCLOSURE UNDER APPLICABLE LAW.

If you are not the addressee, or a person authorized to deliver this document to the addressee,
you are hereby notified that any review, disclosure, dissemination, copying, or other action based
on the content of this communication is not authorized. If you have received this document in
error, please notify us immediately by telephone at (301) 796-2050. Thank you.

CLINICAL COMMENTS TO THE SPONSOR

NDA 22-119: [N-13] Ammonia

February 22, 2007

We refer to your NDA 22-119, Serial No. 000, submission dated October 16, 2006.

We have reviewed the submission and have the following information requests.

Please provide a response to the NDA, in *triplicate* hard copies along with an electronic copy on CD-Rom by **Wednesday, March 14, 2007**.

1. The submitted copy of the SPL label is in XML format and we are unable to edit your submitted version. Please submit a copy of the SPL in MS Word (hard copy and electronic copy on CD-Rom).
2. The clinical section of your NDA submission does not contain any updated safety or efficacy information.
 - a. Please perform a search of the scientific and clinical literature and provide a summary of available data regarding safety (including adverse events) and efficacy of [N-13] Ammonia. Please provide copies of the relevant publications.
 - b. Please summarize the clinical experience with [N-13] Ammonia at your clinical center.

We request that you provide a written response by **Wednesday, March 14, 2007**. To expedite processing, you may send your response to us in an electronic pass-word protected format. Please address these communications to the Dr. Cynthia Welsh, Medical Officer (Cynthia.Welsh@fda.hhs.gov) with copy to Ms. Thuy Nguyen, Project Manager (Thuy.Nguyen@fda.hhs.gov).

If you have any questions, please contact:
Thuy Nguyen, M.P.H., Project Manager, 301-796-2050
Cynthia Welsh, M.D., Medical Officer, 301-796-2168

NDA REGULATORY FILING REVIEW
(Including Memo of Filing Meeting)

NDA # 22-119

Established Name: [N-13] Ammonia Injection
Strengths: 3.75 – 37.5 mCi/mL

Applicant: The Feinstein Institute for Medical Research
Agent for Applicant: Thomas Chaly, Ph.D., Chief, Radiochemistry

Date of Application: October 16, 2006
Date of Receipt: October 25, 2006
Date clock started: October 25, 2006
Date of Filing Meeting: December 6, 2006
Filing Date: December 22, 2006
Action Goal Date (optional): August 15, 2007 **User Fee Goal Date:** August 24, 2007

Indication requested: The use of [N-13] Ammonia Injection in PET imaging of the myocardium under rest or pharmacologic stress conditions to evaluate myocardial perfusion in patients with suspected or existing coronary artery disease (CAD).

Type of Original NDA: (b)(2)

NOTE:

(1) *If you have questions about whether the application is a 505(b)(1) or 505(b)(2) application, see Appendix A. A supplement can be either a (b)(1) or a (b)(2) regardless of whether the original NDA was a (b)(1) or a (b)(2). If the application or efficacy supplement is a (b)(2), complete Appendix B.*

Review Classification: S - Standard
Resubmission after withdrawal? No **Resubmission after refuse to file?** N/A
Chemical Classification: (1,2,3 etc.) 1
Other (orphan, OTC, etc.) N/A

Form 3397 (User Fee Cover Sheet) submitted: YES X

User Fee Status:
Waived (e.g., small business, public health) X

NOTE: *If the NDA is a 505(b)(2) application, and the applicant did not pay a fee in reliance on the 505(b)(2) exemption (see box 7 on the User Fee Cover Sheet), confirm that a user fee is not required by contacting the User Fee staff in the Office of Regulatory Policy. The applicant is required to pay a user fee if: (1) the product described in the 505(b)(2) application is a new molecular entity or (2) the applicant claims a new indication for a use that has not been approved under section 505(b). Examples of a new indication for a use include a new indication, a new dosing regime, a new patient population, and an Rx-to-OTC switch. The best way to determine if the applicant is claiming a new indication for a use is to compare the applicant's proposed labeling to labeling that has already been approved for the product described in the application. Highlight the differences between the proposed and approved labeling. If you need assistance in determining if the applicant is claiming a new indication for a use, please contact the User Fee staff.*

- Is there any 5-year or 3-year exclusivity on this active moiety in any approved (b)(1) or (b)(2) application? YES NO
If yes, explain:

Note: If the drug under review is a 505(b)(2), this issue will be addressed in detail in appendix B.

