Test Technical Training: Xpert® MTB/XDR

CE IVD In Vitro Diagnostic Medical Device

302-3807 July 2022 Rev. D

CE-IVD. *In Vitro* Diagnostic Medical Device. May not be available in all countries. Not available in the United States.

Training Agenda

Xpert® MTB/XDR

1. Reagents
2. Sample collection
3. Kit storage and handling
4. Preparing the cartridge
5. Quality controls
6. Results analysis
7. Discussion

Training Objectives

At the end of the training, users will be able to:

- Properly store and handle the Xpert® MTB/XDR cartridge kit
- Follow proper laboratory safety precautions
- Collect and store appropriate specimen(s)
- Prepare a cartridge and run the Xpert® MTB/XDR test
- Report the various software generated results
- Understand the Xpert® MTB/XDR control strategy

The Cepheid Solution

- Simultaneous detection of:
  - **MTB Complex and extensively drug resistance associated mutations**
- On-board internal controls for each sample
  - Sample Volume Adequacy (SVA)
  - Probe Check Control (PCC)
  - Specimen Processing Control (SPC)
- Results in approximately **90 minutes^**
- Closed cartridge system minimizes risk of contamination
- On-demand results
- Random access

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Intended Use

- The Xpert® MTB/XDR test, performed on the GeneXpert® Instrument Systems, is a qualitative, nested real-time polymerase chain reaction (PCR) *in vitro* diagnostic test for the detection of **extensively drug resistant (XDR)** *Mycobacterium tuberculosis* (MTB) complex DNA in unprocessed sputum samples, concentrated sediments prepared from sputum, or BD™ Mycobacterial Growth Indicator Tube (MGIT™) culture.
- In specimens where MTB is detected, the Xpert® MTB/XDR test can also detect isoniazid (**INH**) resistance associated mutations in the *katG* and *fabG1* genes, *oxyR-ahpC* intergenic region and *inhA* promoter; ethionamide (**ETH**) resistance associated with *inhA* promoter mutations only; fluoroquinolone (**FLQ**) resistance associated mutations in the *gyrA* and *gyrB* quinolone resistance determining regions (QRDR); and second line injectable drug (**SLID**) associated mutations in the *rrs* gene and the *eis* promoter region.
- The Xpert MTB/XDR test is intended for use as a **reflex test** for a specimen (unprocessed sputum, concentrated sputum sediments, or MGIT culture) that is determined to be MTB positive.
- This test is intended as an aid in the diagnosis of XDR tuberculosis (TB) when used in conjunction with clinical and other laboratory findings.

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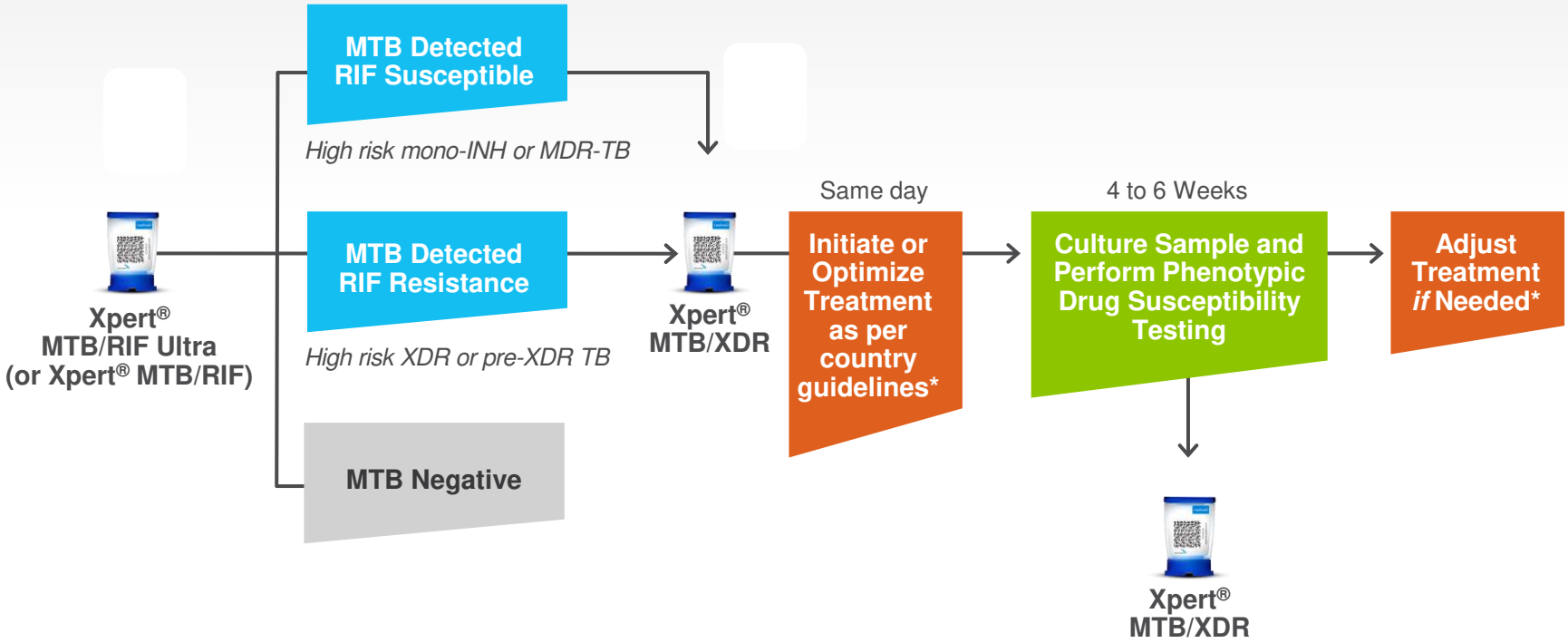
Resistance Associated Mutations Detected

In MTB positive samples, the Xpert® MTB/XDR Assay has been designed to detect:

- **isoniazid (INH)** resistance associated mutations in the *katG* and *fabG1* genes, *oxyR-ahpC* intergenic region and *inhA promoter*
- **ethionamide (ETH)** resistance associated with *inhA promoter* mutations only
- **fluoroquinolone (FLQ)** resistance associated mutations in the *gyrA* and *gyrB* quinolone resistance determining regions (QRDR)
- **second line injectable drug (SLID)** resistance associated mutations in *rrs* gene and the *eis promoter* region

