510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY

A. 510(k) Number:

K143302

B. Purpose for Submission:

Expansion of device Intended Use Statement to include the use of the Xpert MTB/RIF Assay results as an aid in the decision whether continued airborne infection isolation is warranted in patients with suspected active pulmonary tuberculosis.

C. Measurand:

M. tuberculosis complex DNA and rifampin-resistance associated mutations of the *rpoB* gene

D. Type of Test:

Qualitative, nested real-time polymerase chain reaction (PCR)

E. Applicant:

Cepheid®

F. Proprietary and Established Names:

Trade Name: Xpert® MTB/RIF

Common Name: Xpert MTB/RIF Assay

G. Regulatory Information:

1. Regulation section: 21 CFR 866.3373
2. Classification: Class II
3. Product code: PEU
4. Panel: Microbiology (83)

H. Intended Use:

1. Intended use(s):

The Xpert® MTB/RIF Assay, performed on the GeneXpert® Instrument Systems, is a qualitative, nested real-time polymerase chain reaction (PCR) *in vitro* diagnostic test for the detection of *Mycobacterium tuberculosis* complex DNA in raw sputum or concentrated sputum sediment prepared from induced or expectorated sputum. In specimens where *Mycobacterium tuberculosis* complex (MTB-complex) is detected, the Xpert MTB/RIF Assay also detects the rifampin-resistance associated mutations of the *rpoB* gene.

The Xpert MTB/RIF Assay is intended for use with specimens from patients for whom there is clinical suspicion of tuberculosis (TB) and who have received no antituberculosis therapy, or less than three days of therapy. This test is intended as an aid in the diagnosis of pulmonary tuberculosis when used in conjunction with clinical and other laboratory findings.

An Xpert MTB/RIF Assay result of "MTB NOT DETECTED" from either one or two sputum specimens is highly predictive of the absence of *M. tuberculosis* complex bacilli on serial fluorescent acid-fast sputum smears from patients with suspected active pulmonary tuberculosis and can be used as an aid in the decision of whether continued airborne infection isolation (AII) is warranted in patients with suspected pulmonary tuberculosis. The determination of whether testing of either one or two sputum specimens is appropriate for decisions regarding removal from AII should be based on specific clinical circumstances and institutional guidelines. Clinical decisions regarding the need for continued AII should always occur in conjunction with other clinical and laboratory evaluations and Xpert MTB/RIF Assay results should not be the sole basis for infection control practices.

The Xpert MTB/RIF Assay must always be used in conjunction with mycobacterial culture to address the risk of false negative results and to recover organisms when MTB-complex is present for further characterization and drug susceptibility testing. However, decisions regarding the removal of patients from AII need not wait for culture results. Sputum specimens for TB culture, AFB smear microscopy, and Xpert MTB/RIF Assay testing should follow CDC recommendations with regard to collection methods and time frame between specimen collection.

The Xpert MTB/RIF Assay does not provide confirmation of rifampin susceptibility since mechanisms of rifampin resistance other than those detected by this device may exist that may be associated with a lack of clinical response to treatment.

Specimens that have both MTB-complex DNA and rifampin-resistance associated mutations of the *rpoB* gene detected by the Xpert MTB/RIF Assay must have results confirmed by a reference laboratory. If the presence of rifampin-resistance associated mutations of the *rpoB* gene is confirmed, specimens should also be tested for the

presence of genetic mutations associated with resistance to other drugs.

The Xpert MTB/RIF Assay should only be performed in laboratories that follow safety practices in accordance with the CDC/NIH Biosafety in Microbiological and Biomedical Laboratories publication and applicable state or local regulations.

2. Indication(s) for use:

   Same as Intended Use

3. Special conditions for use statement(s):

   The Xpert® MTB/RIF Assay is for prescription use only in accordance with 21 CFR 801.09.

4. Special instrument requirements:

   The Xpert® MTB/RIF Assay is for use with the GeneXpert® Instrument Systems, including the GeneXpert® Diagnostic (Dx) Systems and GeneXpert® Infinity Systems.

I. Device Description:

The Xpert® MTB/RIF Assay is an automated *in vitro* diagnostic test for the qualitative detection of MTB-complex DNA and the genetic mutations associated with rifampin (Rif) resistance in raw sputum samples or concentrated sputum sediments from patients for whom there is clinical suspicion of TB and who have received no antituberculosis therapy, or less than 3 days of therapy. The primers in this test amplify a portion of the *rpoB* gene containing the 81 base pair *core* region. The probes are designed to differentiate between the conserved wild-type sequence and mutations in the core region that are associated with Rifampin (Rif) resistance. The assay is performed on Cepheid GeneXpert® Instrument Systems.

The Xpert® MTB/RIF Assay includes single-use disposable cartridges and sample reagent for sample preparation. The Xpert® MTB/RIF Assay cartridges contain reagents for the detection of MTB-complex DNA and Rif resistance associated mutations. A Sample Processing Control (SPC) and a Probe Check Control (PCC) are also included in the cartridge. The SPC is present to control for adequate processing of the target microorganism and to monitor the presence of inhibitors in the PCR reaction. The Probe Check Control (PCC) verifies reagent rehydration, PCR tube filling in the cartridge, probe integrity and dye stability.

Sputum specimens are collected according to the institution's standard procedures and transported to the GeneXpert® Instrument System area. For raw sputum, Sample Reagent is added to the sample (2:1, v:v). Sample Reagent is added to the resuspended sputum sediment (1.5 mL Sample Reagent to 0.5 mL suspension or 3:1, v:v, for larger volumes of sediment suspension). For both specimen types, the solution is shaken vigorously to

mix, and then incubated at 20-30ºC for 15 minutes. Using the transfer pipette provided, the specimen is transferred to the open port of the Xpert® MTB/RIF Assay cartridge.

The user initiates a test from the system user interface, the Xpert® MTB/RIF Assay cartridge is loaded onto the GeneXpert® Instrument System platform, which performs hands-off, automated sample processing, and real-time PCR for detection of DNA. Summary and detailed test results are obtained in approximately 2 hours and are displayed in tabular and graphic formats.

The Xpert® MTB/RIF Assay simultaneously detects MTB-complex and the genetic mutations associated with rifampin resistance by amplifying a MTB-complex specific sequence of the *rpoB* gene, which is probed with five molecular beacons (Probes A – E) for mutations within the rifampin-resistance determining region (RRDR). Each molecular beacon is labeled with a different fluorophore.