- Does another drug have orphan drug exclusivity for the same indication? YES NO

- If yes, is the drug considered to be the same drug according to the orphan drug definition of sameness [21 CFR 316.3(b)(13)]? YES NO

If yes, consult the Director, Division of Regulatory Policy II, Office of Regulatory Policy (HFD-007).

- Is the application affected by the Application Integrity Policy (AIP)? YES NO
If yes, explain:

- If yes, has OC/DMPQ been notified of the submission? YES NO

- Does the submission contain an accurate comprehensive index? YES NO
If no, explain:

- Was form 356h included with an authorized signature? YES NO
If foreign applicant, both the applicant and the U.S. agent must sign.

- Submission complete as required under 21 CFR 314.50? YES NO
If no, explain:

- Answer 1, 2, or 3 below (do not include electronic content of labeling as an partial electronic submission).

1. This application is a paper NDA YES

2. This application is an eNDA or combined paper + eNDA YES
This application is: Combined paper + eNDA
This application is in: NDA format

Does the eNDA, follow the guidance?
(<http://www.fda.gov/cder/guidance/2353fnl.pdf>) YES NO

If an eNDA, all forms and certifications must be in paper and require a signature.

If combined paper + eNDA, which parts of the application were submitted in electronic format?
ALL

3. This application is an eCTD NDA. YES NO
If an eCTD NDA, all forms and certifications must either be in paper and signed or be electronically signed.

Additional comments:

- Patent information submitted on form FDA 3542a? YES NO

- **Exclusivity requested?** YES, _____ NO
NOTE: An applicant can receive exclusivity without requesting it; therefore, requesting exclusivity is not required.

- **Correctly worded Debarment Certification included with authorized signature?** YES NO
If foreign applicant, both the applicant and the U.S. Agent must sign the certification.

NOTE: Debarment Certification should use wording in FD&C Act section 306(k)(1) i.e., "[Name of applicant] hereby certifies that it did not and will not use in any capacity the services of any person debarred under section 306 of the Federal Food, Drug, and Cosmetic Act in connection with this application." Applicant may not use wording such as "To the best of my knowledge"

- **Are the required pediatric assessment studies and/or deferral/partial waiver/full waiver of pediatric studies (or request for deferral/partial waiver/full waiver of pediatric studies) included?** YES

- **If the submission contains a request for deferral, partial waiver, or full waiver of studies, does the application contain the certification required under FD&C Act sections 505B(a)(3)(B) and (4)(A) and (B)?** YES

- **Is this submission a partial or complete response to a pediatric Written Request?** N/A
If yes, contact PMHT in the OND-IO

- **Financial Disclosure forms included with authorized signature?** YES NO
(Forms 3454 and/or 3455 must be included and must be signed by the APPLICANT, not an agent.)
NOTE: Financial disclosure is required for bioequivalence studies that are the basis for approval.

- **Field Copy Certification (that it is a true copy of the CMC technical section)** YES NO

- **PDUFA and Action Goal dates correct in tracking system?** YES NO
If not, have the document room staff correct them immediately. These are the dates EES uses for calculating inspection dates.

- **Drug name and applicant name correct in COMIS?** YES. If not, have the Document Room make the corrections. Ask the Doc Rm to add the established name to COMIS for the supporting IND if it is not already entered.

- **List referenced IND numbers:** N/A

- **Are the trade, established/proper, and applicant names correct in COMIS?** YES
If no, have the Document Room make the corrections.

- **End-of-Phase 2 Meeting(s)?** _____ NO
If yes, distribute minutes before filing meeting.

- **Pre-NDA Meeting(s)?** _____ NO
If yes, distribute minutes before filing meeting.

- **Any SPA agreements?** _____ NO
If yes, distribute letter and/or relevant minutes before filing meeting.