Diagnostic Algorithm Using Xpert® MTB/XDR



*This test is intended as an aid in the diagnosis of XDR tuberculosis (TB) when used in conjunction with clinical and other laboratory findings.
Please refer to Xpert® MTB/RIF, Xpert® MTB/RIF Ultra package inserts for exact turnaround time

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Targets and Probes

Targets

- 1 target, *inhA promoter*, for TB detection, “low INH” and ETH resistance detection
- 7 additional targets for additional drug resistance detection
- 1 SPC target (used as internal control)

Probes

- 10 mismatch tolerant sloppy molecular beacon probes to identify mutations with the same technology as Xpert® MTB/RIF Ultra*
- 1 probe for the SPC

Assay method

- The assay method relies on melt curves only
- This method of analysis looks at specific melting temperatures (Tm) allowing the differentiation between wild type and mutant sequences

10-colour module with blue line

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Xpert® MTB/XDR Resistance Detection

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Gene Targets and Mutations for Xpert® MTB XDR

Gene	Detection
inhA Promoter	Specifically detect high- and low-level resistance to Isoniazid (INH)
katG	
fabG1	
oxyR-ahpC Intergenic Region	
gyrA	Specifically detect low-R and high-R associated mutations for Fluoroquinolones (FLQ)
gyrB	
rrs	Differentiate between cross-resistance and individual resistance for Second Line Injectable Drugs (SLID)
Eis P	

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Xpert® MTB/XDR Test Requirements

GeneXpert® Dx System

- Full 10-colour GeneXpert® system (all modules identified with a blue line on the door) with **Dx Software v6.2 or higher**

Test Kits

- GXMTB/XDR-10

Materials Required but not Provided

- Leak-proof, sterile screw-capped collection containers.
- Personal Protective Equipment (PPE).
- 1:10 Bleach.
- 70% ethanol or denatured ethanol

Optional

- Uninterruptible Power Supply/ Surge Protector
- Printer

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Good Laboratory Practice Review

Personal Protective Equipment (PPE)	• Wear clean lab coats, safety glasses, and gloves • Change gloves between processing samples
Lab Bench Area	• Clean work surfaces routinely with: ✓ 1:10 dilution of household bleach* ✓ 70% Ethanol Solution • After cleaning, ensure work surfaces are dry
Specimens, Samples, and Kits Storage	• Store specimens and samples away from the kits to prevent contamination
Equipment	• Use filtered pipette tips when recommended • Follow the manufacturer's requirements for calibration and maintenance of equipment

* Final active chlorine concentration should be 0.5% regardless of the household bleach concentration in your country.

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Kit Handling

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Xpert® MTB/XDR Kit Contents

Xpert® MTB/XDR Kit	
Catalog Number	GXMTB/XDR-10
Cartridges per Kit	10
Reagent Vials	10
Kit CD	Assay Definition File (ADF) Assay Import Instructions Package Insert (PDF)
Storage	2–28°C
Disposable transfer pipettes	1bag of 12/kit

Cartridges contain chemically hazardous substances-please see Package Insert and Safety Data Sheet for more detailed information.

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Warnings and Precautions

- Treat all biological specimens, including used cartridges, as if capable of transmitting infectious agents. Because it is often impossible to know which might be infectious, all biological specimens should be treated with standard precautions.

- Guidelines for specimen handling are available from the U.S. Centers for Disease Control and Prevention3 and the Clinical and Laboratory Standards Institute.[6,7,8]

- Follow your institution's safety procedures for working with chemicals and handling biological samples.

- Wear protective disposable gloves, laboratory coats and eye protection when handling specimens and reagents. Wash hands thoroughly after handling specimens and test reagents.

6. Centers for Disease Control and Prevention. Biosafety in microbiological and biomedical laboratories. Chosewood, LC and Wilson, DE (eds) (2009). HHS Publication number (CDC) 21-1112.

7. Clinical and Laboratory Standards Institute (formerly National Committee for Clinical Laboratory Standards). Protection of laboratory workers from occupationally acquired infections; Approved Guideline. Document M29 (refer to latest edition).

8. Clinical and Laboratory Standards Institute (formerly National Committee for Clinical Laboratory Standards). Laboratory Detection and Identification of Mycobacteria; Document M48A(refer to latest edition).

Warnings and Precautions (continued)

- Biological specimens, transfer devices, and used cartridges should be considered capable of transmitting infectious agents requiring standard precautions. Follow your institution's environmental waste procedures for proper disposal of used cartridges and unused reagents. These materials may exhibit characteristics of chemical hazardous waste requiring specific national or regional disposal procedures. If national or regional regulations do not provide clear direction on proper disposal, biological specimens and used cartridges should be disposed per WHO [World Health Organization] medical waste handling and disposal guidelines[9]

- Sample Reagent contains sodium hydroxide (pH > 12.5) and isopropanol. Harmful if swallowed (H302), causes severe skin burns and eye damage (H314). Flammable liquid and vapor (H226).

9. REGULATION (EC) No 1272/2008 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 16 December 2008 on the classification labeling and packaging of substances and mixtures amending and repealing, List of Precautionary Statements, Directives 67/548/EEC and 1999/45/EC (amending Regulation (EC) No 1907/2007)

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Warnings and Precautions (continued)

- Performance characteristics of this test have been established with the specimen types listed in the Intended Use section only. The performance of this test with other specimen types or samples has not been evaluated.
- Follow your institution's safety procedures for working with chemicals and handling biological samples.
- Specimen collection and handling procedures require specific training and guidance.
- Maintain proper storage conditions during specimen transport to ensure the integrity of the specimen. Specimen stability under shipping conditions other than those recommended has not been evaluated.

Warnings and Precautions (continued)

- Reject specimens with obvious food particles or other solid particulates.
- Proper sample collection, storage, and transport are essential for correct results.
- Culture material from a positive MGIT culture bottle may either be used undiluted or diluted 100-fold with PBS or Middlebrook 7H9 media. The test may also be performed with heat inactivated cultures. For heat inactivation, it is recommended that the culture is first diluted 100-folds with PBS or Middlebrook 7H9 media and then heated at 100˚C for 20 minutes.

