DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 21-357/S-006 **SUPPLEMENT APPROVAL**

Bracco Diagnostics, Inc.
Attention: Melanie Benson
Director, US Regulatory Affairs
107 College Road East
Princeton, NJ 08540

Dear Ms. Benson:

Please refer to your supplemental new drug application dated April 17, 2009, received April 20, 2009, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for MultiHance, (Gadobenate Dimeglumine) Injection.

We acknowledge receipt of your submissions dated June 12, 19, and 24, November 5, December 21, 2009; January 20, and 22, February 19, 23, 25, and 26, and March 9 and 10, 2010.

This "Prior Approval" supplemental new drug application provides for the addition of children over 2 years of age to the population in which MultiHance is approved for use.

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

CONTENT OF LABELING

Please resubmit the enclosed content of labeling in SPL format as soon as possible, but no later than 14 days from the date of this letter. For administrative purposes, please designate this submission, "**SPL for approved NDA 21-357/S-006.**"

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication in pediatric patients unless this requirement is waived, deferred, or inapplicable.

We are waiving the pediatric study requirement for ages 0 to 2 years because available data are insufficient to support the safety of conducting clinical studies in this age range. Specifically, accumulating data suggest that inability to eliminate gadolinium-based contrast agents, as may

occur with insufficiently developed renal function or severe renal dysfunction, increases the risk for nephrogenic systemic fibrosis (NSF).

You have fulfilled the pediatric study requirements to evaluate the safety and efficacy of MultiHance in patients 2-16 of years of age with "known or suspected CNS disease" and to conduct a pharmacokinetic study in patients 2-5 years of age with "known or suspected CNS disease."

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit, in triplicate, a cover letter requesting advisory comments, the proposed materials in draft or mock-up form with annotated references, and the package insert(s) 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

As required under 21 CFR 314.81(b)(3)(i), you must submit final promotional materials, and the package insert(s), at the time of initial dissemination or publication, accompanied by a Form FDA 2253. For instruction on completing the Form FDA 2253, see page 2 of the Form. For more information about submission of promotional materials to the Division of Drug Marketing, Advertising, and Communications (DDMAC), see http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm.

LETTERS TO HEALTH CARE PROFESSIONALS

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

MedWatch
Food and Drug Administration
5600 Fishers Lane, Room 12B05
Rockville, MD 20857

REPORTING REQUIREMENTS

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 James Moore, Regulatory Project Manager, at (301) 796-2050.

Sincerely,

{See appended electronic signature page}

Rafel Rieves, M.D.
Director
Division of Medical Imaging Products
Office of Drug Evaluation IV
Center for Drug Evaluation and Research

Enclosure
Content of Labeling

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-21357	SUPPL-6	BRACCO DIAGNOSTICS INC	MULTIHANCE(GADOBENATE DIMEGLUMINE INJ)

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

RAFEL D RIEVES
03/17/2010