K081092

510k Summary

1. Assigned 510(k) number

The assigned 510(k) number is 081092

DEC 11 2009

2. Company

Agendia BV
Sciencepark 406
1098XH Amsterdam
The Netherlands
Telephone : 31 20 462 1523
Facsimile : 31 20 462 1505

3. Contact

Guido Brink, Senior Director Regulatory Affairs and Quality Assurance

4. Date Prepared

April 10th, 2008

5. Proprietary Name

MammaPrint®

6. Classification Name

Gene expression profiling test system, for breast cancer prognosis.

7. Common Name

Multivariate device for cancer prognosis

8. Classification

Class II, regulated under 21 CFR 866.6040, product code NYI

9. Predicate Device

Agendia BV's MammaPrint (k080252)

10. Device Description

The MammaPrint service is a microarray based gene expression analysis of a tumor. The analysis is based on several processes: isolation of RNA from frozen tumor tissue sections, DNA'se treatment of isolated RNA, linear amplification and labeling of DNA'se treated RNA, cRNA purification, hybridization of the cRNA to the MammaPrint microarray, scanning the MammaPrint microarray and data acquisition (feature extraction), index calculation and determination of the risk of distant recurrence in breast cancer patients.

The MammaPrint analysis is designed to determine the gene activity of specific genes in a tissue sample compared to a reference standard. The result is an expression profile, or fingerprint, of the sample.

The correlation of the sample expression profile to a template (the mean expression profile of 44 tumors with a known good clinical outcome) is calculated and the molecular profile index of the sample is determined (Low Risk, High Risk).

11. Intended Use

MammaPrint is a qualitative in vitro diagnostic test service, performed in a single laboratory, using the gene expression profile of fresh breast cancer tissue samples to assess a patient's risk for distant metastasis.

The test is performed for breast cancer patients, with Stage I or Stage II disease, with tumor size <= 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.

12. Performance Data (non-clinical)

Analytical performance

MammaPrint analytical (i.e., non-clinical) performance characteristics investigated comprise Precision, Reproducibility, Cutoff, Sensitivity, Specificity, Accuracy, Robustness and Ruggedness.

The technical validity of MammaPrint is determined on multiple individual validation experiments; a comprehensive three-way inter-laboratory comparison study between three independent laboratories in three different countries (Dutch, French and U.S.); data of about 200 analyses of two reference samples over a period of 12 months, used to monitor experiment-to-experiment quality; and quality controls for which the cut-off for all QCs is based on over 5000 hybridizations (2500 samples) performed at Agendia.

Based on 12 month repeated experiments of a Low Risk and High Risk control sample (i.e., more than 190 independent analyses), the Analytical Accuracy of the measurement is 98,5%.

Classification performance

Based on the analytical performance of MammaPrint, the accuracy of classifying a sample as High Risk or Low Risk, is at least 98.9% (i.e., 1.1% false negative classification).

Borderline Sample

As a result of the technical inaccuracy, analytical measurements (i.e., MammaPrint Index) can fall within a pre-defined area around the classification cut-off between the High Risk and Low Risk profile (i.e., "Borderline Sample").

Based on the results of independent MammaPrint analyses over a time period of over 2 years, it has been shown that less than 5% of the analyzed samples are considered to be "Borderline Samples".

"Borderline Samples" have approximately a 90% classification accuracy (i.e. 10% chance of false classification).

Conclusion

Analytical methodology used is identical to the FDA cleared MammaPrint device with 510k number k070675. Therefore substantially equivalence does not have to be shown for analytical performance.