Warnings and Precautions (continued)

- Do not substitute Xpert® MTB/XDR test reagents with other reagents.
- Do not open the Xpert® MTB/XDR test cartridge lid except when adding sample.
- Do not use a cartridge that has been dropped after removing from the kit or shaken after the cartridge lid has been opened. Shaking or dropping the cartridge after opening the lid may yield false or non-determinate results.
- Do not place the sample ID label on the cartridge lid or on the barcode label.
- Do not use a cartridge that has a damaged reaction tube.
- Each single-use Xpert® MTB/XDR test cartridge is used to process one test.
- Do not reuse spent cartridges.

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Warnings and Precautions (continued)

- A single-use disposable pipette is used to transfer one specimen.
- Do not reuse spent disposable pipettes.
- Do not use a cartridge if it appears wet or if the lid seal appears to have been broken.
- Good laboratory practices, including changing gloves between handling patient specimens, are recommended to avoid contamination of specimens or reagents.
- In the event of a spill of specimens or controls, wear gloves and absorb the spill with paper towels. Then, thoroughly clean the contaminated area with a 1:10 dilution of freshly prepared household chlorine bleach. Final active chlorine concentration should be 0.5% regardless of the household bleach concentration in your country. Allow a minimum of two minutes of contact time..

Warnings and Precautions (continued)

- Ensure the work area is dry before using 70% denatured ethanol to remove bleach residue. Allow surface to dry completely before proceeding. Or, follow your institution's standard procedures for a contamination or spill event. For equipment, follow the manufacturer's recommendations for decontamination of equipment.
- The Xpert® MTB/XDR test has been validated using Cepheid GeneXpert® Dx software version 6.2 or higher

Sample Collection, Storage, and Transport

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Sputum Sample Collection

- Collect sputum following your institution's standard procedures.
- Best time to produce sputum: As soon as patient wakes up in the morning
- Sputum should not contain any contain food particles
- Container must be tightly closed after collection

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Sample Collection, Transport and Storage

Sample Type	Volume	Transportation	Storage Conditions
Unprocessed Sputum	1–4 mL	2–35°C	7 days up to 35°C
Sputum Sediment (Re-suspended in 67mM Phosphate/H_20 Buffer)	0.5–2.5 mL	2–8°C	2–8°C up to 7 days
Leftover Specimens Treated with Sample Reagent Buffer	≥2.0 ml	x	35°C up to 2.5 hours 2–8°C up to 4 hours

- Collect sputum following your institution's standard procedures
- Do not accept samples with obvious food particles or other solid particles

Please refer to package insert for detailed instructions.

Cartridge Preparation

Proper Cartridge Handling Techniques

Correct

- Do not touch the reaction tube
- Keep the cartridge upright
- Do not tilt after sample is added

Incorrect

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Cartridge Preparation
Unprocessed Sputum

Xpert® Cartridge Preparation - Unprocessed Sputum

- Xpert MTB/RIF
- Xpert MTB/RIF Ultra
- Xpert MTB/XDR

Refer to the package insert for detailed instructions, precautions, and warnings.

For a copy of the SDS, visit www.cepheid.com or www.cepheidinternational.com
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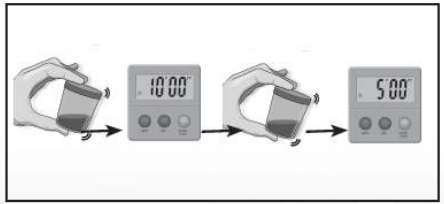
Cepheid
A better way.

1 Obtain one Xpert cartridge, sample reagent (SR), and sputum collection container for each sample.

2 Estimate volume of sputum. Add 2 parts of SR to 1 part of sputum. Replace container lids.

Note: Minimum sputum volume for one test is 1mL.

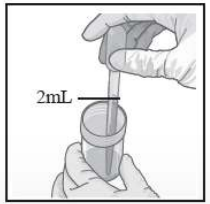
3
- Shake vigorously 10 to 20 times or vortex for at least 10 seconds.
- Incubate at room temperature for 10 minutes.
- Shake again vigorously 10 to 20 times or vortex.
- Incubate for another 5 minutes*.



**Shake and incubate an additional 5 minutes if the sample is not completely liquefied.*

4 Write on the side of the cartridge or affix an ID label. Open the cartridge.

5 Aspirate the liquefied sample to just above the line on the pipette.



6 Slowly empty the sample into the sample chamber of the cartridge.

7 Close the lid firmly.

Start the test within the time frame specified in the package insert.

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301-7000, Rev. B May 2021

Cartridge preparation card 301-7000, Rev. B May 2021 Please refer to Xpert MTB-XDR Package Insert, 302-3514 Rev.D. Sept. 2021.

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Cartridge Preparation
Sputum Sediment

Xpert® Cartridge Preparation - Sputum Sediment

- Xpert MTB/RIF Ultra
- Xpert MTB/XDR

Refer to the package insert for detailed instructions, precautions, and warnings.

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Sputum sediment is prepared according to the method of Kent and Kubica[1]

[1]Kent PT, Kubica GP 1985. Public Health Mycobacteriology—A Guide for Level III Laboratory, Centers of Disease Control, Atlanta, Publication no. PB 86-216546

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1 Obtain one Xpert cartridge, sample reagent (SR), and sediment collection container for each sample.

2 Collect at least 0,5mL of resuspended sediment (RS):
- If < 0,7mL: add 3 parts SR to 1 part RS.
- If ≥ 0,7mL: add 2 parts SR to 1 part RS.

3
- Shake vigorously 10 to 20 times or vortex for at least 10 seconds.
- Incubate at room temperature for 10 minutes.
- Shake again vigorously 10 to 20 times or vortex.
- Incubate for another 5 minutes

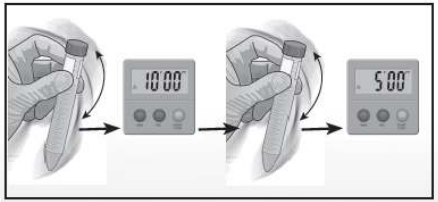
4 Bring the cartridge to room temperature. Write on the side of the cartridge or affix an ID label. Open the cartridge.