The valid maximum cycle threshold (Ct) of 39.0 for Probes A, B and C and 36.0 for Probes D and E are set for data analysis.

- "MTB DETECTED", is reported when at least two probes result in Ct values within the valid range and a delta Ct min (the smallest Ct difference between any pair of probes) of less than 2.0.

- "Rif Resistance NOT DETECTED" is reported if the delta Ct max (the Ct difference between the earliest and latest probe) is ≤4.0.

- "Rif Resistance DETECTED" is reported if the delta Ct max is >4.0.

- "Rif Resistance INDETERMINATE" is reported when the following two conditions are met:

  1. the Ct value of any probe exceeds the valid maximum Ct (or is zero, i.e. no threshold crossing); and
  2. the earliest *rpoB* Ct value is greater than [(Valid maximum Ct of probe in condition1) - (delta Ct max cut-off of 4.0)]

- "MTB NOT DETECTED" is reported when there is only one or no positive probe.

All assay settings are included as automatic calculations in the Xpert® MTB/RIF Assay protocol and cannot be modified by the user.

J. Substantial Equivalence Information:

1. Predicate device name(s): Xpert® MTB/RIF Assay

2. Predicate 510(k) number(s): K131706

3. Comparison with predicate:

Similarities		
Item	Device (K143302)	Predicate (K131706)
Technology	Same	Real-time PCR
Assay Targets	Same	MTB-complex DNA and rifampin resistance associated mutations
Specimen Type	Same	Raw sputum samples or concentrated sputum sediments
Nucleic Acid Extraction Method	Same	Sample preparation integrated in GeneXpert Cartridge and GeneXpert Instrumentation System
Assay Results	Same	Qualitative
Instrument System	Same	Cepheid GeneXpert Instrumentation System
Assay Internal Controls	Same	Sample Processing Control (SPC) and Probe Check Control (PCC). Failures result in a single repeat test.
Total Time to Test Result	Same	120 minutes for sample preparation and real-time PCR.

Difference		
Item	Device (K143302)	Predicate (K131706)
Intended Use Statement	The Xpert® MTB/RIF Assay, performed on the GeneXpert® Instrument Systems, is a qualitative, nested real-time polymerase chain reaction (PCR) *in vitro* diagnostic test for the detection of *Mycobacterium tuberculosis* complex DNA in raw sputum or concentrated sputum sediment prepared from induced or expectorated sputum. In specimens where *Mycobacterium tuberculosis* complex (MTB-complex) is detected, the Xpert MTB/RIF Assay also detects the rifampin-resistance associated mutations of the *rpoB* gene. The Xpert MTB/RIF Assay is intended for use with specimens from patients for whom there is clinical suspicion of tuberculosis (TB) and who have received no antituberculosis therapy, or less than three days of therapy. This test is intended as an aid in the diagnosis of pulmonary tuberculosis when used in conjunction with clinical and other laboratory findings. An Xpert MTB/RIF Assay result of "MTB NOT DETECTED" from either one or two sputum specimens is highly predictive of the absence of *M. tuberculosis* complex bacilli on serial fluorescent acid-fast sputum smears from patients with suspected active pulmonary tuberculosis and can be used as an aid in the decision of whether continued airborne infection isolation (AII) is warranted in patients with suspected pulmonary tuberculosis. The determination of whether testing of either one or two sputum specimens is appropriate for decisions regarding removal from AII should be based on specific clinical circumstances and institutional guidelines. Clinical decisions regarding the need for continued AII should always occur in conjunction with other clinical and laboratory evaluations and Xpert MTB/RIF Assay results should not be the sole basis for infection control practices.	The Xpert® MTB/RIF Assay, performed on the GeneXpert® Instrument Systems, is a qualitative, nested real-time polymerase chain reaction (PCR) *in vitro* diagnostic test for the detection of *Mycobacterium tuberculosis* complex DNA in raw sputum or concentrated sediments prepared from induced or expectorated sputum. In specimens where *Mycobacterium tuberculosis* complex (MTB-complex) is detected, the Xpert MTB/RIF Assay also detects the rifampin-resistance associated mutations of the *rpoB* gene. The Xpert MTB/RIF Assay is intended for use with specimens from patients for whom there is clinical suspicion of tuberculosis (TB) and who have received no antituberculosis therapy, or less than 3 days of therapy. This test is intended as an aid in the diagnosis of pulmonary tuberculosis when used in conjunction with clinical and other laboratory findings. The Xpert MTB/RIF Assay does not provide confirmation of rifampin susceptibility since mechanisms of rifampin resistance other than those detected by this device may exist that may be associated with a lack of clinical response to treatment. Specimens that have both MTB-complex DNA and rifampin-resistance associated mutations of the *rpoB* gene detected by the Xpert MTB/RIF Assay must have results confirmed by a reference laboratory. If the presence of rifampin-resistance associated mutations of the *rpoB* gene is confirmed, specimens should also be tested for the presence of genetic mutations associated with resistance to other drugs. The Xpert MTB/RIF Assay must be used in conjunction with mycobacterial culture to address the risk of false negative results and to recover the organisms for further

	The Xpert MTB/RIF Assay must always be used in conjunction with mycobacterial culture to address the risk of false negative results and to recover organisms when MTB-complex is present for further characterization and drug susceptibility testing. However, decisions regarding the removal of patients from AII need not wait for culture results. Sputum specimens for TB culture, AFB smear microscopy, and Xpert MTB/RIF Assay testing should follow CDC recommendations with regard to collection methods and time frame between specimen collection. The Xpert MTB/RIF Assay does not provide confirmation of rifampin susceptibility since mechanisms of rifampin resistance other than those detected by this device may exist that may be associated with a lack of clinical response to treatment. Specimens that have both MTB-complex DNA and rifampin-resistance associated mutations of the *rpoB* gene detected by the Xpert MTB/RIF Assay must have results confirmed by a reference laboratory. If the presence of rifampin-resistance associated mutations of the *rpoB* gene is confirmed, specimens should also be tested for the presence of genetic mutations associated with resistance to other drugs. The Xpert MTB/RIF Assay should only be performed in laboratories that follow safety practices in accordance with the CDC/NIH Biosafety in Microbiological and Biomedical Laboratories publication and applicable state or local regulations.	characterization and drug susceptibility testing. The Xpert MTB/RIF Assay should only be performed in laboratories that follow safety practices in accordance with the CDC/NIH Biosafety in Microbiological and Biomedical Laboratories publication and applicable state or local regulations.

