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APPLICATION NUMBER:

203684Orig1s000

MICROBIOLOGY / VIROLOGY REVIEW(S)

Product Quality Microbiology Review

JULY 10, 2012

NDA: 203684/N000

Drug Product Name

Proprietary: SonoVue [SF₆]

Non-proprietary: Sulfur hexafluoride lipid microspheres

Review Number: 1

Dates of Submission(s) Covered by this Review

| Submit | Received | Review Request | Assigned to Reviewer |
|-------------------|-------------------|-----------------------|-----------------------------|
| December 21, 2011 | December 21, 2011 | January 4, 2012 | January 6, 2012 |

Submission History (for amendments only) – N/A

Applicant/Sponsor

Name: Bracco Diagnostics Inc.

Address: 107 College Rd., Princeton, NJ 08540

Representative: Melani Benson, Director, US Regulatory Operations.

Telephone: 609-514-2254

Name of Reviewer: Vinayak B. Pawar, Ph.D.

Conclusion: Recommend approval.

Product Quality Microbiology Data Sheet

- A.**
- 1. TYPE OF SUBMISSION:** Original NDA
 - 2. SUBMISSION PROVIDES FOR:** SonoVue™ Injection
 - 3. MANUFACTURING SITE:** Bracco Suisse SA, 1228 Plan-les-Ouates, Switzerland.
 - 4. DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:** Sterile Lyophilized powder in a (b) (4) sealed vial, 25 mg/vial. Reconstituted with 5 ml saline and administered intravenously. Reconstituted product will contain equivalent of 45 µg SF₆/mL powder and (b) (4) x 10⁸ microbubbles/mL.
 - 5. METHOD(S) OF STERILIZATION:** (b) (4)
 - 6. PHARMACOLOGICAL CATEGORY:** SonoVue is indicated for use in echocardiography in patients with suboptimal echocardiograms to obtain left ventricular opacification and improve endocardial border delineation.
- B. SUPPORTING/RELATED DOCUMENTS:** None
- C. REMARKS:** Bracco submits an original NDA 203684 for SonoVue™ (sulfur hexafluoride microbubbles) injection. An IQA was filed by ONDQA on February 1, 2012. This is a eCTD submission. The manufacturing facility was assigned for inspection on April 18, 2012.

filename: N203684R1

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 – For the lyophilized powder,**

(b) (4)

The (b) (4) sterilized drug product diluent (saline) is packaged with the drug product in a ready to use syringe.

- B. Brief Description of Microbiology Deficiencies – N/A**
- C. Assessment of Risk Due to Microbiology Deficiencies – N/A**

III. Administrative

- A. Reviewer's Signature** _____
Vinayak B. Pawar, Ph.D., NDMS, OPS, CDER
- B. Endorsement Block** _____
John W. Metcalfe, Ph.D., NDMS, OPS, CDER
- C. CC Block**
N/A

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/s/

VINAYAK B PAWAR
07/15/2012

JOHN W METCALFE
07/16/2012
I concur.

Additional Comments: None.

Reviewing Microbiologist: Vinayak B. Pawar, Ph.D.

Date

Secondary Concurrence: John W. Metcalfe, Ph.D.

Date

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/s/

VINAYAK B PAWAR
01/19/2012

JOHN W METCALFE
01/19/2012
I concur.