DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

FOI

Food and Drug Administration
Rockville MD 20857

JUN 27 1997

TRANSMITTED VIA FACSIMILE

Nancy A. Wood
Regulatory Affairs Supervisor
DuPont Merck Radiopharmaceuticals
331 Treble Cove Road
N. Billercia, MA 01862

RE: **NDA 19-785**
Miraluma (kit for the preparation of Technetium Tc-99m Sestamibi)
MACMIS # 5472

Dear Ms. Wood:

This letter is in reference to DuPont Merck Radiopharmaceuticals' (DuPont) promotional materials for the new indication of breast imaging for Miraluma (kit for the preparation of Technetium Tc-99m Sestamibi). Based on information reviewed as part of our monitoring program, the Division of Drug Marketing, Advertising and Communications (DDMAC) considers that DuPont has made false and/or misleading statements regarding Miraluma that are violative of the Federal Food, Drug, and Cosmetic Act and its implementing regulations. These statements appear in the Press Release for Miraluma located at DuPont's World Wide Web site, and a news release-fact sheet and a case study information sheet distributed at DuPont's booth in the exhibit area at the 1997 Society of Nuclear Medicine Meeting in San Antonio, Texas.

Press Release and News Release

In previous correspondence dated May 13, 1997,, DDMAC advised DuPont, based on draft product labeling, that we considered any statements that: (1) imply superiority of Miraluma imaging over mammography, or (2) claim Miraluma can provide tumor images in difficult-to-image breast tissue, dense or any specific breast tissue types, to be unsupported claims of efficacy. However, DuPont's press release and News Release contains these and other unsupported claims. Specific examples follow:

1. Claims Regarding Difficult-to-Image Breasts

In the releases, DuPont states that "this test is an adjunct to mammography that produces striking pictures of lesions even in the midst of difficult to

image breast tissue." In our May 13, 1997, letter, DDMAC advised DuPont that claims regarding difficult-to-image breast tissue types would be misleading because the data submitted by DuPont do not support claims comparing imaging efficacy in subgroups of patients with and without abnormal types of breast tissue. The approved product labeling for Miraluma states that images from dense and fatty breast tissue were similar, and studies were not designed to compare the performance of Miraluma with the performance of mammography in patients with breast densities or other coexistent breast tissue disorders.

2. Claims of Superiority Over Mammography

In the press release, DuPont states that "while x-ray mammography alone is effective in many women, in the radiographically dense breast the ability of mammography to detect some cancers is reduced. However, the unique value of the Miraluma(TM) test, as an adjunct to mammography, is the accuracy of Miraluma(TM) which is unaffected by breast density." DDMAC considers DuPont's statements implying that Miraluma-aided imaging is superior to x-ray mammography, and that Miraluma is unaffected by breast density to be false and/or misleading.

DDMAC is especially concerned with these statements, because we advised DuPont in our letter dated May 13, 1997, that DuPont should delete all references that imply superior efficacy of Miraluma imaging over x-ray mammography. Further, these statements are contrary to the approved product labeling and the approval letter for Miraluma dated May 23, 1997, that specifically states that "Miraluma may not be promoted as superior to or as a replacement of mammography."

3. Unsupported Claim of Efficacy

In the releases, DuPont states that "the Miraluma(TM) test -- also called sestamibi breast imaging -- uses a radiopharmaceutical (or imaging agent) that is thought to accumulate in areas of increased metabolic activity in malignant cells. According to in vitro studies, the concentration of the drug is up to nine times higher in malignant cells than in normal cells." DDMAC considers these statements to be an unsupported claim that Miraluma can identify malignant cancer cells. In addition, the Agency advised DuPont regarding this claim in the approval letter for Miraluma that specifically states Miraluma is not indicated for confirming the presence or absence of malignancy.

4. Abnormal versus Inconclusive Mammogram

In the press release, DuPont states that "conducting the Miraluma(TM) test after inconclusive mammograms may help us catch more women in the safety net of early detection." DuPont also states that "women facing the possibility of breast cancer will now have a much needed option when faced with an inconclusive mammogram." These statements would be false and/or misleading because they are inconsistent with the Miraluma's recommended use as an adjunct to mammography to assist in the evaluation of breast lesions in patients with an abnormal mammogram or a palpable breast mass (emphasis added).

DDMAC does not consider the terms "abnormal" and "inconclusive" to be synonymous, and considers that there is a marked difference between abnormal and inconclusive mammograms. DDMAC considers the promotion of Miraluma for use after an "inconclusive" mammogram to be the promotion of an unapproved use for Miraluma and therefore in violation of the Act.

5. Diagnostic Sensitivity

In the news release, DuPont states that "diagnostic sensitivity increases in cancers shown to be greater than 1 cm. in largest dimension." The approved product labeling for Miraluma describes greater sensitivity in identifying lesions in breast tissue with palpable lesions than with non-palpable lesions. However, it does not provide information on what dimensions constitute a palpable lesion. Thus, DDMAC considers the statement regarding efficacy relative to lesion size to be false and/or misleading without adequate supporting data.

Case Study Information Sheet

Comparison of Radiographic and Scintigraphic Images of Heterogeneously Dense Breasts

In the case study information sheet, DuPont presents two images of breast scans--one is an image from mammography and one is an image from Miraluma mammoscintigraphy. DuPont's description of the mammographic image is "numerous vague densities, and indeterminate findings." Its description of the Miraluma image is "focal uptake in the right breast." The photographic images show no lesion in the mammograph, but a very clear

image of a lesion in the scintigraph. DDMAC considers DuPont's presentation of these comparative images to be false and/or misleading and a promotion of Miraluma as superior to or as a replacement of mammography. This issue was discussed in this letter under number 2, Claims of Superiority Over Mammography.

Fair Balance

The news release and the case study information are lacking risk balancing information. The press release has adequate information regarding adverse events seen with Technetium labeled sestimibi, but it is presented the end of the press release in a manner that minimizes its importance and readability. In future promotional materials, DDMAC requests that DuPont present risk balancing information in the body of the promotional materials in a manner comparable in prominence and readability as the presentation of information relating to the effectiveness of the drug.

DuPont should immediately cease disseminating the above promotional material and any other promotional materials that include the above cited claims. DDMAC requests that DuPont respond in writing to DDMAC regarding this issue by July 11, 1997.

If you have any questions, please contact me by telephone at (301) 827-2831, 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.

In all future correspondence regarding this matter, please refer to MACMIS # 5472 and NDA 19785.

Sincerely,

Warren Rumble

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