K. Standard/Guidance Document Referenced (if applicable):

1. Guideline for Industry and FDA Staff – Class II Special Controls Guideline: Nucleic Acid-Based In Vitro Diagnostic Devices for the Detection of Mycobacterium tuberculosis Complex and Genetic Mutations Associated with *Mycobacterium tuberculosis* Complex Antibiotic Resistance in Respiratory Specimens, issued October 22, 2014.
2. Class II Special Controls Guidance Document: Nucleic Acid-Based In Vitro Diagnostic Devices for the Detection of *Mycobacterium tuberculosis* Complex in Respiratory specimens – Draft Guidance for Industry and FDA Staff, issued March 19, 2012.
3. CLSI EP5-A2, Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline-Second Edition. CLSI, 940 West Valley Road, Suite 1500, Wayne, PA 19087-1898 USA, 2004.
4. EN 13640, Stability Testing of In Vitro Diagnostic Reagents, June 2002.
5. ASTM D4169-05, Standard Practice for Performance Testing of Shipping Containers and Systems.
6. MM3-A2, Molecular Diagnostic Methods for Infectious Disease; Approved Guideline-Second Edition. CLSI, 940 West Valley Road, Suite 1500, Wayne, PA 19087-1898 USA, 2004.
7. Guidance for Industry and FDA Staff – Format for Traditional and Abbreviated 510(k), issued August 12, 2005.

8. Guidance for Industry and Food and Drug Administration Staff – eCopy Program for Medical Device Submissions, issued October 10, 2013.
9. Guidance for Industry and Food and Drug Administration Staff – Refuse to Accept Policy for 510(k)s, issued December 31, 2012.
10. Guidance for Review Criteria for assessment of In Vitro Diagnostic Device for Direct Detection of Mycobacterium SPP, issued by FDA DCLD/Microbiology Branch, February 28, 1994.
11. Guidance for Industry and FDA Staff – Class II Special Controls Guidance Document: Instrumentation for Clinical Multiplex Test Systems, issued March 10, 2005.
12. Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices – Guidance for Industry and FDA Staff, issued May 11, 2005.
13. Guidance for Industry, FDA Reviewers and Compliance on Off-the-Shelf Software Use in Medical Devices, issued September 9, 1999.
14. Guidance for Industry – Cybersecurity for Networked Medical Devices Containing Off-the-Shelf (OTS) Software, issued January 14, 2005.
15. General Principles of Software Validation; Final Guidance for Industry and FDA Staff, issued January 11, 2002.
16. EMC (Electromagnetic Compatibility) Directive, 2004/108/EC
17. LVD (Low Voltage Directive) 2006/95/EC
18. IEC 61010-1:2001 2nd Edition "Safety Requirements for electrical equipment for measurement, control, and laboratory use-Part 1: General Requirements"
19. EN 61010-1:2001 2nd Edition "Safety Requirements for electrical equipment for measurement, control, and laboratory use-Part 1: General Requirements"
20. UL 61010-1:2004 2nd Edition "Safety Requirements for electrical equipment for measurement, control, and laboratory use-Part 1: General Requirements"
21. EN 61010-2-101:2002 "Safety Requirements for electrical equipment for measurement, control, and laboratory use-Part 2-101: Particular Requirements for in vitro diagnostic (IVD) medical equipment"
22. CAN-CSA 22.2 No. 61010-1: 2004 +G11(R2009) 2nd Edition "Safety Requirements for electrical equipment for measurement, control, and laboratory use-Part 1: General Requirements"
23. CAN-CSA 22.2 No. 61010-1: 2004 2nd Edition "Safety Requirements for electrical equipment for measurement, control, and laboratory use-Part 1: General Requirements"
24. CAN-CSA 22.2 No. 61010-2-101: 2004 "Safety Requirements for electrical equipment for measurement, control, and laboratory use-Part 2-101: Particular Requirements for in vitro diagnostic (IVD) medical equipment"
25. WEEE Directive 2002/96/EC
26. EN 55011:1998 +A1:1999+A2:2002 "Industrial, scientific and medical (ISM) radio-frequency equipment- Electromagnetic disturbance characteristics- Limits and methods of measurements"
27. EN 55011:2007 +A1:2007 "Industrial, scientific and medical (ISM) radio-frequency equipment- Electromagnetic disturbance characteristics- Limits and methods of measurements"
28. EN 61326-1:2006 "Electrical Equipment for measurement, control and laboratory use-EMC Requirements"

29. EN 61326-2-6:2006 "Electrical Equipment for measurement, control and laboratory use- EMC requirements-Part 2-6: Particular Requirement for in vitro diagnostic (IVD) medical equipment"
30. FCC Part 15 Rules and Regulations for Information Technology Equipment
31. FCC Part 18 Rules and Regulations for Information Technology Equipment
32. CISPR 11:2004 "Industrial, scientific and medical equipment- Radio-frequency disturbance characteristics - Limits and methods of measurement" (Class A Radiated Emission Requirements)
33. CISPR 22:1997+A1:2000+A2:2003 "Information technology equipment -Radio disturbance characteristics- Limits and methods of measurement" (Class A Radiated Emission Requirements)
34. CISPR 22:2006 "Information technology equipment -Radio disturbance characteristics- Limits and methods of measurement" (Class A Radiated Emission Requirements

L. Test Principle:

The primers and probes in the Xpert® MTB/RIF Assay detect the presence of a unique gene sequence in MTB-complex DNA by using fluorogenic target-specific hybridization for detection of the amplified DNA. Sputum specimens are collected from patients with clinical suspicion of tuberculosis. The specimen is mixed with Sample Reagent, shaken 10 to 20 times or vortexed for at least 10 seconds, and incubated for 15 minutes at 20-30ºC. At 5 to 10 minutes into the incubation period, the specimen is shaken or vortexed again, and incubated for the remainder of the 15 minute incubation period prior to transferring it to the assay cartridge for testing. The GeneXpert® performs sample preparation by mixing the prepared sample with the lyophilized Sample Processing Control. The cells are filtered and washed with buffer to remove inhibitors and contaminants, and lysed using glass beads and an ultrasonic horn, eluting the released DNA. The DNA is mixed with dry real-time polymerase chain reaction (PCR) reagents and transferred into the integrated PCR tube for real-time PCR amplification and detection of chromosomal DNA gene sequences for MTB-complex.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

   a. Precision/Reproducibility:

   Refer to K131706 for a description of the Reproducibility and Precision performance study results.

   b. Linearity/assay reportable range:

   Not applicable, the Xpert MTB/RIF Assay is a qualitative assay.

   c. Traceability, Stability, Expected values (controls, calibrators, or methods):

Internal Controls

Refer to K131706 for a complete description of Xpert MTB/RIF Assay internal controls.