Project Management

- **If Rx, was electronic Content of Labeling submitted in SPL format?** YES X NO
If no, request in 74-day letter.
- **If Rx, for all new NDAs/efficacy supplements submitted on or after 6/30/06:
Was the PI submitted in PLR format?** YES X NO
If no, explain. Was a waiver or deferral requested before the application was received or in the submission? If before, what is the status of the request:
- **If Rx, all labeling (PI, PPI, MedGuide, carton and immediate container labels) has been consulted to DDMAC?** YES X NO
- **If Rx, trade name (and all labeling) consulted to OSE/DMETS?** YES X NO
- **If Rx, MedGuide and/or PPI (plus PI) consulted to ODE/DSRCS?**
N/A X YES NO
- **Risk Management Plan consulted to OSE/IO?** N/A X YES NO
- **If a drug with abuse potential, was an Abuse Liability Assessment, including a proposal for scheduling submitted?** NA X YES NO

If Rx-to-OTC Switch or OTC application:

- **Proprietary name, all OTC labeling/packaging, and current approved PI consulted to OSE/DMETS?** YES NO
- **If the application was received by a clinical review division, has DNPCE been notified of the OTC switch application? Or, if received by DNPCE, has the clinical review division been notified?** YES NO

Clinical

- **If a controlled substance, has a consult been sent to the Controlled Substance Staff?**
N/A X

Chemistry

- **Did applicant request categorical exclusion for environmental assessment?** YES X NO
If no, did applicant submit a complete environmental assessment? YES NO
If EA submitted, consulted to EA officer, OPS? YES NO
- **Establishment Evaluation Request (EER) submitted to DMPQ?** YES X NO
- **If a parenteral product, consulted to Microbiology Team?** YES X NO

ATTACHMENT

MEMO OF FILING MEETING

DATE: DECEMBER 6, 2006
NDA #: 22-119
DRUG NAMES: [N-13] Ammonia Injection
APPLICANT: The Feinstein Institute for Medical Research

BACKGROUND: A 505(b)(2) NDA – clinical, stat, PK, and P/T data referenced by published literature and FR Notice – March 2000. Proposed Indication: The use of [N-13] Ammonia Injection in PET imaging of the myocardium under rest or pharmacologic stress conditions to evaluate myocardial perfusion in patients with suspected or existing coronary artery disease (CAD).

ATTENDEES: Eldon Leutzinger, CMC PAL, Anastasia Lolas, Microbiologist,
Thuy Nguyen, Project Manager Cynthia Welsh, Medical Reviewer

ASSIGNED REVIEWERS (including those not present at Filing Meeting) :

<u>Discipline/Organization</u>	<u>Reviewer</u>
Medical:	Cynthia Welsh, M.D.
Secondary Medical:	Louis Marzella, M.D.
Statistical:	N/A
Pharmacology:	N/A
Statistical Pharmacology:	N/A
Chemistry:	Ravi Kasliwal, Ph.D.
Environmental Assessment (if needed):	Ravi Kasliwal, Ph.D.
Biopharmaceutical:	N/A
Microbiology, sterility:	Anastasia Lolas, Ph.D.
Microbiology, clinical (for antimicrobial products only):	N/A
DSI:	N/A
OPS:	N/A
Regulatory Project Management:	Thuy Nguyen, M.P.H.
Other Consults:	Diane Smith, OSE, DMETS Samuel Chan, OSE, DSRCS Robin Anderson, SEALD

Per reviewers, are all parts in English or English translation? YES X NO
 If no, explain:

CLINICAL FILE X REFUSE TO FILE

- Clinical site audit(s) needed? NA X
If no, explain:
- Advisory Committee Meeting needed? _____ NO X
- If the application is affected by the AIP, has the division made a recommendation regarding whether or not an exception to the AIP should be granted to permit review based on medical necessity or public health significance?
N/A X YES NO

CLINICAL MICROBIOLOGY	N/A	X	FILE	<input type="checkbox"/>	REFUSE TO FILE	<input type="checkbox"/>		
STATISTICS	N/A	X	FILE	<input type="checkbox"/>	REFUSE TO FILE	<input type="checkbox"/>		
BIOPHARMACEUTICS			N/A	X	REFUSE TO FILE	<input type="checkbox"/>		
Biopharm. study site audits(s) needed?					YES	<input type="checkbox"/>	NO	<input type="checkbox"/>
PHARMACOLOGY/TOX	N/A	X	FILE	<input type="checkbox"/>	REFUSE TO FILE	<input type="checkbox"/>		
• GLP audit needed?					YES	<input type="checkbox"/>	NO	<input type="checkbox"/>
CHEMISTRY			FILE	X	REFUSE TO FILE	<input type="checkbox"/>		
• Establishment(s) ready for inspection?					YES	X	NO	<input type="checkbox"/>
• Sterile product?					YES	X	NO	<input type="checkbox"/>
If yes, was microbiology consulted for validation of sterilization?					YES	X	NO	<input type="checkbox"/>

ELECTRONIC SUBMISSION:

Any comments:

REGULATORY CONCLUSIONS/DEFICIENCIES:
(Refer to 21 CFR 314.101(d) for filing requirements.)

