510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY

A. 510(k) Number:

k133302

B. Purpose for Submission:

Device modification, software revision

C. Manufacturer and Instrument Name:

Luminex Molecular Diagnostics, Inc., FLEXMAP 3D® Instrument System with Luminex xPONENT® v.4.2 Software

D. Type of Test or Tests Performed:

Multiplex nucleic-acid testing

E. System Descriptions:

1. Device Description:

The Luminex FLEXMAP 3D® instrument includes four subsystems: electronic, fluidic, mechanical, and optical.

Luminex FLEXMAP 3D®
The FLEXMAP 3D® system is a compact analyzer that performs up to 500 analytes from a single sample. The instrument includes four subsystems: electronic, fluidic, mechanical, and optical; and utilizes xPONENT® software v.4.2 of the xMAP® (Multi−Analyte Profiling) technology operating system. The electronics system provides the power for operation and control of the FLEXMAP 3D® system and communication between its parts. The fluidics system handles the flow of liquid through the Luminex FLEXMAP 3D® instrument. The mechanical subsystem of the Luminex FLEXMAP 3D® instrument includes a filter system used to aid in cooling of the instrument and pressurized sheath fluid. The optical sub-system consists of the optical assembly and excitation lasers and does not require manual adjustment by the user.

Luminex xPONENT® v.4.2 software
The Luminex xPONENT® v.4.2 or higher software will provide complete control of the FLEXMAP 3D® instrument and perform the analyses. The FLEXMAP 3D® system utilizes software version xPONENT® v.4.2 of the xMAP technology operating system.

2. Principles of Operation:

Luminex's xMAP technology is built on flow cytometry, microspheres, lasers, digital signal processing and traditional chemistry. Systems using xMAP technology perform discrete chemistry on the surface of color coated beads known as microspheres, which are then read in a compact analyzer. The analyzer reads multiplexed assay results by identifying color differences between beads as well as the presence or absence of a fluorescent reporter marker.

The principle of operation for the instrument system is flow cell fluorometry. The fluidics, optics, robotics, temperature control, software, and xMAP microspheres work together to enable simultaneous analysis of up to 500 analytes in a single test sample. Assay analysis requiring temperature control is provided through the enclosed instrument heater block.

There are two fluidics paths in the FLEXMAP 3D® analyzer. The first path involves a syringe driven mechanism that controls the sample uptake. This mechanism permits small sample uptake volumes from small reaction volumes. The syringe-driven system transports a specified volume of sample from a sample container to the cuvette. The sample is injected into the cuvette at a steady rate for analysis. Following analysis, the sample path is automatically purged with sheath buffer by the second fluidics path. This process removes residual sample within the tubing, valves, and probe. The second fluidics path is driven by positive air pressure and supplies sheath fluid to the cuvette and sample path.

Sheath fluid is the delivery medium of the sample to the optics component. The analysis sample is acquired using a sample probe from a 96-well microtiter plate. The sample passes through with sheath fluid at a reduced rate resulting in a narrow sample core to ensure that each microsphere is illuminated individually. The sample injection rate is such that the microspheres are introduced to the optics path as a series of single events. The optics assembly consists of two lasers. One laser excites the dye mixture inside the microspheres and the second laser excites the fluorophore bound to the surface of the microsphere. Avalanche photo diode detectors measure the excitation emission intensities of the color coding classification dye mixtures inside the microspheres and a photomultiplier tube detects the excitation emission intensity of the reporter molecule bound to the surface of the microspheres. High speed digital signal processors and computer algorithms provide analysis of the microspheres as they are processed through the FLEXMAP 3D® analyzer. Results of the analyses are provided in a report format.

3. Modes of Operation:

Automatic/Batch-mode. The FLEXMAP 3D® analyzer utilizes sequential positioning of each well of a 96-well microtiter plate beginning from any well position.

4. Specimen Identification:

The FLEXMAP 3D® analyzer utilizes an optional barcode reader that is available for entry of sample IDs, or they may be entered manually.

5. Specimen Sampling and Handling:

   The samples are manually prepared according to assay manufacturer's suggestions and are transferred to a 96-well microtiter plate for analysis.

6. Calibration:

   The FLEXMAP 3D® analyzer utilizes classification and reporter calibrator microspheres in FLEXMAP 3D® Calibration Kit. Calibration is performed weekly.

7. Quality Control:

   The FLEXMAP 3D® analyzer utilizes classification and reporter verification microspheres in FLEXMAP 3D® Performance Verification Kit.

8. Software:

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

   Yes___X____ or No_____

F. Regulatory Information:

1. Regulation section:

   21 CFR 862.2570, Instrumentation for Clinical Multiplex Test Systems

2. Classification:

   Class II

3 Product code:

   NSU, Instrumentation for Clinical Multiplex Test Systems

4. Panel:

   Clinical Chemistry (75)

G. Intended Use:

1. Indication(s) for Use:

The Luminex FLEXMAP 3D® system with xPONENT® software is a clinical multiplex test system intended to measure and sort multiple signals generated in an *in vitro* diagnostic assay from a clinical sample. This instrumentation is intended for use with specific IVD cleared or approved assays citing its use, to measure multiple similar analytes that establish a single indicator to aid in diagnosis.

2. Special Conditions for Use Statement(s):

   For prescription use only.