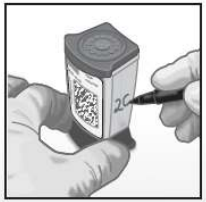
5 Aspirate the liquefied sample just above the line on the pipette.

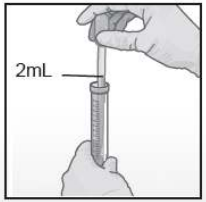
6 Slowly empty the sample into the sample chamber of the cartridge.

7 Close the lid firmly.

Start the test within the time frame specified in the package insert.







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301-7001, Rev. B May 2021

Cartridge preparation card 301-7001, Rev. B May 2021. Please refer to the Xpert® MTB-XDR Package Insert, 302-3514 Rev. D. Sept. 2021

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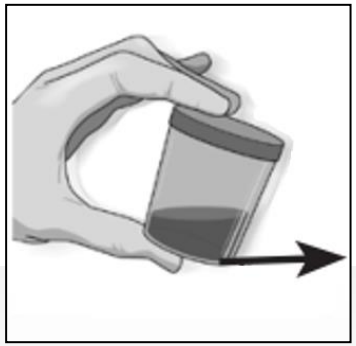
Storage of Leftover Specimens Treated with Sample Reagent Buffer

If the volume of the leftover SR treated specimen is ≥ 2 mL, you can still use the decontaminated liquified sample within:

- 2.5 hours up to 35˚C
- 4 hours if stored at 2˚C–8˚C



The same decontaminated liquified sample prepared for the Xpert® MTB/RIF^ or Xpert® MTB/RIF Ultra* test may be used for the Xpert® MTB/XDR.*

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Cartridge Preparation
Positive MGIT

Xpert® MTB/XDR Cartridge Preparation - Positive MGIT

Refer to the package insert for detailed instructions, precautions, and warnings.

For a copy of the SDS, visit
www.cepheid.com or
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Cepheid Technical Support

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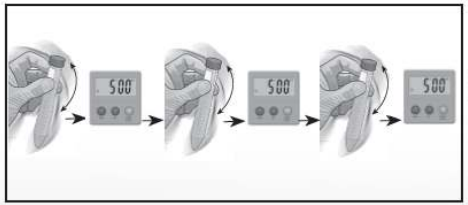
Important Note: The MGIT* culture bottle may be used undiluted or diluted 100 fold with PBS or Middlebrook and/or heat inactivated at 100°C for 20 minutes.

Cepheid. A better way.

1 Obtain one Xpert cartridge, sample reagent (SR), and one tube with 1 mL of inactivated MGIT culture.

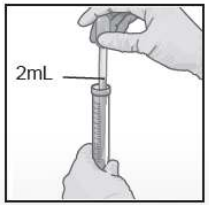
2 Add 2 parts of SR to 1 part inactivated of MGIT culture. The total volume must be at least 2 mL.

3 Incubate at room temperature for 15 minutes. Shake or vortex every 5 minutes to prevent settling.



4 Bring the cartridge to room temperature. Write on the side of the cartridge or affix an ID label. Open the cartridge.

5 Aspirate the liquefied sample just above the line on the pipette.



6 Slowly empty the sample into the sample chamber of the cartridge.

7 Close the lid firmly.

Start the test within the time frame specified in the package insert.

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IMPORTANT NOTE: The MGIT* culture bottle may be used undiluted or diluted 100-fold with PBS or Middlebrook 7H9 media. The test may also be performed with heat inactivated culture at 100°C for 20 minutes.
Refer to the package insert for detailed instructions, precautions, and warnings.

Cartridge preparation card 302-6721, Rev. A May 2021. Please refer to Xpert® MTB-XDR Package Insert, 302-3514 Rev.D. Sept. 2021
BD MGIT (Mycobacteria Growth Indicator Tube; Becton, Dickinson, and Company

Cepheid.

Run a Test

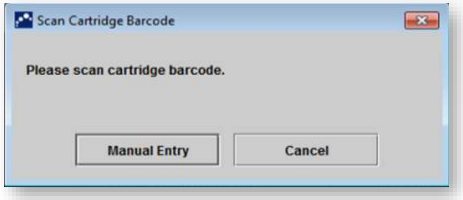
*Before starting the test, make sure the **Xpert® MTB/XDR* assay definition file** is imported into the software.*

1 Create Test.

GeneXpert®

2 Scan barcode messages:

Cartridge/Patient and/or Sample ID



By default, do not click on **Manual Entry** or **Cancel**.

3 Scan the cartridge.

- Unprocessed sputum or sputum sediment: Start the test **within 2.5 hours** of adding SR to the specimen or **within 4 hours if stored at 2–8 °C.**
- MGIT Culture: Start the test **within 30 minutes** of adding SR to the specimen or **within 4 hours if stored at 2–8 °C.**

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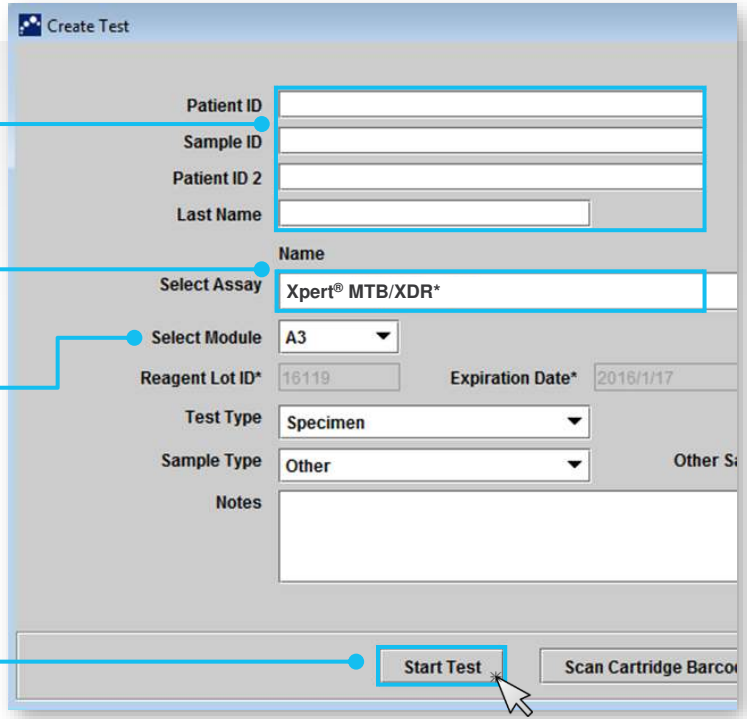
Create a Test on GeneXpert Dx Software

4 Complete the fields as required.

5 The Assay Protocol is selected automatically.

6 The module is selected automatically.

7 Click on Start Test.



8 A green light will flash on the module.

Load the cartridge into module and close the door.

