510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY

A. 510(k) Number:

K092705

B. Purpose for Submission:

Clearance of m2000 system

C. Manufacturer and Instrument Name:

Abbott m2000 system consisting of the m2000sp and m2000rt instruments

D. Type of Test or Tests Performed:

Real-Time PCR

E. System Descriptions:

1. Device Description:

The Abbott *m*2000 System is an instrument platform that automates steps to perform nucleic acid amplification assays from sample processing through amplification, detection, and data reduction. The Abbott *m*2000 System comprises the *m*2000*sp* and *m*2000*rt* instruments, which are operated with separate System Control Center (SCC) workstations. Each instrument contains an independent software application; one for the *m*2000*sp* and a second for the *m*2000*rt*. The *m*2000*sp* instrument is a floor standing, automated sample preparation system. The *m* 2000*rt* instrument is a real-time PCR thermal cycler/reader instrument system. Abbott Molecular is the manufacturer of the m2000 System. The principal hardware components that comprise the m2000*sp* and m2000*rt* were developed by Original Equipment Manufacturer vendors, Tecan Schweiz AG, Mannedorf, Switzerland, and Applied Biosystems, Foster City, CA, respectively. Abbott Molecular developed the software that is uniquely for use with the m2000 System. The Abbott *m*2000 System software processes sample preparation and amplification/detection protocols based on pre-determined, assay-specific parameters that are contained in individual assay application specification files that are installed on the SCC. The Abbott *m*2000sp reads and processes bar coded primary sample tubes and processes up to 96 specimens, controls, and calibrators in batch mode. The *m*2000 System is capable of processing samples from various matrices, depending on the specific assay application. At the completion of the automated sample preparation protocol, the operator seals and manually transfers the PCR plate to the Abbott *m*2000*rt* for nucleic acid detection. Bar code and

*m*2000 *sp* data is transferred to the *m*2000*rt* electronically via removable media (i.e., a CD).

2. Principles of Operation:

The *m*2000*sp*

The sample preparation process consists of releasing the nucleic acid target from its native biological source (e.g., lysis of microorganisms) using chaotropic nucleic acid extraction technology, binding of nucleic acids to a solid phase (i.e., magnetic particles) using silica or iron oxide nucleic acid chemistry, separation of the solid phase from the residual lysis solution using magnetic separation technology, washing to remove unwanted materials, and elution or separation of nucleic acid from the solid phase using conventional fluid handling technology.

The *m*2000*rt*

The Abbott *m*2000*rt* is an amplification/detection system that provides real-time PCR technology with fluorescence capability of up to five distinct dyes per reaction. PCR amplifies specific target DNA sequences through the use of reagents containing target-specific oligonucleotide sequences (or primers), individual nucleic acid triphosphate bases and polymerase enzymes. RNA target sequences must first be converted to complementary DNA (cDNA) sequences before PCR can occur. The system provides thermal cycling temperature control (the process of cycling the reaction mixture between high and low temperatures) with optical read capability for every cycle throughout the amplification protocol. Temperature control for assay reactions is accomplished by heating or cooling all sample wells in the thermal cycler simultaneously per the assay-specific protocol. The block heating and cooling is controlled by Peltier assemblies in thermal contact with the block. Through the process of thermal cycling, the reagents replicate the target nucleic acid sequence many-fold. Multiple target sequences can be amplified in the same reaction by including the appropriate combination of target specific oligonucleotide primer sequences.

The heated lid assembly is held at a high, constant temperature to prevent condensation on the plate lid. The heated lid assembly also contains optical elements to aid in collection of fluorescent light and suppression of light coming from areas other than individual wells.

Detection of fluorescent dyes in the reaction is accomplished by simultaneously illuminating all wells in the plate using the tungsten-halogen lamp. Light from the tungsten-halogen lamp is directed through an excitation filter and dichroic beamsplitter onto the PCR plate, held securely in place in the thermal block. The excitation light excites fluorescent dyes in each well of the PCR plate. The emitted fluorescence light passes through the dichroic beamsplitter and an emission filter and is detected by a charge coupled device (CCD) camera.

The optical filters inside the *m*2000*rt* are arranged in five excitation/emission filter pairs. The excitation and emission center wavelength and bandpass are designed to preferentially excite individual dyes in the reaction mixture. The filter wheel assembly is indexed during the read process to measure fluorescence through each of the five filter pairs. Up to five dye signals may be monitored in each sample well of the PCR plate. The thermal and optical detection system is under computer control and monitored for proper operation.

