

**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
INSTRUMENT ONLY TEMPLATE**

A. 510(k) Number:

k042279

B. Purpose for Submission:

Clearance of new device

C. Manufacturer and Instrument Name:

Affymetrix GeneChip Microarray Instrumentation System

D. Type of Test or Tests Performed:

Hybridization, washing, scanning, and data analysis of GeneChip microarrays

E. System Descriptions:

1. Device Description:

The Affymetrix GeneChip Microarray Instrumentation System is designed to work with microarrays based on Affymetrix GeneChip® technology.

FS450Dx Fluidics Station

The FS450Dx (Fluidics Station) is an instrument consisting of four modules installed in a single Station or housing. Each module holds a single GeneChip microarray and performs the functions required for hybridization, washing, and staining of that array.

Up to 8 stations communicate to a workstation.

Each module contains controls the addition of target and staining fluids to the array cartridge and subsequent washing of the array. The module contains a pump, valve, thermo-electric system, and LCD that are controlled by scripts selected by the system operator and automatically downloaded to each module, then stored in the module's electronic memory.

GCS3000Dx Scanner

The GCC3000Dx Scanner is a wide-field, epifluorescent, confocal, scanning laser microscope which scans the chip after the staining process performed by the Fluidics Station. Array cartridges are loaded into the scanner by an automatic handler (the Autoloader) prior to scanning, and returned to the handler after scanning is complete.

GCOSDx Software

The GeneChip® Operating Software (GCOSDx) provides the interface between the user and instrument systems. It is the software that provides instrument control and the application for processing arrays and data collection. Upon completion of scanning of the array, data is passed through GCOSDx to the assay specific software component that contains the algorithms and reporting functions to produce a clinical result.

2. Principles of Operation:

a. Device Features Controlled by Software

- i. The GeneChip® Operating Software (GCOSDx) provides the interface between the user and the instruments. GCOSDx controls the FS450Dx, GCS3000Dx and the AutoLoaderDx. GCOSDx may also be used to monitor the operations being performed by each instrument.
- ii. GCOSDx controls the fluidics station using fluidics scripts specific to the assay being performed. Fluidics scripts are written to a directory specified during GCOSDx installation.
- iii. GCOSDx aids and controls scanner movement and image capture including grid alignment. GCOSDx displays a picture of the scan image in an image window on the computer workstation. The software represents the fluorescence intensity values from each pixel on the array in a grayscale or pseudocolor mode. This image is saved as a “.dat” file format.
- iv. GCOSDx then uses an alignment algorithm to superimpose a grid on the image to delineate probe cells. The alignment algorithm uses a checkerboard image of control probes, located at the corners of the probe array to superimpose the grid on the scanned image. GCOSDx generates cell intensity data from the image data. The cell analysis algorithm analyzes the image data and computes a single intensity value for each probe cell on the array. This data is saved as a “.cel” file. It is the “.cel” file that is handed to the assay specific software for final data analysis and result reporting.

b. Operational Environment (Off-The-Shelf Software)

GCOSDx is programmed in C++. GCOSDx functions on Microsoft® Windows® 2000 SP3 or SP4 Operating System. The work stations also include Internet Explorer 6.0, Office XP and MDAC 2.7 SP1. The operating system will be moved to Microsoft® XP in the near future. Prior to this shift, the appropriate validations will be performed. Dell workstations included with the system must have 750 MHz to 3.0 GHz Processor speed as well as 256 Mbyte to 1 Gbyte Memory and a 10 Gbyte to 80 Gbyte Hard Drive.

3. Modes of Operation:

batch - the scanner automatically loads and unloads chips from the autoloader

4. Specimen Identification:

The operator enters patients ID information in tied to a barcode on the chip. The barcode is scanned at the level of the fluidics station and the scanner.

5. Specimen Sampling and Handling:

Specimens are processed according to assay instructions. Reagents specific to each assay and fluidics protocol are manually loaded onto the fluidics station.