The application is unsuitable for filing. Explain why:

- X **The application, on its face, appears to be well-organized and indexed. The application appears to be suitable for filing.**
- X **No filing issues have been identified.**
- Filing issues to be communicated by Day 74. List (optional):

ACTION ITEMS:

1. X Ensure that the review and chemical classification codes, as well as any other pertinent classification codes (e.g., orphan, OTC) are correctly entered into COMIS.
2. N/A If RTF, notify everybody who already received a consult request of RTF action. Cancel the EER.
3. N/A If filed and the application is under the AIP, prepare a letter either granting (for signature by Center Director) or denying (for signature by ODE Director) an exception for review.
4. X If filed, complete the Pediatric Page at this time. (If paper version, enter into DFS.)
5. X Convey document filing issues/no filing issues to applicant by Day 74.

Thuy Nguyen, M.P.H., DMIHP
Regulatory Health Project Manager

APPENDIX A to NDA Regulatory Filing Review

NOTE: The term "original application" or "original NDA" as used in this appendix denotes the NDA submitted. It does not refer to the reference drug product or "reference listed drug."

An original application is likely to be a 505(b)(2) application if:

- (1) it relies on published literature to meet any of the approval requirements, and the applicant does not have a written right of reference to the underlying data. If published literature is cited in the NDA but is not necessary for approval, the inclusion of such literature will not, in itself, make the application a 505(b)(2) application,
- (2) it relies for approval on the Agency's previous findings of safety and efficacy for a listed drug product and the applicant does not own or have right to reference the data supporting that approval, or
- (3) it relies on what is "generally known" or "scientifically accepted" about a class of products to support the safety or effectiveness of the particular drug for which the applicant is seeking approval. (Note, however, that this does not mean *any* reference to general information or knowledge (e.g., about disease etiology, support for particular endpoints, methods of analysis) causes the application to be a 505(b)(2) application.)

Types of products for which 505(b)(2) applications are likely to be submitted include: fixed-dose combination drug products (e.g., heart drug and diuretic (hydrochlorothiazide) combinations); OTC monograph deviations (see 21 CFR 330.11); new dosage forms; new indications; and, new salts.

An efficacy supplement can be either a (b)(1) or a (b)(2) regardless of whether the original NDA was a (b)(1) or a (b)(2).

An efficacy supplement is a 505(b)(1) supplement if the supplement contains all of the information needed to support the approval of the change proposed in the supplement. For example, if the supplemental application is for a new indication, the supplement is a 505(b)(1) if:

- (1) The applicant has conducted its own studies to support the new indication (or otherwise owns or has right of reference to the data/studies),
- (2) No additional information beyond what is included in the supplement or was embodied in the finding of safety and effectiveness for the original application or previously approved supplements is needed to support the change. For example, this would likely be the case with respect to safety considerations if the dose(s) was/were the same as (or lower than) the original application, and,
- (3) All other "criteria" are met (e.g., the applicant owns or has right of reference to the data relied upon for approval of the supplement, the application does not rely for approval on published literature based on data to which the applicant does not have a right of reference).

An efficacy supplement is a 505(b)(2) supplement if:

- (1) Approval of the change proposed in the supplemental application would require data beyond that needed to support our previous finding of safety and efficacy in the approval of the original application (or earlier supplement), and the applicant has not conducted all of its own studies for approval of the change, or obtained a right to reference studies it does not own. For example, if the change were for a new indication AND a higher dose, we would likely require clinical efficacy data and preclinical safety data to approve the higher dose. If the applicant provided the effectiveness data, but had to rely on a different listed drug, or a new aspect of a previously cited listed drug, to support the safety of the new dose, the supplement would be a 505(b)(2),
- (2) The applicant relies for approval of the supplement on published literature that is based on data that the applicant does not own or have a right to reference. If published literature is cited in the supplement but is not necessary for approval, the inclusion of such literature will not, in itself, make the supplement a 505(b)(2) supplement, or
- (3) The applicant is relying upon any data they do not own or to which they do not have right of reference.

If you have questions about whether an application is a 505(b)(1) or 505(b)(2) application, consult with your ODE's Office of Regulatory Policy representative.

