DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-064/S-007

Bristol-Myers Squibb Medical Imaging, Inc.
Attention: Heather Nigro
Associate Director, Regulatory Affairs
331 Treble Cove Road, Building 300-2
North Billerica, MA 01862

Dear Ms. Nigro:

Please refer to your supplemental new drug application dated February 26, 2007, received February 27, 2007, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for DEFINITY® Vial for (Perflutren Lipid Microsphere) Injectable Suspension.

We acknowledge receipt of your submissions dated August 29, 2007; October 3 and 4, 2007.

This "Changes Being Effected" supplemental new drug application provides for revision of the product labeling to include the addition of a boxed warning that describes the occurrence of serious cardiopulmonary reactions, including fatalities, during and following Definity administration and a revised Warnings section that also describes the serious cardiopulmonary reaction risks. Additionally, a modified Indications section states that that the safety and efficacy of Definity with exercise stress or pharmacologic stress testing have not been established and the revised label contains new Warnings subsections pertaining to anaphylactoid reactions, QT prolongation risks, high ultrasound mechanical index considerations as well as a revised subsection pertaining to risks for patients with cardiac shunts. The label revision also includes a revised Contraindication section and corrects certain typographical errors, as follows: 1) correction of the Adverse Reactions text to consistently identify "15" patients as having discontinued participation in clinical trials; 2) a correction to the text in the Dosage and Administration, in the subheading of Imaging, to cite the Warning section (instead of Precautions section) when referring to the correct mechanical index and 3) the date of the label is revised from September 2007 to October 2007.

We completed our review of this application, as amended, effective on the date of this letter, for use as recommended in the agreed-upon labeling text.

The final printed labeling (FPL) must be identical to the enclosed labeling text for the package insert.

Please submit an electronic version of the FPL according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDA*. Alternatively, you may submit 20 paper copies of the FPL as soon as it is available but no more than 30 days after it is printed. Individually mount 15 of the copies on heavy-weight paper or similar material. For administrative purposes, designate this/these submission(s) "**FPL for approved supplement NDA 21-064/S-007**." Approval of this submission by FDA is not required before the labeling is used.

We remind you of your postmarketing study commitment in your submission, dated October 4, 2007. This postmarketing commitment supplants post-marketing study commitment number 4 which is described in our action letter, dated July 31, 2001. We regard the status of that commitment (number 4) as "released". In place of that released commitment, you have agreed to:

1. Provide clinical data that evaluate the occurrence of serious adverse reactions among patients who receive Definity in routine clinical practice. The goal of the study will be to capture post-marketing safety information on Definity as it is actually used, from the enrollment of at least 1000 patients.

Protocol submission: November 1, 2007
First patient in (start of study accrual): February 28, 2008
Completion of study report for FDA submission: January 1, 2010

Submit clinical protocols to your IND for this product. Submit non-clinical and chemistry, manufacturing, and controls protocols and all study final reports to this NDA. In addition, under 21 CFR 314.81(b)(2)(vii) and 314.81(b)(2)(viii), you should include a status summary of each commitment in your annual report to this NDA. The status summary should include expected summary completion and final report submission dates, any changes in plans since the last annual report, and, for clinical studies, number of patients entered into each study. All submissions, including supplements, relating to these postmarketing study commitments must be prominently labeled "**Postmarketing Study Commitment Protocol**", "**Postmarketing Study Commitment Final Report**", or "**Postmarketing Study Commitment Correspondence**."

In addition, submit three copies of the introductory promotional materials that you propose to use for this product. Submit all proposed materials in draft or mock-up form, not final print. Send one copy to this division/ the Division of Medical Imaging and Hematology Products and two copies of both the promotional materials and the package insert directly to:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Drug Marketing, Advertising, and Communications
5901-B Ammendale Road
Beltsville, MD 20705-1266

We acknowledge your plans to issue a Dear Healthcare Professional Letter. We request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH
Food and Drug Administration
5515 Security Lane
HFD-001, Suite 5100
Rockville, MD 20852

Please submit one market package of the drug product when it is available.

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, call Tiffany Brown, Regulatory Project Manager, at (301) 796-1972.

Sincerely,

{See appended electronic signature page}

Rafel Dwaine Rieves, M.D.
Acting Director
Division of Medical Imaging and
Hematology Products
Office of Oncology Drug Products
Center for Drug Evaluation and Research

Enclosure: Draft Labeling

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

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