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RESEARCH**

*APPLICATION NUMBER:*

**022494Orig1s000**

**MICROBIOLOGY REVIEW(S)**

# Product Quality Microbiology Review

18 January 2011

**NDA:** 22-494/N-000/SD-011 (Resubmission)

**Drug Product Name**

**Proprietary:** (None)

**Non-proprietary:** Sodium Fluoride [<sup>18</sup>F] Injection

**Review Number:** 2

**Dates of Submission(s) Covered by this Review**

| Submit Date      | Received Date    | Review Request | Assigned to Reviewer |
|------------------|------------------|----------------|----------------------|
| 12 May 2010      | 13 May 2010      | 17 May 2010    | 25 May 2010          |
| 26 July 2010     | 26 July 2010     | na             | na                   |
| 01 December 2010 | 02 December 2010 | na             | na                   |
| 27 December 2010 | 30 December 2010 | na             | na                   |

**Submission History (for amendments only):**

| Submit Date(s)   | Microbiology Review # | Review Date(s) |
|------------------|-----------------------|----------------|
| 30 December 2008 | 1                     | 12 May 2009    |

**Applicant/Sponsor**

**Name:** National Cancer Institute/DCTD/Cancer Imaging Program

**Address:** 6130 Executive Blvd.  
EPN, Suite 6000  
Bethesda, MD 20892-7412

**Representative:** Paula M. Jacobs, Ph.D.  
Deputy Associate Director  
Cancer Imaging Program, NCI

**Telephone:** 301-435-9181

**Name of Reviewer:** Robert J. Mello, Ph.D.

**Conclusion:** Recommend Approval

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## Product Quality Microbiology Data Sheet

- A.**
- 1. TYPE OF SUBMISSION:** Original NDA (Resubmission after Complete Response)
  - 2. SUBMISSION PROVIDES FOR:** Marketing Authorization
  - 3. MANUFACTURING SITES:**  
Siemens/ PETNET Solutions  
Lincoln Park West #107/108  
2310 Presidential Drive  
Durham, NC 27703
  - 4. DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:** Sterile Injection; Intravenous; 10-200mCi/ml EOS (End of Synthesis).
  - 5. METHOD(S) OF STERILIZATION:** (b) (4)
  - 6. PHARMACOLOGICAL CATEGORY:** Positron Emission Tomography (PET) Radiodiagnostic Imaging Agent
- B. SUPPORTING/RELATED DOCUMENTS:**
- DMF #21582 “Type II for Sodium Fluoride F18 Injection as manufactured by PETNET Houston LLC in Houston, TX and PETNET Solutions Inc in Culver City & Palo Alto, CA; Durham, NC; St. Louis, MO; Woburn, MA; Hackensack, NJ for Siemens Molecular Imaging Inc.
  - Product Quality Microbiology review#1 of DMF #21582 dated 12 MAY 2009.
  - Product Quality Microbiology review #2 of DMF #21582 dated 18 January 2011.
- C. REMARKS:**
- The submission is an electronic submission not in CTD format.
  - The original submission listed (b) (4) manufacturers of the Drug Product. In subsequent Amendments the (b) (4) site was deleted (19 February 2009 Amendment) and replaced by (b) (4) sites (10 April 2009 Amendment). In this resubmission, all of the (b) (4) sites have been deleted. The sole remaining manufacturing site is the Siemens PETNET site in Durham, NC.

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## **Executive Summary**

### **I. Recommendations**

- A. Recommendation on Approvability** – Recommend Approval
- B. Recommendations on Phase 4 Commitments and/or Agreements, if Approvable** – N/A

### **II. Summary of Microbiology Assessments**

- A. Brief Description of the Manufacturing Processes that relate to Product Quality Microbiology** – All of the CMC manufacturing and control information was referenced to the Siemens Medical Imaging DMF #21582.
- B. Brief Description of Microbiology Deficiencies** – None
- C. Assessment of Risk Due to Microbiology Deficiencies** – N/A

### **III. Administrative**

- A. Reviewer's Signature** \_\_\_\_\_  
Robert J. Mello, Ph.D.  
Senior Microbiology Reviewer
- B. Endorsement Block** \_\_\_\_\_  
David Hussong, Ph.D.  
Associate Director,  
New Drug Microbiology Staff
- C. CC Block**  
NDA 22-494

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/s/  
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ROBERT J MELLO  
01/25/2011

DAVID HUSSONG  
01/25/2011

I concur with the reviewer's recommendation to approve the application.