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Automated Xpert® MTB/XDR Protocol

1 The cartridge is loaded into the System.

2 Nucleic acids are purified

3 Purified nucleic acids mix with the PCR reagents

4 PCR Melt Curve Analysis

5 Results are ready to view

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Quality Controls

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CONTROL

Cepheid Control Strategy

- **System Control – Check Status**
  - System control checks the optics, temperature of the module and mechanical integrity of each cartridge.
  - If the system controls fail, an ERROR test result will be reported.

- **Assay Quality Controls**

Each Xpert® cartridge is a self-contained test device

Cepheid designed specific molecular methods to include internal controls that enable the system to detect specific failure modes within each cartridge

  - Sample Volume Adequacy (SVA)
  - Sample Processing Control (SPC)
  - Probe Check Controls (PCC)

Internal Quality Controls

- **Sample Volume Adequacy (SVA)**

- Verifies that the correct sample volume is added to the cartridge

- **Probe Check Controls (PCC)**

Before the PCR step, fluorescence signal is measured on all probes and compared with default factory settings to monitor

- bead rehydration
- reaction tube filling
- probe integrity
- dye stability

- **Sample Processing Controls (SPC)**

non-infectious spore in each cartridge

- Verifies adequate sample processing
- Verifies lysis and presence of the organism and detects PCR inhibition
- Should be positive in a negative sample
- Can be positive or negative in a positive sample

Result Interpretation

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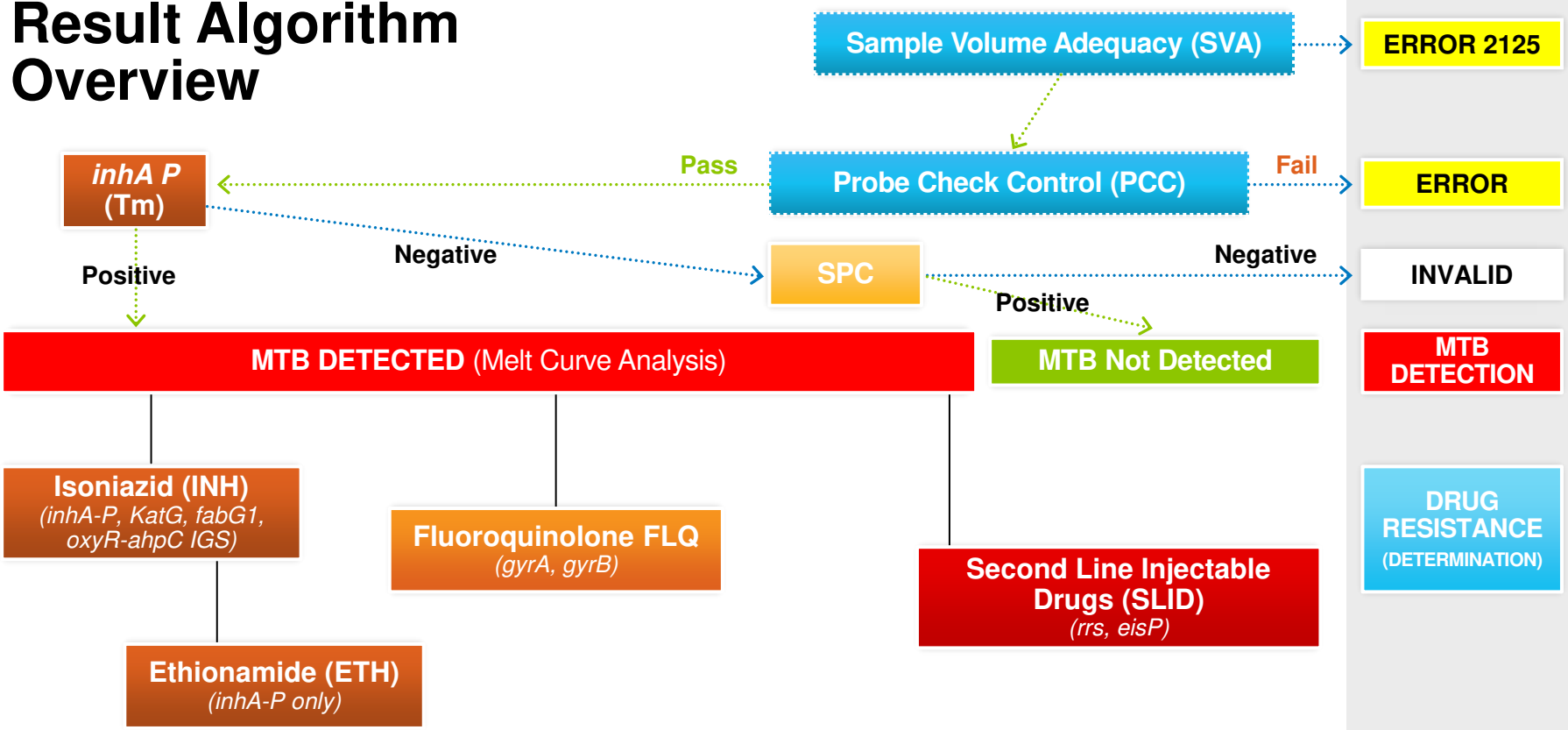
Result Algorithm Overview