APPENDIX B to NDA Regulatory Filing Review
Questions for 505(b)(2) Applications

1. Does the application reference a listed drug (approved drug)? YES NO

If "No," skip to question 3.

2. Name of listed drug(s) referenced by the applicant (if any) and NDA/ANDA #(s):

3. Is this application for a drug that is an "old" antibiotic (as described in the draft guidance implementing the 1997 FDAMA provisions? (Certain antibiotics are not entitled to Hatch-Waxman patent listing and exclusivity benefits.) YES NO

If "Yes," skip to question 7.

4. Is this application for a recombinant or biologically-derived product? YES NO

If "Yes" contact your ODE's Office of Regulatory Policy representative.

5. The purpose of the questions below (questions 5 to 6) is to determine if there is an approved drug product that is equivalent or very similar to the product proposed for approval that should be referenced as a listed drug in the pending application.

- (a) Is there a pharmaceutical equivalent(s) to the product proposed in the 505(b)(2) application that is already approved? YES NO

(Pharmaceutical equivalents are drug products in identical dosage forms that: (1) contain identical amounts of the identical active drug ingredient, i.e., the same salt or ester of the same therapeutic moiety, or, in the case of modified release dosage forms that require a reservoir or overage or such forms as prefilled syringes where residual volume may vary, that deliver identical amounts of the active drug ingredient over the identical dosing period; (2) do not necessarily contain the same inactive ingredients; and (3) meet the identical compendial or other applicable standard of identity, strength, quality, and purity, including potency and, where applicable, content uniformity, disintegration times, and/or dissolution rates. (21 CFR 320.1(c))

If "No," to (a) skip to question 6. Otherwise, answer part (b and (c)).

- (b) Is the pharmaceutical equivalent approved for the same indication for which the 505(b)(2) application is seeking approval? YES NO

- (c) Is the approved pharmaceutical equivalent(s) cited as the listed drug(s)? YES NO

If "Yes," (c), list the pharmaceutical equivalent(s) and proceed to question 6.

If "No," to (c) list the pharmaceutical equivalent and contact your ODE's Office of Regulatory Policy representative.

Pharmaceutical equivalent(s):

6. (a) Is there a pharmaceutical alternative(s) already approved? NO X

(Pharmaceutical alternatives are drug products that contain the identical therapeutic moiety, or its precursor, but not necessarily in the same amount or dosage form or as the same salt or ester. Each such drug product individually meets either the identical or its own respective compendial or other applicable standard of identity, strength, quality, and purity, including potency and, where applicable, content uniformity, disintegration times and/or dissolution rates. (21 CFR 320.1(d)) Different dosage forms and strengths within a product line by a single manufacturer are thus pharmaceutical alternatives, as are extended-release products when compared with immediate- or standard-release formulations of the same active ingredient.)

If "No," to (a) skip to question 7. Otherwise, answer part (b and (c)).

- (b) Is the pharmaceutical alternative approved for the same indication for which the 505(b)(2) application is seeking approval? YES NO

- (c) Is the approved pharmaceutical alternative(s) cited as the listed drug(s)? YES NO

If "Yes," to (c), proceed to question 7.

NOTE: If there is more than one pharmaceutical alternative approved, consult your ODE's Office of Regulatory Policy representative to determine if the appropriate pharmaceutical alternatives are referenced.

If "No," to (c), list the pharmaceutical alternative(s) and contact your ODE's Office of Regulatory Policy representative. Proceed to question 7.

Pharmaceutical alternative(s):

7. (a) Does the application rely on published literature necessary to support the proposed approval of the drug product (i.e. is the published literature necessary for the approval)? YES X

If "No," skip to question 8. Otherwise, answer part (b).

- (b) Does any of the published literature cited reference a specific (e.g. brand name) product? **NO.**
Note that if yes, the applicant will be required to submit patent certification for the product, see question 12.

8. Describe the change from the listed drug(s) provided for in this (b)(2) application (for example, "This application provides for a new indication, otitis media" or "This application provides for a change in dosage form, from capsules to solution").