An optical reading consists of a set of five fluorescence intensity measurements by a CCD camera, one for each of the five filter assembly modules (positioned on a five-position rotating assembly). The five pairs of filters are calibrated for their response to each dye used in the assay using calibration dye plates. The choice of filters allows for the use of the following dyes on the system: FAM™, SYBR® Green, VIC®, NED™, TAMRA™, JOE™, ROX™, and CY™5. A typical amplification/detection protocol for a DNA assay lasts about 120 minutes. RNA assays run about 30 minutes longer due to the reverse transcription step.

3. Modes of Operation:

The Abbott *m*2000 System is an automated, open tube, batch analyzer. Samples are prepared for nucleic acid testing by the *m*2000*sp* through user initiated protocols run on the *m*2000*sp* liquid handling platform using specific reagents. Using the *m*2000*sp* software, users can select a Master Mix addition protocol to automatically distribute the assay reagents and extracted nucleic acid specimens into an Abbott 96-Well Optical Reaction plate, which must be manually loaded onto the *m*2000*rt* instrument. Sample IDs and processing status for each specimen are electronically transferred to the *m*2000*rt* from the *m*2000*sp* and linked to the PCR plate ID. The samples are then amplified and analyzed by the *m*2000*rt* through fluorescent-based real-time PCR using a user initiated protocol associated with the sample preparation protocol run on the *m*2000*sp* selected by plate ID.

The specific protocols that are performed on each instrument for IVD assays depend upon the assay-specific, closed-mode application specifications that are installed on the System. For closed mode assays, the assay protocol selected when initiating the *m*2000*sp* run automatically establishes the protocol to be run on the *m*2000*rt* system. The *m*2000*sp* and *m*2000*rt* instruments are also capable of performing laboratory-defined (user-validated) applications. The *m*2000*sp* instrument is capable of performing sample extractions for open-mode protocols. The *m*2000*rt* instrument is capable of PCR thermal cycling and real-time reading for laboratory-defined applications. Any special requirements or system restrictions for specific open-mode protocols would be communicated upon installation of the protocol. The FDA is not reviewing, clearing or approving any of the open-mode/laboratory-defined functionalities and requires documentation and evidence that these functionalities do not interfere with IVD functionalities.

4. Specimen Identification:

   Samples are identified by the bar code label on the primary sample tube, which is read by the *m*2000*sp* Positive ID Bar Code Reader (PosID). The system identifies the location of the sample by reading the bar coded sample rack ID and the bar coded sample tube IDs as a function of the positions in the rack. The sample location and sample ID map are then electronically transferred to the *m*2000*rt* linked to the PCR plate ID, along with reagent data and the prepared PCR plate.

5. Specimen Sampling and Handling:

   Specific mixing protocols depend on the application specifications of the assay being used on the *m*2000 System. Mixing, if necessary, is performed by pipetting using the Liquid Handling Arm (LiHa). The LiHa pipettes, dilutes, and mixes samples and reagents by aspirating and dispensing liquid through eight different channels, using disposable tips (DiTis).

   Specimens are sampled by direct open tube and transferred automatically by the LiHa from the sample input tubes to Reaction vessels (RVs) in the 1 mL subsystem, then to the output plates of the *m*2000*sp*. Sample input tubes can be primary tubes or secondary aliquot tubes.

6. Calibration:

   The calibration for the *m*2000 system consists of an assay independent optical calibration and an assay specific assay calibration, each described below.

   Abbott *m*2000*rt* Optical Calibration

   The *m*2000*rt* instrument extracts dye fluorescence data from digital images. Four sets of optical calibration data are used in this data extraction process:

   - Region of Interest (ROI) data, specifying what portions of the digital images correspond to the 96 reaction wells of the PCR plate.
   - Background fluorescence data, indicating the signal from each well with no fluorescent dye present.
   - Pure dye spectral data, indicating the relative signal intensity for the five optical filter channels when fluorescence of a single pure dye is measured.
   - Uniformity data, indicating the signal intensity of a given well relative to the other wells for a uniform plate.

   These optical data sets are acquired during the optical calibration process. Their execution involves using the Abbott *m*2000*rt* Optical Calibration Kit, List No. 4J71-93. This kit contains ten 96-well PCR plates as follows:

- A ROI calibration plate, with five dyes in each well. This is used for both the ROI calibration and the uniformity calibration.

