DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-064/SCM-004

Bristol-Myers Squibb Medical Imaging, Inc.
Attention: William J. Regan
Director Regulatory Affairs
331 Treble Cove Road, Bldg. 500-2
North Billerica, MA 01862

Dear Mr. Regan:

Please refer to your supplemental new drug application dated September 30, 2002, received October 1, 2002, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for DEFINITY® Vial for (Perflutren Lipid Microsphere) Injectable Suspension.

We also acknowledge receipt of your submissions dated January 13, 17, 23, and 27, 2003.

This supplemental new drug application provides for an alternate buffered formulation of DEFINITY®. This formulation differs only in that a phosphate buffer has been added to better control the solution pH of the formulation and tighten the pH range. The addition of the phosphate buffer necessitates a change from the current rubber stopper (closure) to a more compatible non-zinc stopper in order to avoid the formation of insoluble zinc phosphates.

We completed our review of this application, as amended. This application is approved, 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 submitted labeling (package insert submitted January 13, 2003, immediate container and carton labels submitted January 13, 2003).

Please submit the FPL electronically 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, in no case more than 30 days after it is printed. Please individually mount ten of the copies on heavy-weight paper or similar material. For administrative purposes, this submission should be designated "FPL for approved supplement NDA 21-064/SCM-004". Approval of this submission by FDA is not required before the labeling is used.

If you issue a letter communicating important information about this drug product (i.e., a "Dear Health Care Professional" letter), we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH, HF-2
FDA
5600 Fishers Lane
Rockville, MD 20857

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 Lynn Panholzer, Pharm.D., Regulatory Project Manager, at (301) 827-3247.

Sincerely,

{See appended electronic signature page}

Eldon E. Leutzinger, Ph.D.
Chemistry Team Leader for the
Division of Medical Imaging and
Radiopharmaceutical Drug Products (HFD-160)
DNDC II, Office of New Drug Chemistry
Center for Drug Evaluation and Research

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/s/

Eldon Leutzinger
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