9. Is the application for a duplicate of a listed drug and eligible for approval under section 505(j) as an ANDA? (Normally, FDA may refuse-to-file such NDAs (see 21 CFR 314.101(d)(9)). NO X

10. Is the application for a duplicate of a listed drug whose only difference is that the extent to which the active ingredient(s) is absorbed or otherwise made available to the site of action less than that of the reference listed drug (RLD)? (See 314.54(b)(1)). If yes, the application may be refused for filing under 21 CFR 314.101(d)(9)). NO X

11. Is the application for a duplicate of a listed drug whose only difference is that the rate at which the product's active ingredient(s) is absorbed or made available to the site of action is unintentionally less than that of the RLD (see 21CFR 314.54(b)(2))? If yes, the application may be refused for filing under 21 CFR 314.101(d)(9). NO X

12. Are there certifications for each of the patents listed in the Orange Book for the listed drug(s) referenced by the applicant (see question #2)? (This is different from the patent declaration submitted on form FDA 3542 and 3542a.) N/A

13. Which of the following patent certifications does the application contain? (Check all that apply and identify the patents to which each type of certification was made, as appropriate.)

Not applicable (e.g., solely based on published literature. See question # 7)

21 CFR 314.50(i)(1)(i)(A)(1): The patent information has not been submitted to FDA. (Paragraph I certification)
Patent number(s):

21 CFR 314.50(i)(1)(i)(A)(2): The patent has expired. (Paragraph II certification)
Patent number(s):

21 CFR 314.50(i)(1)(i)(A)(3): The date on which the patent will expire. (Paragraph III certification)
Patent number(s):

21 CFR 314.50(i)(1)(i)(A)(4): The patent is invalid, unenforceable, or will not be infringed by the manufacture, use, or sale of the drug product for which the application is submitted. (Paragraph IV certification)
Patent number(s):

NOTE: IF FILED, and if the applicant made a "Paragraph IV" certification [21 CFR 314.50(i)(1)(i)(A)(4)], the applicant must **subsequently** submit a signed certification stating that the NDA holder and patent owner(s) were notified the NDA was filed [21 CFR 314.52(b)]. The applicant must also submit documentation showing that the NDA holder and patent owner(s) received the notification [21 CFR 314.52(e)]. OND will contact you to verify that this documentation was received.

21 CFR 314.50(i)(3): Statement that applicant has a licensing agreement with the patent owner (must also submit certification under 21 CFR 314.50(i)(1)(i)(A)(4) above).
Patent number(s):

Written statement from patent owner that it consents to an immediate effective date upon approval of the application.
Patent number(s):

21 CFR 314.50(i)(1)(ii): No relevant patents.

21 CFR 314.50(i)(1)(iii): The patent on the listed drug is a method of use patent and the labeling for the drug product for which the applicant is seeking approval does not include any indications that are covered by the use patent as described in the corresponding use code in the Orange Book. Applicant must provide a statement that the method of use patent does not claim any of the proposed indications. (Section viii statement)
Patent number(s):

14. Did the applicant:

- Identify which parts of the application rely on the finding of safety and effectiveness for a listed drug or published literature describing a listed drug or both? For example, pharm/tox section of application relies on finding of preclinical safety for a listed drug.

NO X

If "Yes," what is the listed drug product(s) and which sections of the 505(b)(2) application rely on the finding of safety and effectiveness or on published literature about that listed drug

Was this listed drug product(s) referenced by the applicant? (see question # 2)

YES NO

- Submit a bioavailability/bioequivalence (BA/BE) study comparing the proposed product to the listed drug(s)?

N/A

15. (a) Is there unexpired exclusivity on this listed drug (for example, 5 year, 3 year, orphan or pediatric exclusivity)? Note: this information is available in the Orange Book.

NO X

If "Yes," please list:

Application No.	Product No.	Exclusivity Code	Exclusivity Expiration

**This is a representation of an electronic record that was signed electronically and
this page is the manifestation of the electronic signature.**

/s/

Thuy Nguyen
12/7/2006 02:38:42 PM
CSO

Form Approved: OMB No. 0910 - 0297 Expiration Date: December 31, 2006 See instructions for OMB Statement.

