

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*

**202008Orig1s000**

**MICROBIOLOGY REVIEW(S)**

# Product Quality Microbiology Review

2 March 2012

**NDA:** 202-008/N-000

**Drug Product Name**

**Proprietary:** AMYVID™

**Non-proprietary:** Florbetepir F18 (<sup>18</sup>F-AV-45)

**Review Number:** 2

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

Submit	Received	Review Request	Assigned to Reviewer
7 October 2011	7 October 2011	12 December 2011	12 December 2011

**Submission History (for amendments only)**

Submit Date(s)	Microbiology Review #	Review Date(s)
17 September 2010	1	11 February 2011
28 January 2011	1	11 February 2011

**Applicant/Sponsor**

**Name:** Avid Pharmaceuticals  
**Address:** 3711 Market St. 7<sup>th</sup> Floor  
Philadelphia, PA 19104

**Representative:** Alan P. Carpenter, Jr. Ph.D., J.D.  
**Telephone:** (215) 298-0707

**Name of Reviewer:** Stephen E. Langille, Ph.D.

**Conclusion:** Recommended for approval

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## Product Quality Microbiology Data Sheet

- A.**
- 1. TYPE OF SUBMISSION:** Original NDA - resubmission
  - 2. SUBMISSION PROVIDES FOR:** Sterility assurance and endotoxin control information for a sterile injectable drug product.
  - 3. MANUFACTURING SITES:** Multiple. See Table 3.
  - 4. DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:**
    - Sterile Injectable
    - Intravenous
    - 370 MBq/10 mL
  - 5. METHOD(S) OF STERILIZATION:** (b) (4)
  - 6. PHARMACOLOGICAL CATEGORY:** Imaging agent
- B. SUPPORTING/RELATED DOCUMENTS:** DMF (b) (4) and DMF (b) (4)
- C. REMARKS:** This NDA was originally recommended for approval by the New Drug Microbiology Staff in February of 2011. The NDA was re-submitted in October of 2011 in response to the Agency's CR letter of 17 March 2011. The submission was provided in eCTD format.

**filename:** N202008r2.doc

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## **Executive Summary**

### **I. Recommendations**

- A. Recommendation on Approvability -**  
NDA 202-008 is recommended for approval from the standpoint of product quality microbiology.
- B. Recommendations on Phase 4 Commitments and/or Agreements, if Approvable -**  
Not applicable

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

- A. Brief Description of the Manufacturing Processes that relate to Product Quality Microbiology -**  
The drug product will be (b) (4) processed at 19 different manufacturing sites.
- B. Brief Description of Microbiology Deficiencies -**  
No deficiencies were identified based upon the information provided.
- C. Assessment of Risk Due to Microbiology Deficiencies -**  
Not applicable

### **III. Administrative**

- A. Reviewer's Signature** \_\_\_\_\_  
Stephen E. Langille, Ph.D.  
Senior Microbiology reviewer
- B. Endorsement Block** \_\_\_\_\_  
David Hussong Ph.D.  
Associate Director –  
New Drug Microbiology Staff
- C. CC Block**  
N/A

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/s/  
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STEPHEN E LANGILLE  
03/08/2012

DAVID HUSSONG  
03/08/2012

This NDA provides for a P.E.T. drug. I agree with the reviewer's assessment that the application may be approved from the perspective of CMC-microbiology.

## PRODUCT QUALITY MICROBIOLOGY FILING CHECKLIST

**NDA Number: 202-008**

**Applicant: Avid  
Radiopharmaceuticals**

**Letter Date: October 7, 2011**

**Drug Name: AMYVID™**

**NDA Type: Resubmission**

**Stamp Date: October 7, 2011**

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		Sections 3.2.P.3.3 and 3.2.P.3.5
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
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
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	The drug product is not preserved and container closure integrity study data was not provided.
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		Section 3.2.P.5.3
8	Has the applicant submitted all special/critical studies/data requested during pre-submission meetings and/or discussions?		X	No such information requests were made.
9	Is this NDA fileable? If not, then describe why.	X		

Additional Comments: This is a resubmission in response to a complete response letter. The original submission was recommended for approval on the basis of product quality microbiology on February 11, 2011.

