

Section 5: 510(k) Summary**1. Assigned 510(k) number**The assigned 510(k) number is K080252

JUL 21 2008

2. Company

Agendia BV

Slotervaart Medical Center 9D

Louwesweg 6, 1066EC Amsterdam

The Netherlands

Telephone : 31 20 512 9161

Facsimile : 31 20 5129162

3. Contact

Guido Brink, Director Quality Management and Regulatory Affairs

4. Date Prepared

January 21, 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 (k070675)

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), calculation and determination of the risk of 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 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 who are less than 61 years old, 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 and Reproducibility compared to the predicate device.

First, the technical validity of the high density microarray platform was established by method validation (i.e., precision evaluation) according the EP5-2A protocols of NCCLS. This experimental design consisted of repeated runs over 20 days in which 3 samples with different outcome levels, high, low and borderline, were performed on MammaPrint index High Density 8-pack arrays. Per day one run is performed consisting of two replicates of each sample level. Additionally both control samples high and low risk

control (HRC, LRC) as used for MammaPrint were also be taken along with one of the replicates.

The repeatability and precision of the MammaPrint index of all levels of sample outcomes, were at least as good as the performance of the predicate device (Standard Deviation and Variance of 0.030 and 0.001 respectively).

Second, a comparison was made between the FDA cleared Low Density (LD) microarray and, under QSR design controlled, High Density (HD) microarray. For the LD and HD comparison 98 samples will be selected for MammaPrint service from the period 2004 through 2007. All samples will be re-hybridized on 8-pack HD arrays. However, samples originating from 2004 through 2005 will be relabeled and hybridized for both LD and HD 8-pack arrays.

From 2006 onwards the original MammaPrint Index from previous LD hybridizations will be used. For these samples the labeled cRNA will be taken and re-hybridized on HD 8-pack MammaPrint arrays. Subsequently, a comparison of the MammaPrint index of both array types were performed.

Results showed a 98.9% concordance in MammaPrint outcome between HD and LD microarray which falls with the 97.7% technical accuracy of the predicate device.

Third the High Density sample set from the precision evaluation was used to determine the performance between the Agilent DNA microarrays. A set of 26 newly hybridized slides (104 samples) were scanned first on the FDA cleared scanner (serial nr: US22502555, Agendia DPd Id: 002) and subsequently on the new scanner (serial nr: US45103019 Agendia DPd Id: 112). The hybridized samples included: three samples with either high, low, borderline results with repeated results were generated per sample. Additionally, control samples LRC and HRC were included. MammaPrint indices were compared between both scans using Passing and Bablok regression analysis and a comparison of the variance per scanner.

The difference between the mean, median and standard deviation for all samples levels between both scanners fall within the accepted variance of the predicate device of $1.96 \cdot 0.030$.

Classification performance

Based on the analytical performance of MammaPrint using the High Density microarray platform, the accuracy of classifying a sample as High Risk or Low Risk, is 98,9%, (i.e., 0.5% false negative classification). This performance is better than the predicate device which has a classification accuracy of 97.7% (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).

Looking at all generated data it is concluded that the MammaPrint analysis on a High Density microarray platform using the Agilent DNA microarray scanner G2505B with serial number US45103019 is considered to be substantially equivalent to the FDA cleared MammaPrint device with 510k number k070675.

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 (LNO, <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) |

14. Conclusion

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.



JUL 21 2008

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

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

Re: k080252

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: May 7, 2008
Received: May 9, 2008

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 application (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 such 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.

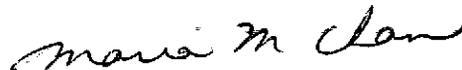
Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820). This letter will allow you to begin marketing your device as described in your Section 510(k) premarket notification. The

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FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801), please contact the Office of In Vitro Diagnostic Device Evaluation and Safety at (240) 276-0450. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding postmarket surveillance, please contact CDRH's Office of Surveillance and Biometric's (OSB's) Division of Postmarket Surveillance at 240-276-3474. For questions regarding the reporting of device adverse events (Medical Device Reporting (MDR)), please contact the Division of Surveillance Systems at 240-276-3464. 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 (240) 276-3150 or at its Internet address <http://www.fda.gov/cdrh/industry/support/index.html>.

Sincerely yours,

A handwritten signature in cursive script that reads "maria m chan".

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

Enclosure

Section 4: Indications for Use Statement

Indications for Use Form

510(k) Number (if known): K080252

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.

The test is performed for breast cancer patients who are less than 61 years old, 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 a 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 Device Evaluation (ODE)

Manu M Chan
Division Sign-Off

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Office of In Vitro Diagnostic Device
Evaluation and Safety

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