DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

FEB - 6 2007

Agendia BV
c/o Mr. Guido Brink
Director Quality Management & Regulatory Affairs
Slotervaart Hospital, Floor 9D
Louwesweg 6, 1066 EC Amsterdam
The Netherlands

Re: k062694
Evaluation of Automatic Class III Designation
MammaPrint®
Regulation Number: 21 CFR 866.6040
Classification: Class II
Product Code: NYI

Dear Mr. Brink:

The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) has completed its review of your petition for classification of the MammaPrint® that is intended as a qualitative *in vitro* diagnostic test service, performed in a single laboratory, using the gene expression profile of fresh frozen breast cancer tissue samples to assess a patient's risk for distant metastasis. The test is performed for breast cancer patients who are less than 61 years old, with Stage I or Stage II disease, with tumor size $\leq$ 5.0 cm and who are lymph node negative. The MammaPrint® result is indicated for use by physicians as a prognostic marker only, along with other clinicopathological factors.

FDA concludes that this device should be classified into class II. This order, therefore, classifies the MammaPrint® into class II under the generic name, gene expression profiling test system for breast cancer prognosis. This order also identifies the special controls applicable to this device and to substantially equivalent devices of this generic type.

FDA identifies this generic type of device as:

21 CFR 866.6040 Gene Expression Profiling Test System for Breast Cancer Prognosis. A gene expression profiling test system for breast cancer prognosis is a device that measures the RNA expression level of multiple genes and combines this information to yield a signature (pattern or classifier or index) to aid in prognosis of previously diagnosed breast cancer.

In accordance with section 513(f)(1) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360c(f)(1)) (the act), devices that were not in commercial distribution prior to May 28, 1976 (the date of enactment of the Medical Device Amendments of 1976 (the amendments)), generally referred to as postamendments devices, are classified automatically by statute into class III without any FDA

rulemaking process. These devices remain in class III and require premarket approval, unless and until the device is classified or reclassified into class I or II or FDA issues an order finding the device to be substantially equivalent, in accordance with section 513(i) of the act (21 U.S.C. 360c(i)), to a predicate device that does not require premarket approval. The agency determines whether new devices are substantially equivalent to previously marketed devices by means of premarket notification procedures in section 510(k) of the act (21 U.S.C. 360(k)) and Part 807 of the FDA regulations (21 CFR 807).

Section 513(f)(2) of the act provides that any person who submits a premarket notification under section 510(k) for a device may, within 30 days after receiving an order classifying the device in class III under section 513(f)(1), request FDA to classify the device under the criteria set forth in section 513(a)(1). FDA shall, within 60 days of receiving such a request, classify the device. This classification shall be the initial classification of the device type. Within 30 days after the issuance of an order classifying the device, FDA must publish a notice in the **Federal Register** classifying the device type.

On January 19, 2007, FDA issued an order classifying the MammaPrint® into class III because it was not substantially equivalent to a class I or class II device. On January 30, 2007, FDA filed your petition requesting classification of the MammaPrint® into class II. The petition was submitted under section 513(f)(2) of the act.

In order to classify the MammaPrint® into class I or II, it is necessary that the proposed class have sufficient regulatory controls to provide reasonable assurance of the safety and effectiveness of the device for its intended use. After review of the information submitted in the petition, FDA has determined that the MammaPrint®, intended as a qualitative *in vitro* diagnostic test service, performed in a single laboratory, using the gene expression profile of fresh frozen breast cancer tissue samples to assess a patient's risk for distant metastasis, can be classified in class II with the establishment of special controls.

A gene expression profiling test system for breast cancer prognosis is intended to provide prognostic information to aid in clinical evaluation of breast cancer patients. Failure of this device to perform as indicated may lead to erroneous test results. False positive results will misclassify the patient into a higher risk group and false negative results will misclassify the patient into a lower risk group. Misclassification of cancer recurrence risk may lead to incorrect prognosis with attendant psychological distress, inaccurate counseling and suboptimal patient care. The measures FDA recommends to mitigate these risks are described in the guidance document, "Class II Special Controls Guidance Document: Gene expression profiling test system for breast cancer prognosis," which includes recommendations for performance validation and labeling.

In addition to the general controls of the act, gene expression profiling test system for breast cancer prognosis is subject to the following special controls: "Class II Special Controls Guidance Document: Gene expression profiling test system for breast cancer prognosis." Section 510(m) of the act provides that FDA may exempt a class II device from the premarket notification requirements under section 510(k) of the act, if FDA determines that premarket notification is not necessary to

provide reasonable assurance of the safety and effectiveness of the device. FDA has determined premarket notification is necessary to provide reasonable assurance of the safety and effectiveness of the device and, therefore, the device is not exempt from the premarket notification requirements. Thus, persons who intend to market this device must submit to FDA a premarket notification submission containing information on the gene expression profiling test system for breast cancer prognosis they intend to market prior to marketing the device.

A notice announcing this classification order will be published in the **Federal Register**. A copy of this order and supporting documentation are on file in the Dockets Management Branch (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Room 1061, Rockville, MD 20852 and are available for inspection between 9 a.m. and 4 p.m., Monday through Friday.

As a result of this order, you may immediately market this device, subject to the general control provisions of the act and the special controls identified in this order. If you have any questions concerning this classification order, please contact Reena Philip at (240) 276-1286.

Sincerely yours,

Steven I. Gutman, M.D., M.B.A.
Director
Office of *In Vitro* Diagnostic Device
Evaluation and Safety
Center for Devices and Radiological Health