External Controls

During the clinical trial, three external controls (MTB Negative, MTB Positive rifampin susceptible, MTB Positive rifampin resistant) were run each day that study specimens were tested. Of the 1862 external controls samples that were run, 96.9% (1805/1862) gave expected results on the first attempt. Of the 57 external controls that failed to give expected results on the first attempt (i.e., a non-determinate result of INVALID, ERROR, or NO RESULT), 51 gave expected results when retested. No study specimens were tested on days without valid controls.

d. Detection limit:

Refer to K131706 for a description of the Limit of Detection (LoD) study results.

e. Analytical specificity:

Potential cross-reactivity of eight microorganisms was evaluated by *in silico analysis*. All eight microorganisms tested revealed no potential for cross-reactivity. See Tables 1A, 1B, and 1C below.

Table 1A. Microorganisms Predicted to be Non-cross Reactive by *in silico* Analysis (RpoB For1 + RpoB Rev Probe)

Organism	Accession	Max Score	Query Cov	E value	Identity
Mycobacterium franklinii Taxid:948102	HQ662080.1	22.3	83%	0.36	100%
M. massiliense, M. bolletii, M. abscessus subsp. bolletii Taxid:319705	NC_018150.2	32.2	100%	0.21	95%
Mycobacterium chimaera Taxid:222805	AY943187.1	26.3	83%	0.016	90%
Mycobacterium avium subsp. paratuberculosis Taxid:1770	AF057479.1	36.2	85%	0.005	100%
Mycobacterium avium subsp. silvaticum Taxid:44282	AY544889.1	28.2	85%	0.004	94%
Mycobacterium avium subsp. hominissuis Taxid:439334	AP012555.1	30.2	100%	0.15	100%
Mycobacterium immunogenum Taxid:83262	HM454251.1	32.2	48%	5E-04	95%

Table 1B. Microorganisms Predicted to be Non-cross Reactive by *in silico* Analysis (RpoB For2 + RpoB Rev Probe)

Organism	Accession	Max Score	Query Cov	E value	Identity
Mycobacterium franklinii Taxid:948102	HQ662038.1	22.3	83%	0.36	100%
M. massiliense, M. bolletii, M. abscessus subsp. bolletii Taxid:319705	NC_018150.2	32.2	100%	0.21	100%
Mycobacterium chimaera Taxid:222805	AY943187.1	40.1	91%	1E-06	96%
Mycobacterium avium subsp. paratuberculosis Taxid:1770	AF057479.1	36.2	59%	0.005	100%
Mycobacterium avium subsp. silvaticum Taxid:44282	AY544889.1	28.2	79%	0.004	94%
Mycobacterium avium subsp. hominissuis Taxid:439334	AP012555.1	32.2	100%	0.038	100%
Mycobacterium immunogenum Taxid:83262	HQ662101.1	24.3	36%	0.13	100%

Table 1C. Microorganisms Predicted to be Non-cross Reactive by *in silico* Analysis (All RpoB Probes with no stem sequences)

Organism	Accession	Max Score	Query Cov	E value	Identity
Mycobacterium franklinii Taxid:948102	HQ662092.1	24.3	88%	0.16	100%
M. massiliense, M. bolletii, M. abscessus subsp. bolletii Taxid:319705	DQ987717.1	75.8	75%	3E-14	92%
Mycobacterium chimaera Taxid:222805	AY943187.1	91.7	100%	6E-22	90%
Mycobacterium avium subsp. paratuberculosis Taxid:1770	CP005928.1	83.8	100%	4E-17	89%
Mycobacterium avium subsp. silvaticum Taxid:44282	AY544889.1	107	100%	8E-27	90%
Mycobacterium avium subsp. hominissuis Taxid:439334	AP012555.1	107	100%	1E-24	90%
Mycobacterium immunogenum Taxid:83262	HM454251.1	95.1	97%	1E-22	87%

f. Assay cut-off:

Refer to K131706 for a complete description of Assay Cut-Off.

2. Comparison studies:

a. Method comparison with predicate device:

Not applicable. Refer to Clinical Studies section.

b. Matrix comparison:

Not applicable

3. Clinical studies:

A prospective multi-center study (Study 2) was conducted at multiple sites in the United States, as well as South Africa and Brazil. Performance of the MTB/RIF Assay was assessed as an alternative to fluorescent stained AFB-smear microscopy as an aid in determining the need for continued airborne infection isolation in patients with suspected active pulmonary tuberculosis. Results from Xpert MTB/RIF Assay testing of two serial sputum specimens in study subjects with suspected active pulmonary tuberculosis were compared to results of fluorescent stained AFB smears of the same specimens; a subset of subjects had a third sputum specimen tested by AFB-smear but not by the Xpert MTB/RIF Assay. Each specimen was cultured for MTB-complex using liquid and solid

culture media, with mycobacterial growth confirmed for MTB-complex and rifampin drug susceptibility testing performed via the Middlebrook agar proportion method. Study 2 was also designed to evaluate the clinical performance of the Xpert MTB/RIF Assay using prospectively collected sputum specimens in HIV-infected and HIV-uninfected populations

Study subjects 18 years or older were eligible for enrollment if they were suspected of pulmonary tuberculosis, on no treatment or had fewer than 48 hours of TB treatment within 180 days prior to collection of the first sputum specimen, and had determination/documentation of HIV status. Subjects were included in the analysis if they produced at least two sputum specimens collected in sufficient volume for testing by Xpert MTB/RIF Assay, AFB smear, and MTB culture, and interpretable results were available for all three methods. A third specimen for analysis was collected at some sites based on standard of care protocols. Of 992 eligible and tested subjects, thirty-two subjects (3.2%) were excluded from the analysis: 7 due to absence of culture results and 3 due to MTB culture contamination. Twenty-two subjects (2.2%) were excluded due to Xpert MTB/RIF Assay non-determinate results (i.e., INVALID, ERROR, or NO RESULT). Therefore, 960 subjects were used in the analysis based on the first Xpert MTB/RIF Assay result. Twenty of the 22 subjects excluded from analysis based on the first Xpert MTB/RIF Assay result gave valid results for the second Xpert MTB/RIF Assay test specimen, therefore, analysis based on two Xpert MTB/RIF Assay test specimens included a total of 980 subjects.