- A background plate, with non-fluorescent buffer in each well. Water or diluent in a normal PCR plate may also be used for background calibrations.

- Eight pure dye calibration plates, each with wells filled with a specific dye (FAM, VIC, NED, ROX, Cy5, SYBR, JOE, or TAMRA), used for the pure dye spectral calibration.

Optical calibrations are performed at installation, when the lamp is changed, and after six months. Background calibrations are also performed monthly.

Assay Calibration

Abbott RealTi*m*e assays are calibrated by processing calibrators as samples on the *m*2000*sp* and *m*2000*rt* instrument.

Quantitative assays require between two and ten calibrators, as specified by the assay, to yield a log-linear calibration curve (cycle number vs. log of calibrator concentration). Quantitative calibration curves must satisfy slope and y-intercept validity criteria specified for each assay. Assays must be recalibrated for each lot of assay reagents and as directed by assay reagent labeling.

Qualitative assays use cutoff controls with each batch of samples, from which the qualitative criteria are determined. The number of valid cutoff controls and mean cutoff control cycle number must meet validity criteria specified by the assay.

7. Quality Control:

   Quality control is addressed for each separately cleared specific assay to be run on the instrument.

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:

   862.2570 Instrumentation for clinical multiplex test systems

2. Classification:

   Class II

3 Product code:

   OOI (Real-Time Nucleic Acid Amplification System) for *rt* instrument.

   JJH (Clinical Sample Concentrator) for *sp* instrument.

4. Panel:

   Clinical Chemistry (75)

G. Intended Use:

1. Indication(s) for Use:
   The Abbott *m*2000 system is intended for in vitro diagnostic use in performing FDA cleared and approved nucleic acid testing in clinical laboratories. It comprises the Abbott *m*2000*sp* and the Abbott *m*2000*rt* instruments. The Abbott *m*2000*sp* is an automated system for performing sample preparation for nucleic acid testing. The Abbott *m*2000*rt* is an automated system for performing fluorescence-based PCR to provide quantitative and qualitative detection of nucleic acid sequences.

2. Special Conditions for Use Statement(s):

   Prescription use only

H. Substantial Equivalence Information:

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

   Roche COBAS TaqMan Analyzer (K012966) for the m2000*rt*. The m2000*sp* instrument is considered an accessory device to the *rt* instrument since it automates sample preparation.

2. Comparison with Predicate Device:

Similarities		
Item	Device	Predicate
Intended Use	The Abbott *m*2000 system is intended for in vitro diagnostic use in performing FDA cleared and approved nucleic	Fully automated amplification and detection system for nucleic acids using 5′-nuclease technology.

Similarities		
Item	Device	Predicate
	acid testing in clinical laboratories. It comprises the Abbott *m*2000*sp* and the Abbott *m*2000*rt* instruments. The Abbott *m*2000*sp* is an automated system for performing sample preparation for nucleic acid testing. The Abbott *m*2000*rt* is an automated system for performing fluorescence-based PCR to provide quantitative and qualitative detection of nucleic acid sequences.	Intended for use by laboratory professionals trained in laboratory techniques and on the use of the analyzer
Assay Format	Homogeneous, closed tube PCR	Homogeneous, closed tube PCR
Degree of Automation	Requires manual transfer of amplification mixture to amplification/detection instrument Automated control of amplification, detection, and data analysis	Requires manual transfer of amplification mixture to amplification/detection instrument Automated control of amplification, detection, and data analysis
Primary Operational Amplification and Detection Components	Integrated thermocycler and microvolume fluorimeter for walk away PCR amplification and detection	Integrated thermocycler and microvolume fluorimeter for walk away PCR amplification and detection
Heating Method for Amplification	Peltier device with sample block	Peltier device with sample block
Detection Procedure	Optical detection of stimulated fluorescence	Optical detection of stimulated fluorescence
Detection Chemistries	Fluorescence labeled, target-specific probes	Fluorescence labeled, target-specific probes
User Interface	PC with instrument-specific software	PC with instrument-specific software

Differences		
Item	Device	Predicate
Amplification Reaction Volume	25-100 µL in 96-well PCR plates	100 µL in 200 µL K-tubes
Sample Preparation	Pairing with the m2000sp instrument provides automated sample processing.	No automated sample processing instrument offered in conjunction with COBAS TaqMan Analyzer.