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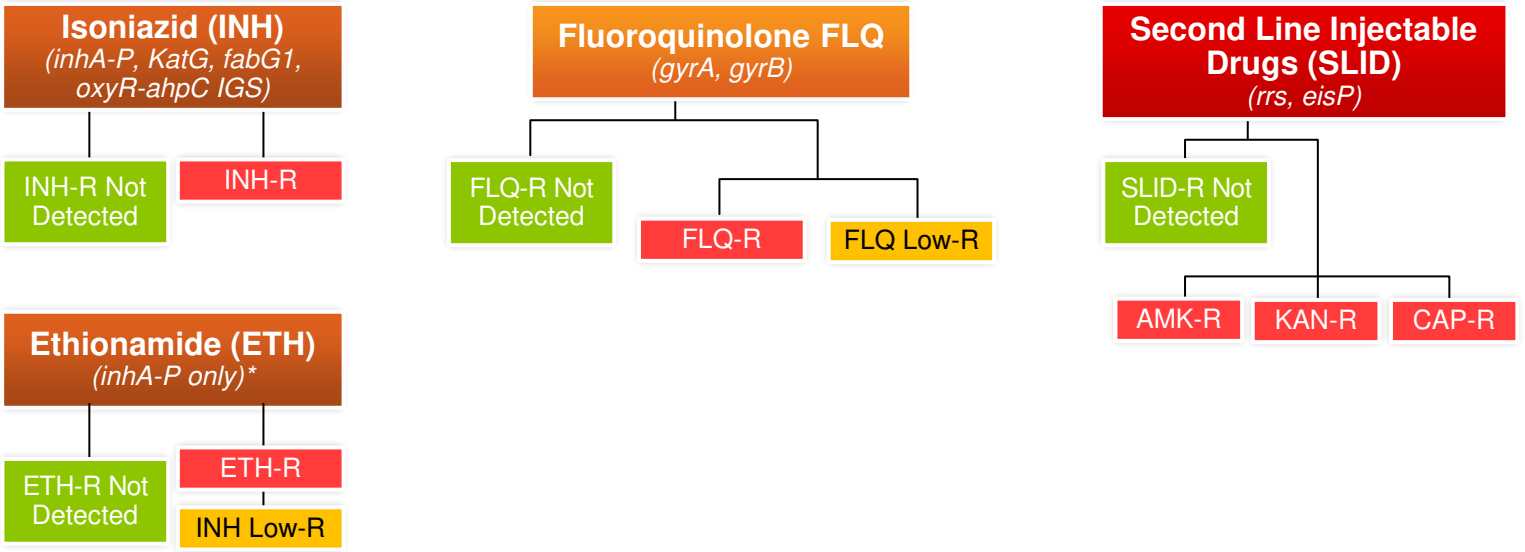
Result Algorithm
Resistance specific



*Warning: The absence of mutations in the *inhA* promoter region does not exclude ETH resistance. Mutations conferring ETH resistance are reported to be present in genomic regions not targeted by the Xpert® MTB-XDR* assay.

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Xpert® MTB/XDR* Assay Result Output Algorithm

Analyte	Tm Detected	WT Tm Detected	MUT Tm Detected
inhA Promoter	MTB Detected	INH-R Not Detected/ ETH-R Not Detected	Low INH-R Detected/ ETH-R Detected
katG		INH-R Not Detected	INH-R Detected
fabG1			
oxyR-ahpC IGR			
gyrA1		FLQ-R Not Detected	Low FLQ-R (specific Tm patterns)/FLQ-R Detected
gyrA2			
gyrA3			
gyrB2			FLQ-R Detected
rrs		AMK/KAN/CAP-R Not Detected	AMK/KAN/CAP-R Detected
eis P		AMK/KAN-R Not Detected	AMK/KAN-R Detected