Study subjects were 62% male, 38% female. Sixty-five (65%) percent of subjects were from the U.S., and 35% were from non-U.S. sites. Forty-five (45%) percent of study subjects were HIV-infected and 55% were HIV-uninfected subjects. Expectorated and induced sputa represented 59.6% and 33.6% of specimens respectively; 7% of sputum specimens were unspecified. Twenty-eight percent of specimens were raw sputa and 72% were concentrated sputum sediments.

Xpert MTB/RIF Assay Performance as Predictive of Results of Serial Fluorescent Stained AFB Smears

Of 215 study subjects with culture confirmed MTB-complex (14.2% [88/618] of U.S. subjects and 37.1% [127/342] of non-U.S. subjects), 99% of subjects (97% of U.S. subjects and 100% of non-U.S. subjects) with suspected pulmonary tuberculosis where MTB-complex was detected by acid-fast microscopy of two or three serial sputum specimens also had MTB-complex detected by testing of a single sputum by the Xpert MTB/RIF Assay. Results from testing of two serial sputum specimens by the Xpert MTB/RIF Assay detected MTB-complex in all AFB-smear-positive subjects (100% in the U.S. subjects and 100% in non-U.S. subjects).

A single negative Xpert MTB/RIF Assay result predicted the absence of AFB smear-positive pulmonary tuberculosis with an overall negative predictive value (NPV) of 99.7% (99.6% in the U.S. and 100% in non-U.S.). Two serial negative Xpert MTB/RIF Assay results predicted the absence of AFB smear-positive pulmonary tuberculosis with an

overall NPV of 100%.

One Xpert MTB/RIF Assay Result as Predictive of Results of Serial Fluorescent Stained AFB Smears

Tables 2 and 3 present the overall performance of one Xpert MTB/RIF Assay result compared to the results of MTB culture, stratified by AFB smear result (Table 2). Table 3 is a side-by-side comparison of the performance of one Xpert MTB/RIF Assay result versus the composite result of two AFB smears in U.S. and non-U.S. subjects (N=960).

Overall sensitivity of one Xpert MTB/RIF Assay in AFB smear-positive and AFB smear-negative subjects (based on two AFB smears) was 98.5% (95% CI: 94.6%, 99.6%) and 54.8% (95% CI: 44.1%, 65.0%) respectively, and overall specificity was 98.7% (95% CI: 97.5%, 99.3%). One Xpert MTB/RIF Assay result of "MTB Not Detected" was associated with a probability of MTB culture-positive/AFB smear-positive results of 0.4% for U.S. subjects and 0.0% for non-U.S. subjects.

Table 2. Performance of One Xpert MTB/RIF Assay Result Stratified by Two AFB Smears Relative to MTB Culture in U.S. and non-U.S. Subjects

		Culture						
		Positive			Negative			Total
		AFB Smear +	AFB Smear -	Overall Culture +	AFB Smear +	AFB Smear -	Overall Culture -	
Xpert MTB/RIF Assay	Positive	129	46	175	1	9	10[a]	185
	Negative	2	38	40	17	718	735	775
	Total	131	84	215	18[b]	727	745	960

Performance of Xpert MTB/RIF Assay for Smear Positive:
Sensitivity: 98.5% (129/131), 95% CI: 94.6%,99.6%
Specificity: 94.4% (17/18), 95% CI: 74.2%, 99.0%

Performance of Xpert MTB/RIF Assay for Smear Negative:
Sensitivity: 54.8% (46/84), 95% CI: 44.1%, 65.0%
Specificity: 98.8% (718/727), 95% CI: 97.7%, 99.4%

Prevalence of MTB Culture Positive: 22.4% (215/960)
Prevalence of MTB Culture Positive in U.S. subjects: 14.2% (88/618)
Prevalence of MTB Culture positive in non-U.S. subjects: 37.1% (127/342)

Percent of AFB smear positive subjects among subjects with MTB Culture Positive Result: 60.9% (131/215)

Overall Probability of MTB Culture Positive among subjects with an Xpert MTB/RIF Negative Result: 5.2% (40/775), 95% CI: 3.8%, 7.0%
Probability of MTB Culture Positive among subjects with an Xpert MTB/RIF Negative Result (U.S. subjects): 2.4% (13/539), 95% CI: 1.4%, 4.1%

Probability of MTB Culture Positive among subjects with an Xpert MTB/RIF Negative Result (non-U.S. subjects): 11.4% (27/236), 95% CI: 8.0%, 16.1%

Overall Probability of MTB Culture Positive and AFB smear positive among subjects with an Xpert MTB/RIF Negative Result: 0.3% (2/775), 95% CI: <0.1%, 0.9%

Probability of MTB Culture Positive and AFB smear positive among subjects with an Xpert MTB/RIF Negative Result (U.S. subjects): 0.4% (2/539), 95% CI: 0.1%, 1.3%

Probability of MTB Culture Positive and AFB smear positive among subjects with an Xpert MTB/RIF Negative Result (non-U.S.) subjects: 0.0% (0/236), 95% CI: 0.0%, 1.6%

[a]Of the 10 MTB culture-negative specimens that were positive by Xpert MTB/RIF Assay, 5 grew non-tuberculosis mycobacteria (NTM). MTB-complex was isolated and identified using standard of care methods not associated with the study protocol in 4 of the 5 specimens.
[b]Of the 18 MTB culture-negative/AFB smear-positive specimens, 14 grew NTM.

One Xpert MTB/RIF Assay was associated with a sensitivity of 81.4% (95% CI: 75.7%, 86.0%) for identifying MTB culture-positive subjects compared to a sensitivity of 60.9% (95% CI: 54.3%, 67.2%) for two AFB smears.