DEPARTMENT OF HEALTH AND HUMAN
SERVICES
FOOD AND DRUG ADMINISTRATIONPRESCRIPTION DRUG USER FEE
COVERSHEET

A completed form must be signed and accompany each new drug or biologic product application and each new supplement. See exceptions on the reverse side. If payment is sent by U.S. mail or courier, please include a copy of this completed form with payment. Payment instructions and fee rates can be found on CDER's website: <http://www.fda.gov/cder/pdufa/default.htm>

1. APPLICANT'S NAME AND ADDRESS THE FEINSTEIN INSTITUTE FOR MEDICAL RESEARCH Thomas Chaly 350 Community Drive Manhasset NY 11030 US	4. BLA SUBMISSION TRACKING NUMBER (STN) / NDA NUMBER 22-119
2. TELEPHONE NUMBER 516-5621042	5. DOES THIS APPLICATION REQUIRE CLINICAL DATA FOR APPROVAL? <input checked="" type="checkbox"/> YES <input type="checkbox"/> NO IF YOUR RESPONSE IS "NO" AND THIS IS FOR A SUPPLEMENT, STOP HERE AND SIGN THIS FORM. IF RESPONSE IS "YES", CHECK THE APPROPRIATE RESPONSE BELOW: <input type="checkbox"/> THE REQUIRED CLINICAL DATA ARE CONTAINED IN THE APPLICATION <input checked="" type="checkbox"/> THE REQUIRED CLINICAL DATA ARE SUBMITTED BY REFERENCE TO: Circulation 1989; 79, 825-35

3. PRODUCT NAME amonia N13injection	6. USER FEE I.D. NUMBER PD3006849
---	---

7. IS THIS APPLICATION COVERED BY ANY OF THE FOLLOWING USER FEE EXCLUSIONS? IF SO, CHECK THE APPLICABLE EXCLUSION.

<input type="checkbox"/> A LARGE VOLUME PARENTERAL DRUG PRODUCT APPROVED UNDER SECTION 505 OF THE FEDERAL FOOD, DRUG, AND COSMETIC ACT BEFORE 9/1/92 (Self Explanatory)	<input type="checkbox"/> A 505(b)(2) APPLICATION THAT DOES NOT REQUIRE A FEE
<input type="checkbox"/> THE APPLICATION QUALIFIES FOR THE ORPHAN EXCEPTION UNDER SECTION 736(a)(1)(E) of the Federal Food, Drug, and Cosmetic Act	<input type="checkbox"/> THE APPLICATION IS SUBMITTED BY A STATE OR FEDERAL GOVERNMENT ENTITY FOR A DRUG THAT IS NOT DISTRIBUTED COMMERCIALY

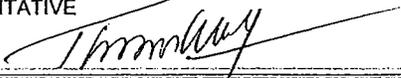
8. HAS A WAIVER OF AN APPLICATION FEE BEEN GRANTED FOR THIS APPLICATION? YES NO

Public reporting burden for this collection of information is estimated to average 30 minutes per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:

Department of Health and Human Services
 Food and Drug Administration
 CBER, HFM-99
 1401 Rockville Pike
 Rockville, MD 20852-1448

Food and Drug Administration
 CDER, HFD-94
 12420 Parklawn Drive, Room 3046
 Rockville, MD 20852

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.

SIGNATURE OF AUTHORIZED COMPANY REPRESENTATIVE 	TITLE CHIEF, RADIOCHEMISTRY ASSOCIATE PROFESSOR	DATE 11/07/06
--	--	-------------------------

9. USER FEE PAYMENT AMOUNT FOR THIS APPLICATION
 \$.00

Form FDA 3397 (12/03)

(IBE PRMT CLOSE G) (Print Cover sheet)



Division of Medical Imaging and
Hematology Products
Office of Oncology Drug Products
Center for Drug Evaluation and Research
Food and Drug Administration

FACSIMILE TRANSMITTAL SHEET

DATE: NOVEMBER 2, 2006

TO: DR. THOMAS CHALY	From: Thuy Nguyen Regulatory Health Project Manager
COMPANY: Feinstein Institute for Medical Research	Division of Division of Medical Imaging and Hematology Products
FAX Number: (516) 562-1041	Fax Number: (301) 796-9849
PHONE Number: (516) 562-1042	Phone Number: (301) 796-2050

SUBJECT: NDA 22-119: Ammonia [N-13] Injection

TOTAL No. of Pages (including cover): 2

COMMENTS: Please find attached the Division's comments regarding
NDA 22-119: Ammonia [N-13], submission dated October 16, 2006.

Please provide an official response to the NDA [in hard copy triplicate along with
Form FDA 356(h)] by 12:00 pm, Monday, November 6, 2006.

Please note that these comments are subject to changes (additions and deletions) and
additional new comments may be forthcoming.

If you have any questions, please feel free to contact me. Thank you.