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

Class II Special Controls Guidance Document: Instrumentation for Clinical Multiplex Test Systems:
http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm077819.htm

J. Performance Characteristics*:*

All assay analytical and clinical testing was reviewed in K092704. This submission is linked to the assay data presented there.

1. Analytical Performance:

   a. *Accuracy*:
   Accuracy was assessed during the clearance of the assay (K092704) and will be addressed for each assay to be run on this system.

   b. *Precision/Reproducibility*:
   Precision/Reproducibility was assessed during the clearance of the assay (K092704) and will be addressed for each assay to be run on this system.

   c. *Linearity*:

   N/A since CT/NG is a qualitative assay.

   d. *Carryover*:
   Carryover was assessed during the clearance of the assay (K092704) and will be addressed for each assay to be run on this system.

   e. *Interfering Substances*:
   Interfering Substances were assessed during the clearance of the assay (K092704) and will be addressed for each assay to be run on this system.

2. Other Supportive Instrument Performance Data Not Covered Above:

Fluid Pipetting Performance Testing

Requirements for fluid pipetting are stated in product requirements SPS4, SPS5, SPS6, and SPS7, found in MD0036 "*m*2000 Instrument System Product Requirements Document":

- Accuracy within ± 8% for 25 to 49 µL and within ± 5% for 50 to 900 µL, using 1000 µL pipette tips (SPS4)
- Accuracy within ± 8% for 10 to 49 µL and within ± 5% for 50 to 150 µL, using 200 µL pipette tips (SPS5)
- Precision < 1.0% coefficient of variation (CV) for 100 µL dispenses using 1000 µL pipette tips (SPS6)
- Precision < 0.75% CV for 100 µL dispenses and 3.5% CV for 10 µL dispenses using 200 µL pipette tips (SPS7)

Satisfaction of these requirements was demonstrated by functional testing of the *m*2000 instrument, performed by Original Equipment Manufacturer (OEM), Tecan Schweiz AG. Testing was performed with water at room temperature. Tecan also verified positioning accuracy within ± 0.4 mm. Verification is documented in MD12502 *m*2000 Instrument System Revision 3.0 Design Verification Record – Tecan *m*2000 *sp* EVO Verification.

Thermal Cycler Performance Testing

Functional design verification testing demonstrated that the *m*2000 *rt* design satisfies its design input requirements for thermal accuracy and uniformity, which are found in MD0036 "*m*2000 Instrument System Product Requirements Document":

- Thermal block temperature accuracy within ± 0.5°C from setpoint, specified in product requirement ADH2 (MD0036)
- Thermal block well temperature nonuniformity within ± 0.5°C range within 30 seconds of reaching hold state, specified in product requirement ADH4 (MD0036)

Optical Detection Verification

Performance requirements for optical detection are stated in the Abbott *m*2000 product requirements and in the technical requirements for the Abbott *m*2000*rt* reader specific to the vendor (design specification document MD10085 "*m*2000 Instrument System Design Specifications – Airjuice Thermalcycler Reader Technical Requirements,"). These requirements include:

- Dynamic range sufficient to measure fluorescence of 100 µL of selected dyes over concentration range of 10 nM to 200 nM at temperature range of 35 to 65° C, specified in product requirement ADH15 (MD0036)

- Linearity such that the square of the correlation coefficient (r^2) exceeds 0.95 over the dye concentration range, specified in technical requirement FD.4.1 and FD.4.2 (MD10085)

- Cycle-to-cycle signal variability not exceeding 1.0% of the average signal in any well, specified in technical requirement FD.5.1 (MD10085)

- Signal drift not exceeding 1.0% over a one hour period, specified in technical requirement FD.5.2 (MD10085)

- Run-to-run signal variability not exceeding 5% of the average signal in any well, specified in technical requirement FD.5.3 (MD10085)

- Measurement reliability such that instances of measurements outside a ± 5 standard deviation range are less than 1 per 50,000 measurements, specified in technical requirement FD.5.4 (MD10085)

Satisfaction of these requirements was demonstrated by performance testing executed by Applied Biosystems, documented in their verification testing records. Vendor verification testing records are cited by Abbott design verification records as summarized in MD10122 "*m*2000 Instrument Systems Initial Development Design Verification Summary Report."

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.