

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*

**203137Orig1s000**

**MICROBIOLOGY REVIEW(S)**

# Product Quality Microbiology Review

18 June 2013

**NDA:** 203-137/N-000

**Drug Product Name**

**Proprietary:**

**VIZAMYL™**

**Non-proprietary:**

**Flutemetamol [F-18] Injection**

**Review Number:** 1

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

<b>Submit</b>	<b>Received</b>	<b>Review Request</b>	<b>Assigned to Reviewer</b>
26 October 2012	26 October 2012	26 October 2012	29 October 2012
30 January 2013	31 January 2013	n/a	n/a
08 February 2013	11 February 2013	n/a	n/a

**Submission History (for 2<sup>nd</sup> Reviews or higher):** N/A

**Applicant/Sponsor**

**Name:**

GE Healthcare

**Address:**

101 Carnegie Center

Princeton, NJ 08540

**Representative:**

Kevin Darryl White, MBA, RAC

Sr. Dir. /Americas Head, Reg. Affairs

**Telephone:**

609-228-5604

**Name of Reviewer:**

Robert J. Mello, Ph.D.

**Conclusion:**

Recommended for Approval

## Product Quality Microbiology Data Sheet

- A. 1. **TYPE OF SUBMISSION:** New Drug Application, 505(b)(1)
2. **SUBMISSION PROVIDES FOR:** Marketing Authorization
3. **MANUFACTURING SITE:** There are eight (8) manufacturing sites listed for the drug product and one site listed for the manufacture of the formulation buffer vial. See Review Section P.3.1, below for full addresses.

Drug Product sites:

(b) (4)

(b) (4)

Formulation buffer vial site: GE Healthcare AS  
Nycoveien 1-2  
P.O. Box 4220 Nydalen  
0401 Oslo  
Norway

4. **DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:** Sterile Injection, Intravenous, 185MBq (5 mCi) packaged in either a 10mL/20mm (GE Healthcare AS, Oslo, Norway) or 30mL/20mm (b) (4) multiple dose vials sealed with (b) (4) (10mL vial) or (b) (4) (30mL vial) (b) (4) closure and 20mm aluminum overseals. The 10mL vials (b) (4) The 30mL vials (b) (4)
5. **METHOD(S) OF STERILIZATION:** Sterile (b) (4)
6. **PHARMACOLOGICAL CATEGORY:** [F-18] PET Radiopharmaceutical imaging agent

B. **SUPPORTING/RELATED DOCUMENTS:**

- Letter of Authorization - (b) (4)
- Microbiology Review (b) (4)



## **Executive Summary**

### **I. Recommendations**

- A. Recommendation on Approvability - Recommended for 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 -** The drug product is an F-18 PET radioisotope. It is produced in an (b) (4)

This formulation vial is produced at the GE Healthcare facility in Norway. The final formulated drug product is subsequently sterile (b) (4) empty vials (10mL or 30mL) produced by GE Healthcare (Norway) (b) (4)

- B. Brief Description of Microbiology Deficiencies - None**
- C. Assessment of Risk Due to Microbiology Deficiencies – N/A**
- D. Contains Potential Precedent Decision(s)-  Yes  No**

### **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 203137

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/s/  
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ROBERT J MELLO

06/20/2013

DAVID HUSSONG

06/20/2013

The NDA describes manufacture of the product at several sites and refers to a master file for one of the two final containers. The review notes that adequate controls and specifications are described on the submission and the (b) (4) was appropriately simulated. I concur with the recommendation for approval.

## PRODUCT QUALITY MICROBIOLOGY FILING CHECKLIST

**NDA Number:** 203-137      **Applicant:** GE Healthcare      **Submit Date:** 26 October 2012

**Drug Name:** VIZAMYL®      **NDA Type:** 505(b)(1)      **Received Date:** 26 October 2012  
 Flutemetamol [F-18] Injection

The following are necessary to initiate a review of the NDA application:

	<b>Content Parameter</b>	<b>Yes</b>	<b>No</b>	<b>Comments</b>
1	Is the product quality microbiology information described in the NDA and organized in a manner to allow substantive review to begin? Is it legible, indexed, and/or paginated adequately?	X		Information is in eCTD format accessible via EDR. Section 3.2.P.2.5
2	Has the applicant submitted an overall description of the manufacturing processes and microbiological controls used in the manufacture of the drug product?	X		Section 3.2.P.3.3 (Flow charts and narrative)
3	Has the applicant submitted protocols and results of validation studies concerning microbiological control processes used in the manufacture of the drug product?	X		Section 3.2.P.3.5 (b)(4) validation plus data from 3 batches(each site) in Section 3.2.P.5.4
4	Are any study reports or published articles in a foreign language? If yes, has the translated version been included in the submission for review?		X	
5	Has the applicant submitted preservative effectiveness studies (if applicable) and container-closure integrity studies?	X		Product is not preserved. Container closure integrity studies were summarized for the 10ml and 30ml vials.
6	Has the applicant submitted microbiological specifications for the drug product and a description of the test methods?	X		Section 3.2.P.5.1
7	Has the applicant submitted the results of analytical method verification studies?		X	Batch analysis data is provided. Section 3.2.P.5.2.1 but additional information is needed.
8	Has the applicant submitted all special/critical studies/data requested during pre-submission meetings and/or discussions?	X	-	As requested by this reviewer, the Applicant has provided information from each of the manufacturing sites
9	Is this NDA fileable? If not, then describe why.	X		<b>The submission is fileable.</b>

**Additional Comments: The submission is fileable.**

The Applicant lists 9 US manufacturing sites in 9 states. Relevant data for each site was submitted for review. The overall submission appears to be comprehensive and complete. Details of the sterility and bacterial endotoxins test methodologies were lacking and will be requested.

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Robert J. Mello, Ph.D.  
Senior Review Microbiologist

Date

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David Hussong, Ph.D.  
Director, OPS/NDMS

Date

**Product Quality Microbiology Assessment**

Details of the sterility and bacterial endotoxins test methods were lacking in that there was only a simple reference to USP <71> and <85>, respectively. The following information request will be conveyed to the applicant.

*Please provide the following additional information:*

- 1. A description of the bacterial endotoxins test method to include relevant assay qualification data as well as the determination of the Maximum Valid Dilution, the routine sample dilution and the sensitivity of the test.*
- 2. A description of the sterility test method to include the media used, sample volume and incubation conditions.*

(b) (4)

[END]

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/s/  
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ROBERT J MELLO  
11/09/2012

DAVID HUSSONG  
11/09/2012

The submission appears complete enough for a microbiology review.