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Reviewing Microbiologist  
Stephen E. Langille

Date

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James McVey Team Leader

Date

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/s/  
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STEPHEN E LANGILLE  
11/02/2011

JAMES L MCVEY  
11/02/2011

# Product Quality Microbiology Review

11 February 2011

**NDA:** 202-008/N-000

**Drug Product Name**

**Proprietary:** AMYVID™

**Non-proprietary:** Florbetepir F18 (<sup>18</sup>F-AV-45)

**Review Number:** 1

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

Submit	Received	Review Request	Assigned to Reviewer
17 September 2010	17 September 2010	21 September 2010	23 September 2010
28 January 2011	31 January 2011	Not applicable	Not applicable

**Submission History (for amendments only):** Not applicable

**Applicant/Sponsor**

**Name:** Avid Pharmaceuticals

**Address:** 3711 Market St. 7<sup>th</sup> Floor  
Philadelphia, PA 19104

**Representative:** Alan P. Carpenter, Jr. Ph.D., J.D.

**Telephone:** (215) 298-0707

**Name of Reviewer:** Stephen E. Langille, Ph.D.

**Conclusion:** Recommended for approval

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## Product Quality Microbiology Data Sheet

- A.**
- 1. TYPE OF SUBMISSION:** Original NDA
  - 2. SUBMISSION PROVIDES FOR:** Sterility assurance and endotoxin control information for a sterile injectable drug product.
  - 3. MANUFACTURING SITE:** Multiple. See Table 3.
  - 4. DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:**
    - Sterile Injectable
    - Intravenous
    - 370 MBq/10 mL
  - 5. METHOD(S) OF STERILIZATION:** (b) (4)
  - 6. PHARMACOLOGICAL CATEGORY:** Imaging agent
- B. SUPPORTING/RELATED DOCUMENTS:** DMF (b) (4) and DMF (b) (4)
- C. REMARKS:** The submission was provided in eCTD format. A request for additional product quality microbiology information was sent to the applicant on 10 January 2011.

**filename:** N202008r1.doc

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## **Executive Summary**

### **I. Recommendations**

- A. Recommendation on Approvability -**  
NDA 202-008 is recommended for approval from the standpoint of product quality microbiology.
- B. Recommendations on Phase 4 Commitments and/or Agreements, if Approvable -**  
Not applicable

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

- A. Brief Description of the Manufacturing Processes that relate to Product Quality Microbiology -**  
The drug product will be (b) (4) processed at one of 19 different manufacturing sites.
- B. Brief Description of Microbiology Deficiencies -**  
No deficiencies were identified based upon the information provided.
- C. Assessment of Risk Due to Microbiology Deficiencies -**  
Not applicable

### **III. Administrative**

- A. Reviewer's Signature** \_\_\_\_\_  
Stephen E. Langille, Ph.D.  
Senior Microbiology reviewer
- B. Endorsement Block** \_\_\_\_\_  
David Hussong Ph.D.  
Associate Director –  
New Drug Microbiology Staff
- C. CC Block**  
N/A

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/s/  
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STEPHEN E LANGILLE  
02/11/2011

DAVID HUSSONG  
02/11/2011

I concur that the application may be recommended for approval. The microbiologists note that the applicant has committed to providing bacteriostasis and fungistasis studies to complete the validation of their sterility test.

## PRODUCT QUALITY MICROBIOLOGY FILING CHECKLIST

**NDA Number:** 202-008

**Applicant:** Avid  
Radiopharmaceuticals

**Letter Date:** 17 September  
2010

**Drug Name:** AMYVID  
(Florbetapir F 18) Injection

**NDA Type:** Priority

**Stamp Date:** 17 September  
2010

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		
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
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
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		Single dose, not preserved. Integrity test information was provided in section 3.2.P.2
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?			Section 3.2.P.5.3
8	Has the applicant submitted all special/critical studies/data requested during pre-submission meetings and/or discussions?	N/A		No such requests were sent for product quality microbiology information
9	Is this NDA fileable? If not, then describe why.	X		

**Additional Comments:** The application was submitted in eCTD format. On 7 October 2010, Avid Pharmaceuticals provided background information on the submission in a face-to-face meeting with the review division. No major product quality microbiology deficiencies were identified during the meeting with Avid Pharmaceuticals or during a preliminary review of the electronic submission.

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Reviewing Microbiologist Stephen E. Langille, Ph.D.	13 October 2010 Date
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Microbiology Secondary Reviewer James McVey – Team Leader	13 October 2010 Date
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/s/

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STEPHEN E LANGILLE  
10/14/2010

JAMES L MCVEY  
10/14/2010  
I concur.