13. Clinical Data

Clinical performance testing is based on the following studies:

Study	Purpose	Time Frame	Comments
Nature Paper (1)	Development of breast cancer prognosis 70-gene profile (LNO, <55)	2002, 78 patients, 6.4% adjuvant treatment	Within 5 year metastasis risk by profile multivariate OR 18
NEJM Paper (2)	Validation of the 70-gene profile in consecutive series of breast cancer patients (LNO, <53)	2002, 151 patients, 5.2% adjuvant treatment	Metastasis-free survival by profile at 10 yrs: low risk profile 87%, high risk profile 44% (at 5 yrs: 93% and 56% respectively)
MammaPrint Paper (3)	Development of MammaPrint	2006,reproducibility of (1) and (2) on MammaPrint	Highly reproducible MammaPrint as diagnostic tool
Transbig Paper (4)	Independent European validation of 70-gene signature (LN0, <61)	2006, 302 patients, no adjuvant treatment	Metastasis-free survival by profile at 10 yrs: low risk profile 88%, high risk profile 71% (at 5 yrs: 96% and 83% respectively)
"Older Age" NKI/AVL series (5)	Validation of the 70-gene profile in consecutive series of breast cancer patients (55-87 yrs)	2008/2009, 177 patients, no adjuvant treatment	Metastasis-free survival by profile at 5 yrs: low risk profile 94%, high risk profile 75%

14. Conclusion

Clinical validation data contained in this submission demonstrate equivalent performance of MammaPrint in the age extended patient group up to 87 years old at 5 years metastasis free survival.

MammaPrint is a clinically and analytically accurate prognostic marker for providing a risk assessment of distant metastasis of breast cancer.

(1) Gene expression profiling predicts clinical outcome of breast cancer;
Laura J. Van 't Veer et al; Nature (2002) 415, p530-536.
(2) A Gene-Expression Signature as a Predictor of Survival in Breast Cancer;
Marc J. Van de Vijver et al;. New Engl J Med (2002) 347, p1999-2009.

(3) Converting a breast cancer microarray signature into a high-throughput diagnostic test; Annuska M. Glas et al; BMC Genomics (2006) accepted.
(4) Validation and clinical utility of a 70-gene prognostic signature for women with node-negative breast cancer; Marc Buyse et al; J Natl Cancer Inst (2006), 98, p1183-1192.
(5) Clinical Validation report of MammaPrint Service usage in Breast Cancer Patients of "All ages" – VR-CR-099

DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Building 66
Silver Spring, MD 20993

Agendia BV
c/o Mr. Guido Brink
Senior Director Regulatory Affairs and Quality Assurance
Kruislaan 406
1098 SM Amsterdam
The Netherlands

DEC 11 2009

Re: k081092
Trade/Device Name: MammaPrint®
Regulation Number: 21 CFR §866.6040
Regulation Name: Gene expression profiling test system for breast cancer prognosis
Regulatory Class: Class II
Product Code: NYI
Dated: June 17, 2009
Received: June 23, 2009

Dear Mr. Brink:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801); medical device reporting (reporting of medical

device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801), please go to http://www.fda.gov/AboutFDA/CentersOffices/CDRH/CDRHOffices/ucm115809.htm for the Center for Devices and Radiological Health's (CDRH's) Office of Compliance. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely yours,

Maria M. Chan

Maria M. Chan, Ph.D.
Director
Division of Immunology and Hematology Devices
Office of In Vitro Diagnostic Device Evaluation and Safety
Center for Devices and Radiological Health

Enclosure

Indications for Use

510(k) Number (if known): K081092

Device Name: MammaPrint®

Indications for Use:

MammaPrint® is a qualitative in vitro diagnostic test service, performed in a single laboratory, using the gene expression profile of fresh breast cancer tissue samples to assess a patients' risk for distant metastasis (up to 10 years for patients less than 61 years old, up to 5 years for patients ≥ 61 years).

The test is performed for breast cancer patients with Stage I or Stage II disease, with a tumor size of ≤ 5.0 cm and lymph node negative. The MammaPrint result is indicated for use by physicians as a prognostic marker only, along with other clinicopathological factors.

Prescription Use ___XX____ (Part 21 CFR 801 Subpart D) AND/OR Over-The-Counter Use _____ (21 CFR 801 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE OF NEEDED)

Concurrence of CDRH, Office of In Vitro Diagnostic Devices (OIVD)

Reena Philip

Division Sign-Off

Office of In Vitro Diagnostic Device Evaluation and Safety

510(k) K081092