THIS DOCUMENT IS INTENDED ONLY FOR THE USE OF THE PARTY TO WHOM IT IS ADDRESSED
AND MAY CONTAIN INFORMATION THAT IS PRIVILEGED, CONFIDENTIAL, AND PROTECTED
FROM DISCLOSURE UNDER APPLICABLE LAW.

If you are not the addressee, or a person authorized to deliver this document to the addressee,
you are hereby notified that any review, disclosure, dissemination, copying, or other action based
on the content of this communication is not authorized. If you have received this document in
error, please notify us immediately by telephone at (301) 796-2050. Thank you.

DIVISION COMMENTS TO THE SPONSOR

NDA 22-119: Ammonia [N-13] Injection

November 2, 2006

We have the following comments and request for information regarding your **NDA 22-119: Ammonia [N-13] Injection**, submission dated October 16, 2006.

According to the Federal Register Notice – March 10, 2006, regarding PET products, there are no approved Ammonia [N-13] Injection products for any indications. Therefore, NDA 22-119, is a fee paying NDA 505(b)(2) application. However, the FR Notice states that the Agency would waive the application fee for Ammonia [N-13] Injection products submitted in accordance with the FR Notice only if the sponsor/applicant submits with the NDA a statement that it waives any right to market exclusivity to which it may be entitled under the Act.

1. Please submit the appropriate market exclusivity waiver statement if you wish to have the application fee waived.
2. Please obtain at the FDA's website, a User Fee ID Number and have a Form 3397 generated (the fee should be calculated to be zero if the waiver box is checked). We note that you currently have both the waiver box and the 505(b)(2) exclusion box checked in the paper form that is not electronically generated [the 505(b)(2) exclusion is not correct].
3. Please revise the User Fee Waiver letter requirements. Please note that what was true for NDA 21-870 (FDG) is not true for this NDA 22-119: Ammonia [N-13] Injection.

If you have any questions regarding the above User Fee comments, please contact:
Office of Regulatory Policy
Mike Jones, Special Assistant
Office: (301) 594-2041

DIVISION OF MEDICAL IMAGING AND HEMATOLOGY PRODUCTS

TELECONFERENCE MEETING MINUTES

NDA: 22-119

DRUG NAME: [N-13] Ammonia

SUBMISSION DATE: October 16, 2006

SPONSOR: Thomas Chaly, Ph.D., for The Feinstein Institute

DATE: Wednesday, August 8, 2007

SPONSOR PARTICIPANTS

Thomas Chaly, Ph.D., Regulatory Contact

FDA PARTICIPANTS

Thuy Nguyen, M.P.H., Regulatory Health Project Manager

AGENDA: To discuss the FDA proposed draft labeling dated 08\08\07.
See NDA dated 10\16\06.

The Project Manager (PM) discussed and reviewed the FDA draft labeling dated 08\08\07.

The PM reviewed each of the new labeling changes, 08\08\07, since the previous draft labeling, 05\14\07, with the Sponsor. The Sponsor will review the draft labeling, 08\08\07, and provide a concurrence by August 9, 2007, with an agreement to revise the labeling in SPL and PLR format.

TCON Meeting Minutes Recorded By: T. Nguyen, DMIHP

DIVISION OF MEDICAL IMAGING AND HEMATOLOGY PRODUCTS

TELECONFERENCE MEETING MINUTES

NDA: 22-119
DRUG NAME: [N-13] Ammonia
SUBMISSION DATE: October 16, 2006
SPONSOR: The Feinstein Institute (Thomas Chaly, Ph.D.)
DATE: Monday, May 14, 2007

SPONSOR PARTICIPANTS

Thomas Chaly, Ph.D.

FDA PARTICIPANTS

Thuy Nguyen, M.P.H., Regulatory Health Project Manager

AGENDA: To discuss the FDA proposed draft labeling dated 05\14\07.
See NDA dated 10\16\06.

The Project Manager (PM) discussed and reviewed the FDA draft labeling dated 05\14\07, and referred the Sponsor to the FDA labeling web sites for references.

The PM explained that the format of the Sponsor's labeling should reflect the format of the fictitious labeling – Imdicon, since the Sponsor's proposed labeling submitted in the NDA date d10\16\06, was not in SPL or PLR format. The Sponsor agreed to revised the labeling in accordance with the SPL and PLR requirements and will submit a revised draft labeling to the FDA.

TCON Meeting Minutes Recorded By: T. Nguyen, DMIHP