DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville MD 20857

FOI

TRANSMITTED VIA FACSIMILE

APR 15 1999

June Bray
Director, Regulatory Affairs
Berlex Laboratories, Inc.
340 Changebridge Road
PO Box 1000
Montville, NJ 07045-1000

RE: **NDA 19-596**
Magnevist (gadopentetate dimeglumine) Injection
MACMIS # 7836

Dear Ms. Bray:

This letter is in reference to Berlex Laboratories, Inc.'s (Berlex) submissions, dated December 8, 1998, and January 26, 1999, of promotional materials under cover of Form FDA 2253 for Magnevist. The submissions included exhibit panels and a brochure titled "MRI Perspectives" identified as 98-MAG-060. The Division of Drug Marketing, Advertising, and Communications (DDMAC), in consultation with the Division of Medical Imaging and Radiopharmaceutical Drug Products, has reviewed these promotional materials and has concluded that they are false or misleading under the Federal Food, Drug, and Cosmetic Act and its implementing regulations. Our specific objections follow:

Promotion of Unapproved New Uses

As you know, promotional claims must be supported by substantial evidence. Further, they should not be inconsistent with the approved product labeling. Your promotion of arteriography is inconsistent with the approved product labeling and constitutes an unapproved new use for Magnevist.

In the promotional brochure titled "MRI Perspectives," Berlex presented two case studies and an introduction[1] by Gordon Sze, MD regarding imaging the carotid arteries. Among Berlex's claims in this brochure are the use of Magnevist in magnetic resonance arteriography (MRA) to: 1) identify stenosis and its severity in the carotid arteries, 2) assess other arteries including the proximal common carotid artery, and 3) confirm ultrasound, which may obviate the need for angiography. These claims also are not supported by substantial evidence.

Berlex also promoted Magnevist for use in angiography in a poster identified as

1 Gordon Sze, MD, "Virtues of Contrast Enhanced MRA for Imaging the Carotid Arteries." *MRI Perspectives.* Berlex Laboratories, Inc. January 1999.

98MMRA-R. This poster presented an unlabeled MRI image of angiography, presumably of the aorta and iliac arteries.

We are especially concerned with Berlex's promotion of these unapproved new uses for Magnevist because the Agency and Berlex have discussed Magnevist's approved indications and which clinical studies have been adequate to support promotional claims. We concluded that you have no basis to promote Magnevist for MRA, and specifically we are not aware of evidence to support the efficacy of Magnevist in identifying stenosis in MRA.

Further, in the exhibit poster identified as 98MPSL, you claim that Magnevist is useful for enhancing specific regional tissues in the body including musculoskeletal. In prior discussions with the Agency, Berlex was advised that it was not appropriate to promote Magnevist for use in identifying lesions in the musculoskeletal tissues of the body because we did not consider this claim to be supported by substantial evidence.

Thus, DDMAC requests that Berlex immediately cease the dissemination of these violative promotional materials and any other violative promotional materials that promote Magnevist for unapproved new uses. You should respond to DDMAC regarding this violation by April 29, 1999, providing the date Mallinckrodt ceased the dissemination of the promotional materials.

If you have any questions, please contact me by facsimile at (301) 594-6771, or by written communication at the Division of Drug Marketing, Advertising, and Communications, HFD-40; Room 17B-20; 5600 Fishers Lane; Rockville, MD 20857. DDMAC reminds Berlex that only written communications are considered official.

In all future correspondence regarding this matter, please refer to MACMIS # 7836 and NDA 19-596.

Sincerely,

Warren F. Rumble
Regulatory Review Officer
Division of Drug Marketing,
Advertising and Communications