# Product Quality Microbiology Review

12 MAY 2009

**NDA:** 22-494/N-000,(BC),(BC)

**Drug Product Name**

**Proprietary:** (None)

**Non-proprietary:** Sodium Fluoride [<sup>18</sup>F] Injection

**Review Number:** 1

**Dates of Submission(s) Covered by this Review**

| Letter           | Stamp            | Review Request  | Assigned to Reviewer |
|------------------|------------------|-----------------|----------------------|
| 30 December 2008 | 31 December 2008 | 12 January 2009 | 13 January 2009      |
| 19 February 2009 | 23 February 2009 | n/a             | n/a                  |
| 10 April 2009    | 13 April 2009    | n/a             | n/a                  |

**Submission History (for amendments only):** N/A

**Applicant/Sponsor**

**Name:** National Cancer Institute/DCTD/Cancer Imaging Program

**Address:** 6130 Executive Blvd.  
EPN, Suite 6000  
Bethesda, MD 20892-7412

**Representative:** Paula M. Jacobs, Ph.D.  
Contractor; Cancer Imaging Program, NCI

**Telephone:** 301-496-9531

**Name of Reviewer:** Robert J. Mello, Ph.D.

**Conclusion:** The application is approvable pending receipt of additional information. (See Section H).

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## Product Quality Microbiology Data Sheet

- A.
1. **TYPE OF SUBMISSION:** Original NDA
  2. **SUBMISSION PROVIDES FOR:** Marketing Authorization
  3. **MANUFACTURING SITES:** Six (6) sites were listed.



- 6) Siemens/ PETNET Solutions  
2310 Presidential Drive  
Durham, NC 27703

4. **DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:** Sterile Injection; Intravenous; 10-400mCi/ml EOS (End Of Synthesis).
5. **METHOD(S) OF STERILIZATION:**  Processing
6. **PHARMACOLOGICAL CATEGORY:** Positron Emission Tomography (PET) Radiodiagnostic Imaging Agent

B. **SUPPORTING/RELATED DOCUMENTS:**

- DMF  (b) (4)
- Product Quality Microbiology review of DMF  (b) (4) dated 12 MAY 2009.
- DMF #21582 "Type II for Sodium Fluoride F18 Injection as manufactured by PETNET Houston LLC in Houston, TX and PETNET Solutions Inc  (b) (4)
- Product Quality Microbiology review of DMF #21582 dated 12 MAY 2009.
- USP <823> Radiopharmaceuticals for Positron Emission Tomography—Compounding

C. **REMARKS:**

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- An ONDQA PAL Initial Quality Assessment was not submitted into DFS. The Chemist's Fileability Checklist noted that a separate microbiological section was not submitted (but should have been).
  - The submission is an electronic submission not in CTD format.
  - On 26 February 2009, the Division designated this submission as a PRIORITY review application with a User Fee Goal date of 30 June 2009.
  - The original submission listed [REDACTED] (b) (4) [REDACTED] manufacturers of the Drug Product. In subsequent Amendments the [REDACTED] (b) (4) site was deleted (19 February 2009 Amendment) and replaced by [REDACTED] (b) (4) sites (10 April 2009 Amendment).

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## **Executive Summary**

### **I. Recommendations**

- A. Recommendation on Approvability** – Approvable pending receipt of additional information.
- B. Recommendations on Phase 4 Commitments and/or Agreements, if Approvable** – N/A

### **II. Summary of Microbiology Assessments**

- A. Brief Description of the Manufacturing Processes that relate to Product Quality Microbiology** – All of the CMC manufacturing and control information was referenced to the (b) (4) and the Siemens Medical Imaging DMF #21582. Both DMFs were reviewed and found to be deficient and as such are not adequate to support this application.
- B. Brief Description of Microbiology Deficiencies** – Separate DMF deficiency letters have been sent to (b) (4) and to Siemens Medical Imaging.
- C. Assessment of Risk Due to Microbiology Deficiencies** – Due to the DMF deficiencies, the sterility assurance of the final drug product cannot be adequately assessed. Therefore, a potential risk to drug product sterility assurance exists.

### **III. Administrative**

- A. Reviewer's Signature** \_\_\_\_\_  
Robert J. Mello, Ph.D.
- B. Endorsement Block** \_\_\_\_\_  
Bryan S. Riley, Ph.D.
- C. CC Block**  
NDA 22-494

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/s/

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Robert Mello  
5/15/2009 02:20:10 PM  
MICROBIOLOGIST

Approvable pending additional information

Bryan Riley  
5/15/2009 02:21:36 PM  
MICROBIOLOGIST  
I concur.