6. Calibration:

Installation and calibration are performed by the sponsor. No user calibration required.

7. Quality Control:

Quality control is addressed for each specific assay to be run on the system (separately cleared)

8. Software:

FDA has reviewed applicant's Hazard Analysis and Software Development processes for this line of product types:

Yes 3 or No _____

F. Regulatory Information:

1. Regulation section:

None

2. Classification:

Class III

3. Product code:

NSU, Instrumentation for Clinical Multiplex Test Systems

4. Panel:

Clinical Chemistry (75)

G. Intended Use:

1. Indication(s) for Use:

The Affymetrix GeneChip® Microarray Instrumentation System consisting of GeneChip® 3000Dx scanner with autoloader, FS450Dx fluidics station and GCOSDx software is intended to measure fluorescence signals of labeled DNA target hybridized to GeneChip® arrays.

2. Special Conditions for Use Statement(s):

For use with separately cleared GeneChip microarray assays

H. Substantial Equivalence Information:

1. Predicate Device Name(s) and 510(k) numbers:

This device has no predicate device.

2. Comparison with Predicate Device:

This device has no predicate device.

I. Special Control/Guidance Document Referenced (if applicable):

FDA Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices

J. Performance Characteristics:

1. Analytical Performance:

a. Accuracy:

Not applicable – accuracy for each assay to be run on this system will be assessed during the clearance of the assay.

b. Precision/Reproducibility:

For the reproducibility study, intensity readings generated by Scanner 3000Dx were not changed, manipulated or revised after scanning was completed. Raw .CEL file data was used for the analysis of uniformity, and calculation of intra- and inter-chip, intra- and inter-scanner and intra- and inter-fluidics and fluidics port reproducibility (CV, correlation coefficients). ANOVA analysis to establish whether there are any random effects of FS, FS port or scanner was performed post-data analysis. No arrays were scaled to a fixed value nor normalized since the study was designed to observe variability

in all system components with raw data. (Scaling and normalization are tools for controlling differences between arrays and scanners.)

Array design:

Two different array types were used in order to assess instrumentation performance:

- The first array was used to assess scanner performance alone (without the hybridization step). The 32x32 cell array was designed to have photobleaching stability and can be scanned over 100 times. A single array was scanned at the study start and in-between every 2 scans, on each of 3 scanners tested, leading to total of 12 scans (4 scans per scanner). This experiment was used to demonstrate uniformity of the scanner performance by calculating CV for global (<10% CV) and local uniformity (<1% CV; each 400 μM^2 gridded cell with surrounding 4 cells; averaged over alternating cells of the 32x32 array).
- The second array was used to assess overall system performance using a single chip lot.

Probes: Control probes - random generated synthetic sequence. On the array this probes is located in a specific pattern across the array. Chip probe length of varies from 16-25mer. Probes were used for grid alignment, and to evaluate variability introduced by hybridization.

Discrimination controls - 4 control probe sets; 30 tiled Perfect Match (PM) / Mismatch (MM) probe pairs for each. Probes on array are complementary to one of four 5'-biotinylated oligonucleotides. These probes were used to measure discrimination of PM from MM.

Sample type:

Target - Hybridization Cocktail: two target sets (for control and discrimination, respectively) at concentrations 0.1, 0.5, 1 and 3nM were pooled and spiked into hybridization buffer.

Single lots of buffer, oligonucleotides, and reagents were used.

Study design:

Goal: to generate reproducibility data for consistent system performance independent of assay type.

Primary metric - discrimination score (PM vs. MM).

Design: components-of-variance (random effects) replicated full factorial fully nested. One target aliquot was hybridized to 12 chips on 3 Fluidics Stations (12 ports) - each array was scanned in duplicate on each of 3 scanners 3000Dx (6 scans/chip), resulting in 72 scans of the same test material.