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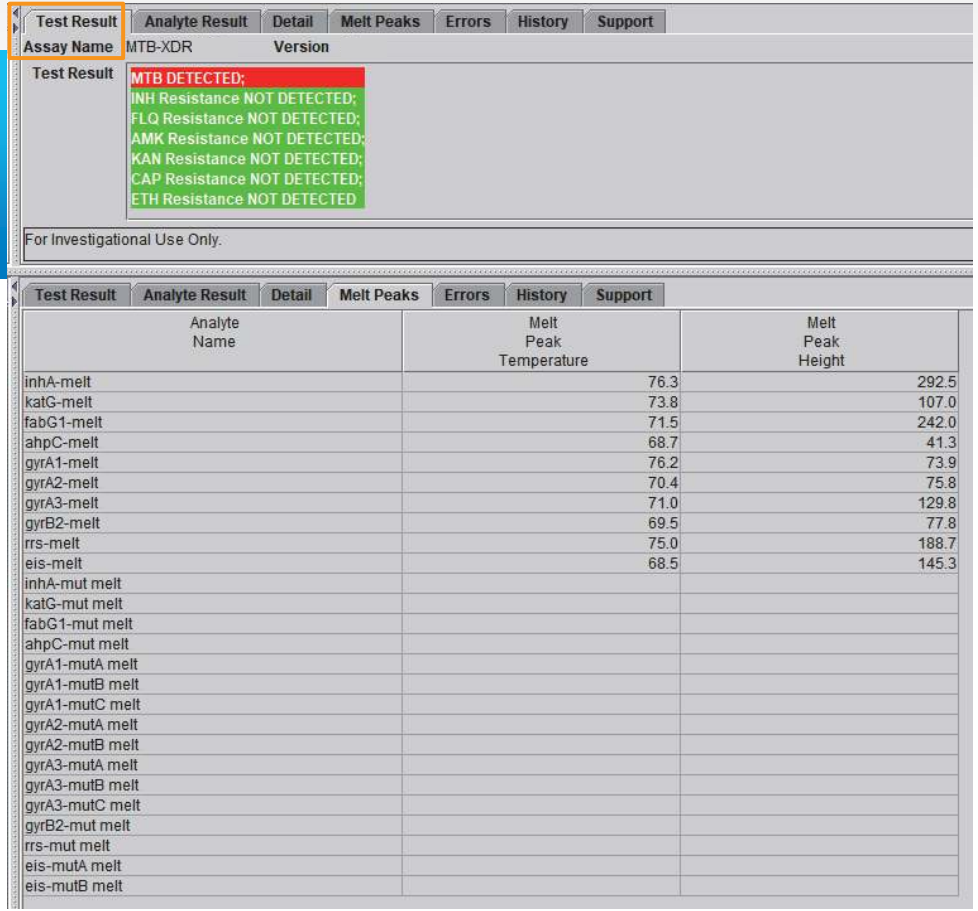
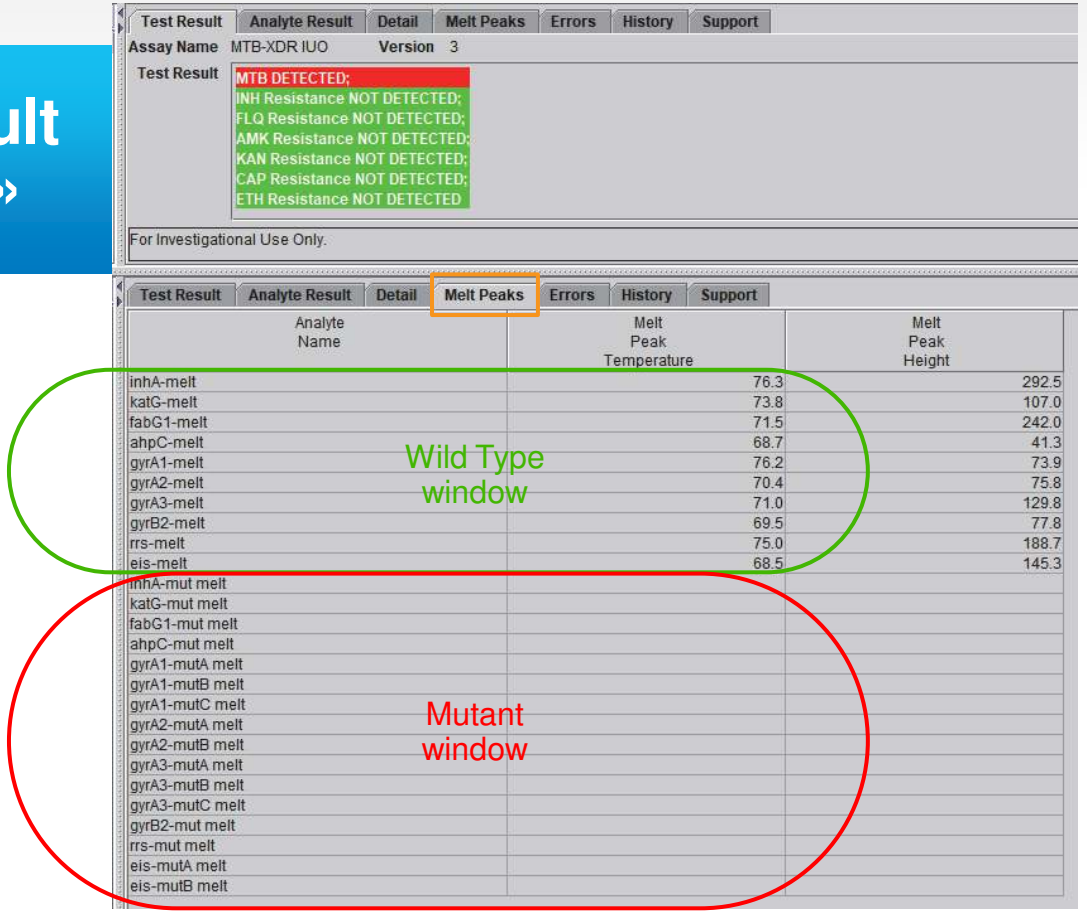
Xpert® MTB/XDR Result Display: « Test Results»



*CE-IVD. In Vitro Diagnostic Medical Device. May not be available in all countries. Not available in the United States.

Xpert® MTB/XDR* Result Display: « Melt Peaks »



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Xpert® MTB/XDR* Result Display: « Melt Peaks »

Test Result | Analyte Result | Detail | **Melt Peaks** | Errors | History | Support

Analyte Name	Melt Peak Temperature	Melt Peak Height
inhA-melt	76.7	185.3
katG-melt	74.0	38.1
fabG1-melt		
ahpC-melt	69.2	31.7
gyrA1-melt	76.5	76.9
gyrA2-melt	70.2	31.1
gyrA3-melt	71.3	66.0
gyrB2-melt	69.9	33.8
rrs-melt	75.3	119.1
eis-melt	68.7	114.5
inhA-mut melt		
katG-mut melt		
fabG1-mut melt		
ahpC-mut melt		
gyrA1-mutA melt		
gyrA1-mutB melt		

No valid Tm for *fabG1*

The absence of Tms for *fabG1* or *oxyR-ahpC IGR* or *gyrB* does not affect the result, provided the other calls in the same group are valid.

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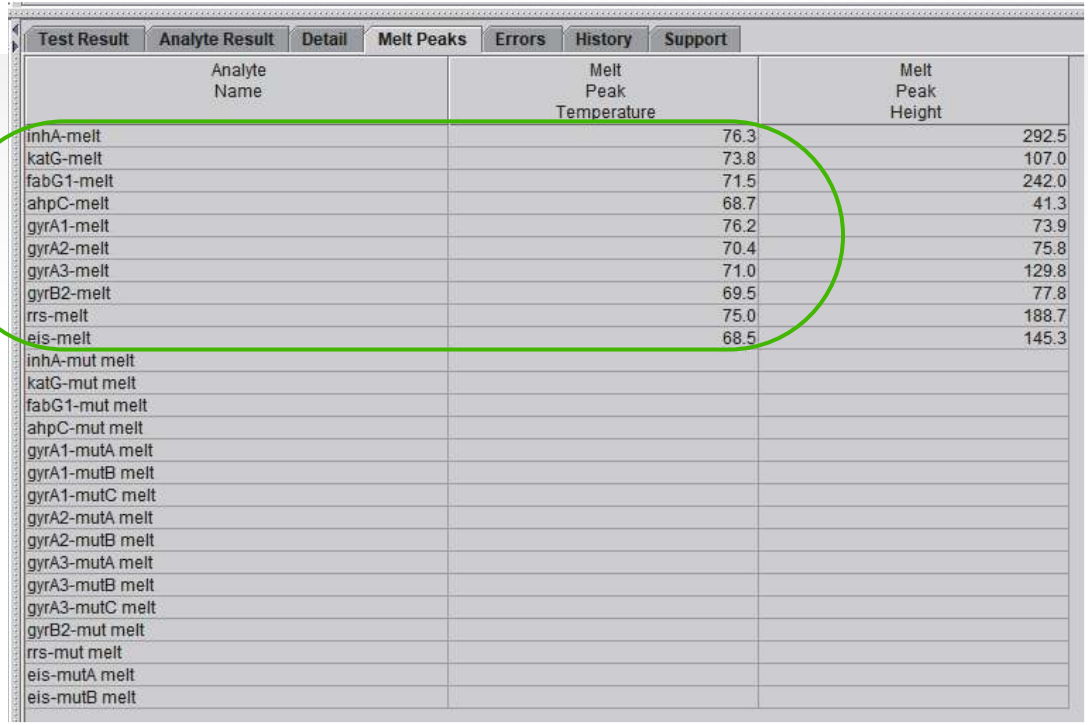
No Resistance Detected