H. Substantial Equivalence Information:

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

   k121399, Luminex® FLEXMAP 3D® Instrument System with xPONENT® v.4.0 SP1 Software

2. Comparison with Predicate Device:

Similarities		
Item	FLEXMAP 3D® with xPONENT® v.4.2 software New Device	FLEXMAP 3D® with xPONENT® v.4.0 SP1 software Predicate
Intended Use	The Luminex FLEXMAP 3D® system with xPONENT® software is a clinical multiplex test system intended to measure and sort multiple signals generated in an in vitro diagnostic assay from a clinical sample. This instrumentation is intended for use with cleared or approved assays citing its use, to measure multiple similar analytes that establish a single indicator to aid in diagnosis. The device includes a signal reader unit, raw data storage mechanisms, data acquisition software and software to process detected signals.	Same
Assays used to establish performance	One Lambda LABType® SSO DNA Typing Tests	Same
Optics Principle	Lasers/APDs1/PMTs2	Same
Hardware Principle	Flow Cytometry based	Same
500-plex Read Time	~ 25 min./96-well plate	Same
100-plex Read Time	~ 20 min./96-well plate	Same

Similarities		
Item	FLEXMAP 3D® with xPONENT® v.4.2 software New Device	FLEXMAP 3D® with xPONENT® v.4.0 SP1 software Predicate
Calibration	System calibration is performed on a monthly basis as part of regularly scheduled maintenance. This is independent of assay calibration.	Same
Calibration kit	Luminex FLEXMAP 3D® Calibration Kit.	Same
Applications	Protein/Nucleic Acid	Same
Dynamic Range	≥ 4.5 logs	Same
Multiplex Capacity	500	Same
Microtiter Plate	96 well	Same

Differences		
Item	FLEXMAP 3D® with xPONENT® v.4.2 software New Device	FLEXMAP 3D® with xPONENT® v.4.0 SP1 software Predicate
Software	xMAP Technology Operating System xPONENT® v.4.2	xMAP Technology Operating System xPONENT® v.4.0 SP1

The software changes included in the update from xPONENT® v.4.0 SP1 to xPONENT® v.4.2 consist of the following:

- Added support for Windows 7.
- Added minor graphical user interface abilities.
- Updated instrument maintenance capabilities.
- Added the ability to schedule a system warm-up at a user-specified time (this is an instrument-only daily start up procedure that facilitates laser initiation and warm up prior to running IVD assays).
- Updates to running a batch
- Added a weekly xPONENT® software restart feature.
- Sample ID entry
- Improved software operational abilities
- Import, Export and Archive Capabilities
- Reports

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

IEC 60825 Safety of Laser products, 2nd edition, 2007

IEC 62304 Medical Device Software – Software Life Cycle Processes, 2006+AC: 2008

BS EN ISO 15223-1 Medical Devices – Symbols to be Used with Medical Device Labels, Labelling, and Information to be Supplied, 2012

J. Performance Characteristics*:*

1. Analytical Performance:

a. Accuracy:

Because the instrument performance specifications and characteristics (for FLEXMAP 3D®) have not changed only a regression analysis of data collected on the FLEXMAP 3D® system with the predicate software (xPONENT v.4.0 SP1) and the new software (xPONENT® v.4.2) was performed. The specimens included a recommended panel of 48 highly characterized cell line HLA genomic DNA samples demonstrated a high degree of concordance between the test results.

Three representative LABType® SSO DNA Typing assays from One Lambda [LABType® SSO DRB1 Typing Test (RSS02B1), LABType® HD Class I B Locus Typing Test (RSSOH1B), and LABType® SSO DQA/DQB Typing Test (RSS02Q)] were used to compare the Luminex FLEXMAP 3D® System using the test (xPONENT® v.4.2) software with the Luminex FLEXMAP 3D® System using the reference (xPONENT® v.4.0 SP1) software. The reference samples used for this evaluation conformed with quality and quantity requirements meeting criteria described in each assay's product insert (20 ng/µL with OD_{260}/OD_{280} ratio of 1.65 – 1.80 and less than 0.5 mM of chelating reagent). These reference samples were selected for each locus with maximum diversification of HLA typing to test as rigorously as possible. HLA typing for all samples was confirmed in accordance with requirements established by CBER.

Each LABType® SSO DNA Typing assay was tested with 48 samples in duplicate. Raw MFI values were compared in a regression analysis for each sample replicate in order to establish the correlation between results using each software version with each typing kit. All data obtained was further analyzed with One Lambda's HLA Fusion software (see BK070070, http://www.fda.gov/downloads/biologicsbloodvaccines/bloodbloodproducts/approvedproducts/substantiallyequivalent510kdeviceinformation/ucm374745.pdf) to assign HLA typing results. The HLA typing results acquired using the Luminex xPONENT® v.4.0 SP1 software and the xPONENT® v4.2 software were compared. The concordance analysis of the HLA typing obtained from the test (xPONENT® v.4.2) and the reference (xPONENT® v.4.0 SP1) Luminex software showed 100% agreement and demonstrate that the data obtained are essentially identical and produce concordant HLA typing results under the conditions tested. The results of the regression analyses are provided in the table below.

LABType® SSO Product	No. of samples	Regression equation	Correlation coefficient (R^2)
DRB1 Typing Test (RSS02B1)	48	y = 0.9965x - 4.4259	0.9999
HD Class I B Locus Typing Test (RSSOH1B)	48	y = 1.0008x + 0.1045	1.00

LABType® SSO Product	No. of samples	Regression equation	Correlation coefficient (R^2)
DQA/DQB Typing Test (RSS02Q)	48	y = 0.9994x - 2.4714	1.00

b. Precision/Reproducibility:

No change from k121399.

c. Linearity:

No change from k121399.

d. Carryover:

No change from k121399.

e. Interfering Substances:

No change from k121399.

K. Proposed Labeling:

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

L. Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.