Table 3. Comparison Of Performance of One Xpert MTB/RIF Assay Result vs Two AFB Smears Each Versus MTB Culture in U.S. and non-U.S. Subjects

		Culture		
		Positive	Negative	Total
Xpert	Positive	175	10	185
	Negative	40	735	775
	Total	215	745	960
Sensitivity:		81.4% (95% CI: 75.7, 86.0)		
Specificity:		98.7% (95% CI: 97.5, 99.3)		
U.S. prevalence		14.2% (95% CI: 11.7, 17.2)		
PPV:		94.9% (95% CI: 87.7, 98.0)		
NPV:		97.6% (95% CI: 95.9, 98.6)		
Non-U.S. prevalence		37.1% (95% CI: 32.2, 42.4)		
PPV		94.3% (95% CI: 88.2, 97.4)		
NPV		88.6 (95% CI: 83.9, 92.0)		

		Culture		
		Positive	Negative	Total
AFB Smear	Positive	131	18	149
	Negative	84	727	811
	Total	215	745	960
Sensitivity:		60.9% (95% CI: 54.1, 67.5)		
Specificity:		97.6% (95% CI: 96.2, 98.6)		
U.S. prevalence		14.2% (95% CI: 11.7, 17.2)		
PPV:		77.2% (95% CI: 66.8, 85.1)		
NPV:		95.0% (95% CI: 92.8, 96.5)		
Non-U.S. Prevalence:		37.1% (95% CI: 32.2, 42.4)		
PPV		100% (95% CI: 94.8, 100)		
NPV		79.0% (95% CI: 73.8, 83.5)		

In U.S. subjects, the NPV for one Xpert MTB/RIF Assay result was 97.6% (95% CI: 95.9%, 98.6%) while the NPV for two AFB smears results was 95.0% (95% CI: 92.8%, 96.5%) with a prevalence of TB in U.S. subjects of 14.2%. The difference in NPVs was 2.6% with 95% CI: 1.2%, 4.2%.

Two Xpert MTB/RIF Assay Results as Predictive of Results of Serial Fluorescent Stained AFB Smears

Tables 4 and 5 present the overall performance of two Xpert MTB/RIF Assay results compared to the results of MTB culture, stratified by AFB smear result (Table 4). Table 5 compares the performance of two Xpert MTB/RIF Assays versus the composite result of two AFB smears in U.S. and non-U.S. subjects (N=980).

Overall sensitivity of two Xpert MTB/RIF Assay results in AFB smear-positive and AFB smear-negative subjects based on two AFB smears was 100.0% (95% CI: 97.2%, 100.0%) and 69.4% (95% CI: 59.0%,78.2% respectively, and the overall specificity was 97.9% (95% CI: 96.6%, 98.7%). No MTB culture-positive/AFB smear-positive results were observed in subjects with two serial negative Xpert MTB/RIF Assay results.

Table 4. Performance of Two Xpert MTB/RIF Assay Results Stratified by Two AFB Smears Relative to MTB Culture in U.S. and non-U.S. Subjects

		Culture						
		Positive			Negative			Total
		AFB Smear +	AFB Smear -	Overall Culture +	AFB Smear +	AFB Smear -	Overall Culture -	
Xpert MTB/RIF Assay	Positive	133	59	192	1	15	16[a]	208
	Negative	0	26	26	17	729	746	772
	Total	133	85	218	18[b]	744	762	980

Performance of Xpert MTB/RIF Assay for Smear Positive:
Sensitivity: 100% (133/133), 95% CI: 97.2%, 100%
Specificity: 94.4% (17/18), 95% CI: 74.2%, 99.0%

Performance of Xpert MTB/RIF Assay for Smear Negative:
Sensitivity: 69.4% (59/85), 95% CI: 59.0%, 78.2%
Specificity: 98.0% (729/744), 95% CI: 96.7%, 98.8%

Prevalence of MTB Culture Positive: 22.2% (218/980)
Prevalence of MTB Culture Positive in U.S. subjects: 14.4% (91/633)
Prevalence of MTB Culture positive in non-U.S. subjects: 36.6% (127/347)

Percent of AFB smear positive subjects among subjects with an MTB Culture Positive Result: 61.0% (133/218)

Probability of MTB Culture Positive among subjects with Xpert MTB/RIF Negative Results: 3.4% (26/772), 95% CI: 2.3%, 4.9%
Probability of MTB Culture Positive among subjects with Xpert MTB/RIF Negative Results (U.S. subjects): 1.5% (8/544), 95% CI: 0.7%, 2.9%
Probability of MTB Culture Positive among subjects with Xpert MTB/RIF Negative Results (non-U.S. subjects): 7.9% (18/228), 95% CI: 5.1%, 12.1%

Probability of MTB Culture Positive and AFB smear positive among subjects with Xpert MTB/RIF Negative Results: 0% (0/772), 95% CI: 0.0%, 0.5%
Probability of MTB Culture Positive and AFB smear positive among subjects with Xpert MTB/RIF Negative Results (U.S. subjects): 0% (0/544), 95% CI: 0.0%, 0.7%
Probability of MTB Culture Positive and AFB smear positive among subjects with Xpert MTB/RIF Negative Results (non-U.S. subjects): 0.0% (0/228), 95% CI:0.0%, 1.7%

[a] Of the 16 MTB culture-negative specimens that were positive by Xpert MTB/RIF Assay, 6 grew non-tuberculosis mycobacteria (NTM). MTB-complex was isolated and identified using standard of care methods not associated with the study protocol in 4 of the 6 specimens.
[b] Of the 18 MTB culture-negative/AFB smear-positive specimens, 14 grew NTM.

Table 5 compares performance of two Xpert MTB/RIF Assay Results and two AFB Smears to MTB Culture. Xpert MTB/RIF Assay results identified 88.1% (95% CI: 83.1%, 91.7%) of MTB culture-positive subjects compared to 61.0% (95% CI:54.4%, 67.2%) two AFB smears.