Methods:

Hybridization - 30 minutes; all data collection within 1 week

Replicate samples processed sequentially (3 replicates/aliquots)

2 scans per array - 2 separate .DAT files

ANOVA (Analysis of Variance) analysis

Data generated:

- Feature position check -The scanner introduced no more than 2.5 microns of feature displacement.
- Intra-chip local and global uniformity data (CV of fluorescent features on the array)

The intensities of the features which were tiled on the array at different positions were measured. There were 643 identical features on the array that were distributed across the array. The signal %CV for all of the features for the control oligonucleotide demonstrated that the features were hybridized uniformly on the array. The overall average of CVs for 72 images was 8.0%. Since the variability of signal for the hybridized control oligonucleotide was measured, the %CV reflects the cumulative variability of all system components, including user handling. Hybridization uniformity was consistent across 36 arrays.

Between-scan %CVs

Percent CVs of bright feature signal over time, of the array, for each of the three scanners were provided. Data from each scanner were derived from the four scans of the same array during the study. The between-scan %CV range for all bright features was 4.2-5.2% for scanner 1, 3.2-4.0% for scanner 2, and 0.3-1.9% for scanner 3.

Between-scanner %CVs

Percent CVs of bright feature signals over time, of the same array, across the three scanners are shown below. Data from all three scanners were derived from the same time point of the same array during the study. The %CV ranges for all bright feature signals across the scanners at the different time points were as follows:

Time point	% CV Range
1	4.4 – 6.8
2	5.0 – 7.4
3	5.7 – 9.2
4	8.9 – 10.9

- Discrimination score: normalized difference between intensity from targets bound to PM and ones bound to MM. Intrinsic binding affinities (e.g. GC content function) are designed to be factored out; the discrimination score is a measure of the amount and quality of information from a probe pair, and is background corrected. Results: 36 average discrimination scores from all arrays fell within 95% confidence interval (average = ave of 2 scanned images/array x 36 arrays).

- ANOVA - looking at random effects of FS, FS port and scanner - P-values >0.05 => no statistically significant variability introduced.

- Chip-to-chip % CV :

The average signal of the duplicate scans for 36 arrays for every feature from the

control oligonucleotides was used to determine their variation, independently. Figures 1 and 2 below demonstrate the variation of the perfect match and mismatch features, respectively. One perfect match feature had a signal CV > 13% while no mismatch features had signal variation >15%.

c. Linearity:

Not applicable – linearity for each assay to be run on this system will be assessed during the clearance of the assay

d. Carryover:

Not applicable – carryover for each assay to be run on this system will be assessed during the clearance of the assay

e. Interfering Substances:

Not applicable – interferences for each assay to be run on this system will be evaluated during the clearance of the assay

2. Other Supportive Instrument Performance Data Not Covered Above:

K. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

L. Conclusion:

This device has no predicate device. However, the submitted information in this premarket notification is complete, and this device would be a good candidate for de novo classification and clearance.

Note: This device was declared NSE for lack of a predicate. On November 3, 2004, the sponsor petitioned to have this device reclassified into Class II via the de novo classification process. FDA has reviewed the sponsor's petition and has proposed the following classification:

§ 862.2570 Instrumentation for Clinical Multiplex Test Systems.

(a) *Identification.* Instrumentation for clinical multiplex test systems is a device intended to measure and sort multiple signals generated by an assay from a clinical sample. This instrumentation is used with a specific assay to measure multiple similar analytes that establish a single indicator to aid in diagnosis. Such instrumentation may be compatible with more than one specific assay. The device includes a signal reader unit, and may also integrate reagent handling, hybridization, washing, dedicated instrument control, and other

hardware components, as well as raw data storage mechanisms, data acquisition software, and software to process detected signals.

(b) *Classification.* Class II (special controls). The special control is FDA's guidance document entitled "Class II Special Controls Guidance Document: Instrumentation for Clinical Multiplex Test Systems." See § 862.1(d) for the availability of this guidance document.