Table 5. Comparison Of Performance of Two Xpert MTB/RIF Assay Results vs Two AFB Smears Each Versus MTB Culture in U.S. and non-U.S. Subjects

Two Xpert MTB/RIF Assay Results		Culture		
		Positive	Negative	Total
Xpert	Positive	192	16	208
	Negative	26	746	772
	Total	218	762	980
Sensitivity:		88.1% (95% CI: 83.1, 91.7)		
Specificity:		97.9% (95% CI: 96.6, 98.7)		
U.S. prevalence		14.4% (95% CI: 11.9, 17.3)		
PPV:		93.3% (95% CI: 86.1, 96.9)		
NPV:		98.5% (95% CI: 97.1, 99.3)		
Non-U.S. prevalence		36.6% (95% CI: 31.7, 41.8)		
PPV		91.6% (95% CI: 85.2, 95.4)		
NPV		92.1 (95% CI: 87.9, 94.9)		

Two AFB Smears		Culture		
		Positive	Negative	Total
AFB Smear	Positive	133	18	151
	Negative	85	744	829
	Total	218	762	980
Sensitivity:		61.0% (95% CI: 54.4, 67.2)		
Specificity:		97.6% (95% CI: 96.3, 98.5)		
U.S. prevalence		14.4% (95% CI: 11.9, 17.3)		
PPV:		77.8% (95% CI: 67.6, 85.5)		
NPV:		94.9% (95% CI: 92.8, 96.5)		
Non-U.S. prevalence		36.6% (95% CI: 31.7, 41.8)		
PPV		100% (95% CI: 94.8, 100)		
NPV		79.4% (95% CI: 74.3, 83.8)		

In U.S. subjects, the NPV for two Xpert MTB/RIF Assay results was 98.5% (95% CI: 97.1%, 99.3%) while the NPV for two AFB smears results was 94.9% (95% CI: 92.8%, 96.5%) when the prevalence of TB in the U.S. subjects was 14.4%.

Detailed information of Xpert MTB/RIF Assay performance as compared to AFB smears with regard to time between collection of sputum specimens in U.S. subjects is presented in Table 6.

Table 6. Xpert MTB/RIF Assay Performance vs AFB Smear Microscopy Relative to Collection Time Between Sputum Specimens

Xpert Results	AFB Smear Results
One Xpert Result **Sensitivity = 85.2% (75/88)** Specificity = 99.2% (526/530) Prevalence = 14.2% (88/618) NPV =97.6% (526/539) Probability of MTB culture-positive/AFB smear-positive subjects among Xpert MTB/RIF negative results =0.4% (2/539)	Data not analyzed for one AFB smear.
Two Xpert Results **Sensitivity = 91.2% (83/91)** Specificity = 98.9% (536/542) Prevalence = 14.4% (91/633) NPV=98.5% (536/544) Probability of MTB culture-positive/AFB smear-positive subjects among Xpert MTB/RIF Assay negative results =0.0% (0/544)	**Two AFB Smear Results** **Sensitivity =69.2% (63/91)** Specificity = 96.7% (524/542) Prevalence = 14.4% (91/633) NPV = 94.9% (524/552)

Xpert Results	AFB Smear Results
Two Xpert Results with two sputum specimens collected ≥8 hours apart[a] **Sensitivity = 92.5% (49/53)** Specificity = 98.9% (342/346) Prevalence = 13.3% (53/399) NPV = 98.9% (342/346) Probability of MTB culture-positive/AFB smear-positive subjects among Xpert MTB/RIF Assay negative results =0.0%	**Two AFB Smear Results with two specimens collected ≥8 hours apart**[a] **Sensitivity = 71.7% (38/53)** Specificity = 98.0% (339/346) Prevalence = 13.3% (53/399) NPV = 95.8% (339/354)
Two Xpert Results with two specimens collected <8 hours apart[b] **Sensitivity = 89.5% (34/38)** Specificity = 99.0% (194/196) Prevalence = 16.2% (38/234) NPV = 98.0% (194/198) Probability of MTB culture-positive/AFB smear-positive subjects among Xpert MTB/RIF Assay negative results =0.0%	**Two AFB Smear Results with two specimens collected <8 hours apart**[b] **Sensitivity = 65.8% (25/38)** Specificity = 99.4% (185/196) Prevalence = 16.2% (38/234) NPV = 93.4% (185/198)
No subjects had three specimens tested by the Xpert MTB/RIF Assay.	**Three AFB Smear Results** **Sensitivity = 60.4%** (29/48) Specificity = 96.6% (284/294) Prevalence = 14.0% (48/342) NPV = 93.7% (284/303)
	Three AFB Smear Results with three specimens collected ≥8 hours apart[c] **Sensitivity = 69.2%** (9/13) Specificity = 95.7% (112/117) Prevalence = 10.0% (13/130) NPV = 96.6% (112/116)
	Three AFB Smear Results with three specimens collected <8 hours apart[d] **Sensitivity = 57.1%** (20/35) Specificity = 97.2% (172/177) Prevalence = 16.5% (35/212) NPV = 92.0% (172/187)

[a]The time frame between the collection of the first sputum specimen and the second sputum specimen is greater than or equal to 8 hours.

[b]The time frame between the collection of the first sputum specimen and the second sputum specimen is less than 8 hours.

[c]The time frame between the collection of the first sputum specimen and the second sputum specimen was greater than or equal to 8 hours, and the time frame between the collection of the second sputum specimen and the third sputum specimen was greater than or equal to 8 hours.

[d]Three AFB smears with less than 8 hour means that at least one of the time intervals between specimen collection was less than 8 hours apart.

Xpert MTB/RIF Assay Performance in an HIV Population

To compare performance of the Xpert MTB/RIF Assay in HIV-infected and HIV-uninfected subjects, data from Study 2 were analyzed by smear status of specimens and HIV status of the population. Tables 7 and 8 compare the sensitivities and specificities of one Xpert MTB/RIF Assay result in specimens obtained from HIV-infected and HIV-uninfected subjects stratified by AFB smear-positive and AFB smear-negative results, respectively. For both HIV-infected and HIV-uninfected subjects, the sensitivity of the Xpert MTB/RIF Assay for detection of MTB-complex was higher in AFB smear-positive specimens (100.0% and 97.8%, respectively) than in AFB smear-negative specimens (52.1% and 58.3%, respectively). These data are summarized in Table 8.

Table 7. Comparison of Sensitivity and Specificity of One Xpert MTB/RIF Assay Result in HIV-Infected and HIV-Uninfected Subjects – AFB Smear Positive Only

Xpert MTB/RIF	Overall	HIV-infected	HIV-uninfected	Difference (95% CI)
Sensitivity	98.5% (129/131)	100% (39/39)	97.8% (90/92)	2.2% (-0.8%, 5.2%)
Specificity	94.4% (17/18)	100% (7/7)	90.9% (10/11)	9.1% (-7.9%, 26.1%

Table 8. Comparison of Sensitivity and Specificity of One Xpert MTB/RIF Assay Result in HIV-Infected and HIV-Uninfected Subjects – AFB Smear Negative Only

Xpert MTB/RIF	Overall	HIV-infected	HIV-uninfected	Difference (95% CI)
Sensitivity	54.8% (46/84)	52.1% (25/48)	58.3% (21/36)	-6.3% (-27.7%, 15.2%)
Specificity	98.8% (718/721)	98.2% (332/338)	99.2% (386/389)	-1.0% (-2.7%, 0.7%)

4. Clinical cut-off**:**

   Not applicable

5. Expected values/Reference range:

   The likelihood that a positive test result is a true positive will vary based on the prevalence of the tuberculosis in the population being tested and whether the AFB smear is positive or negative.

   In two multicenter prospective clinical evaluations of Xpert MTB/RIF Assay performance in subjects in the United States with suspected active TB, overall prevalence of culture-confirmed disease was 13.2%. Of subjects with culture confirmed TB, 71.6% were AFB smear-positive.

Predictive Values for One Xpert MTB/RIF Assay Result

Hypothetical estimated positive and negative predictive values of MTB detection for different prevalence rates for detecting MTB using the Xpert MTB/RIF Assay are shown in Table 9. These calculations are based on hypothetical prevalences and the overall sensitivity and specificity (when compared to culture) observed in the multi-center clinical studies. The sensitivity of the Xpert MTB/RIF Assay for AFB smear-positive specimens was 99.4% (479/482) and sensitivity for AFB smear-negative specimens was 67.2% (135/201). Overall specificity of Xpert MTB/RIF Assay was 98.7% (1355/1373). The prevalence of MTB was 11.8% in the first U.S. prospective study and 14.2% in the second prospective U.S. study.

Table 9. Hypothetical Predictive Values of One Xpert MTB/RIF Assay Result vs. MTB Culture

Prevalence of MTB Culture Positive	Probability of MTB Culture Positive Among		Probability of MTB Culture Negative Among
	Xpert MTB/RIF DETECTED AFB Smear Pos.	Xpert MTB/RIF DETECTED AFB Smear Neg.	Xpert MTB/RIF NOT DETECTED
1%	89.69%	13.67%	99.90%
2%	94.61%	24.24%	99.80%
3%	96.38%	32.65%	99.70%
4%	97.29%	39.51%	99.59%
5%	97.84%	45.20%	99.48%
10%	98.97%	63.52%	98.91%
11.8%	99.14%	67.71%	98.70%
14.2%	99.30%	72.18%	98.39%
20%	99.54%	79.67%	97.59%
40%	99.83%	91.27%	93.82%
50%	99.88%	94.00%	91.01%

Predictive Values Based on Two Xpert MTB/RIF Assay Results

Hypothetical estimated positive and negative predictive values of MTB detection for different prevalence rates for detecting MTB using two Xpert MTB/RIF Assay results are shown in Table 10. These calculations are based on hypothetical prevalence and the overall sensitivity and specificity (when compared to culture) observed in the second of the two multi-center studies where two Xpert MTB/RIF Assays were performed on each subject. The sensitivity of two Xpert MTB/RIF Assay results for AFB smear-positive specimens was 100% (133/133) and the sensitivity for AFB smear-negative specimens was 69.4% (59/85). Overall specificity of two Xpert MTB/RIF Assay results was 97.9% (746/762).

Table 10. Hypothetical Predictive Values of Two Xpert MTB/RIF Assay Results vs. MTB Culture[a]

Prevalence of MTB Culture Positive	Probability of MTB Culture Positive Among		Probability of MTB Culture Negative Among
	Two Xpert MTB/RIF DETECTED, AFB Smear Pos.	Two Xpert MTB/RIF DETECTED AFB Smear Neg.	Two Xpert MTB/RIF NOT DETECTED
1%	84.40%	9.19%	99.91%
2%	91.62%	16.98%	99.82%
3%	94.31%	23.66%	99.72%
4%	95.71%	29.46%	99.63%
5%	96.57%	34.54%	99.53%
10%	98.35%	52.69%	99.02%
11.8%	98.62%	57.28%	98.82%
14.2%	98.88%	62.39%	98.54%
20%	99.26%	71.48%	97.81%
40%	99.72%	86.98%	94.37%
50%	99.81%	90.93%	91.79%

[a]Sensitivity of 100% for two Xpert MTB/RIF assay results for AFB smear positive subjects was considered as 99.9% in this table.

N. Instrument Name:

GeneXpert® Instrument Systems to include the following instruments:

- GeneXpert® Dx
- GeneXpert® Infinity-48
- GeneXpert® Infinity-48s
- GeneXpert® Infinity-80

O. System Descriptions:

Refer to K131706 for a complete description of the GeneXpert Instrument Systems.

1. Modes of Operation:

   Does the applicant's device contain the ability to transmit data to a computer, webserver, or mobile device?

   Yes __**X**__ or No _____

   Does the applicant's device transmit data to a computer, webserver, or mobile device using wireless transmission?

   Yes _____ or No ____**X**____

2. Software:

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

   Yes __**X**__ or No _____

   Refer to K131706 for a complete description of the GeneXpert Instrument Systems software.

3. Specimen Identification:

   Barcode

4. Specimen Sampling and Handling:

   Refer to K131706 for a complete description of the GeneXpert Instrument Systems specimen sampling and handling.

5. Calibration:

   Refer to K131706 for a complete description of the GeneXpert Instrument Systems calibration.

6. Quality Control:

   Refer to K131706 for a complete description of the GeneXpert Instrument Systems quality control.

P. Other Supportive Instrument Performance Characteristics Data Not Covered In The "Performance Characteristics" Section above:

Shelf-Life Testing Update:

The Xpert MTB/RIF Assay shelf-life studies have demonstrated acceptable stability using real-time stability results and linear regression analysis for a shelf-life of 24 months when reagents and cartridges are stored at 2-28°C.

The shelf-life stability of the product was evaluated at four temperatures (5°± 3°C, 25° ± 3°C, 35º ± 3°C, and 45º ± 3°C) at predefined time points up to 36 months, following the study plan described in the 510k submission. At the 24 month time point and subsequent time points, the storage condition at 25° ± 3°C was changed to 30° ± 3°C and the storage condition of 35º ± 3°C was changed to 37º ± 2°C.

Refer to K131706 for a complete description of the Xpert MTB/RIF Assay open package stability study results.

Q. Proposed Labeling:

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

R. Conclusion:

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