Test Result | Analyte Result | Detail | Melt Peaks | Errors | History | Support

Analyte Name	Melt Peak Temperature	Melt Peak Height
inhA-melt	76.3	292.5
katG-melt	73.8	107.0
fabG1-melt	71.5	242.0
ahpC-melt	68.7	41.3
gyrA1-melt	76.2	73.9
gyrA2-melt	70.4	75.8
gyrA3-melt	71.0	129.8
gyrB2-melt	69.5	77.8
rrs-melt	75.0	188.7
eis-melt	68.5	145.3
inhA-mut melt		
katG-mut melt		
fabG1-mut melt		
ahpC-mut melt		
gyrA1-mutA melt		
gyrA1-mutB melt		
gyrA1-mutC melt		
gyrA2-mutA melt		
gyrA2-mutB melt		
gyrA3-mutA melt		
gyrA3-mutB melt		
gyrA3-mutC melt		
gyrB2-mut melt		
rrs-mut melt		
eis-mutA melt		
eis-mutB melt		

MTB DETECTED

INH Resistance NOT DETECTED

FLQ Resistance NOT DETECTED

AMK Resistance NOT DETECTED

KAN Resistance NOT DETECTED

CAP Resistance NOT DETECTED

ETH Resistance NOT DETECTED

- *InhA* melt peak temperature present—MTB DETECTED
- All melt peak temperatures in the wild type window—no mutation—wild type isolate

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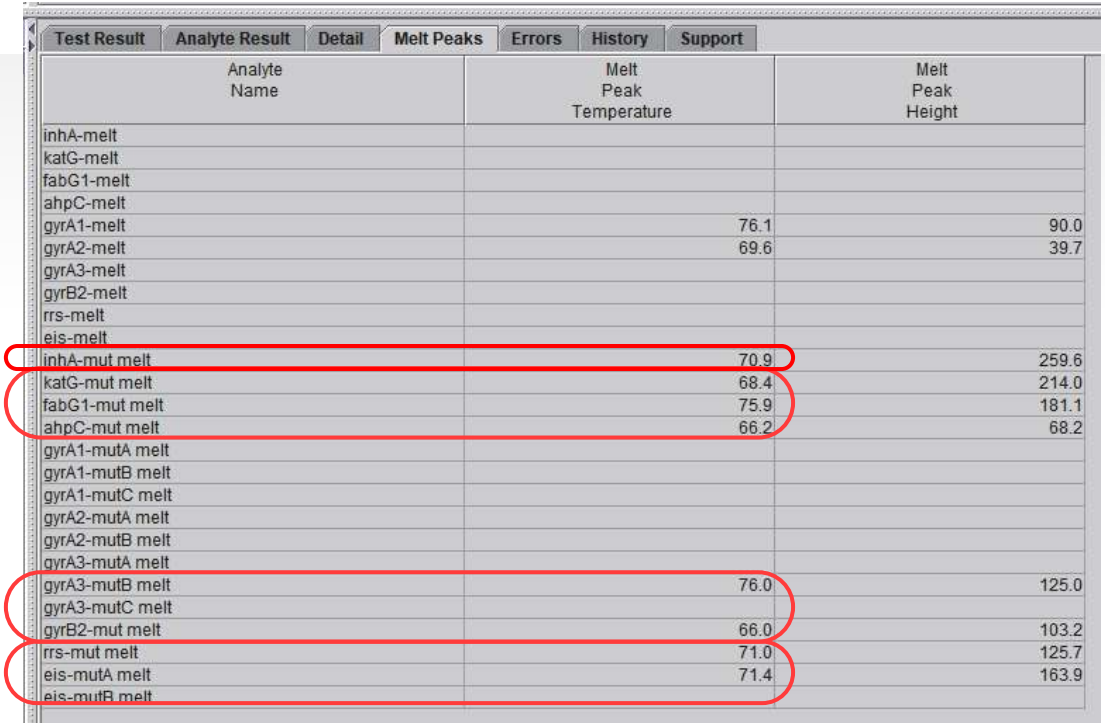
INH-FLQ-SLID-ETH Resistance



Test Result | Analyte Result | Detail | Melt Peaks | Errors | History | Support

Analyte Name	Melt Peak Temperature	Melt Peak Height
inhA-melt		
katG-melt		
fabG1-melt		
ahpC-melt		
gyrA1-melt	76.1	90.0
gyrA2-melt	69.6	39.7
gyrA3-melt		
gyrB2-melt		
rrs-melt		
eis-melt		
inhA-mut melt	70.9	259.6
katG-mut melt	68.4	214.0
fabG1-mut melt	75.9	181.1
ahpC-mut melt	66.2	68.2
gyrA1-mutA melt		
gyrA1-mutB melt		
gyrA1-mutC melt		
gyrA2-mutA melt		
gyrA2-mutB melt		
gyrA3-mutA melt		
gyrA3-mutB melt	76.0	125.0
gyrA3-mutC melt		
gyrB2-mut melt	66.0	103.2
rrs-mut melt	71.0	125.7
eis-mutA melt	71.4	163.9
eis-mutB melt		

MTB DETECTED

INH Resistance DETECTED

FLQ Resistance DETECTED

AMK Resistance DETECTED

KAN Resistance DETECTED

CAP Resistance DETECTED

ETH Resistance DETECTED

- In the mutant window:
  - *katG*
  - *gyrA3, gyrB2*
  - *rrs*

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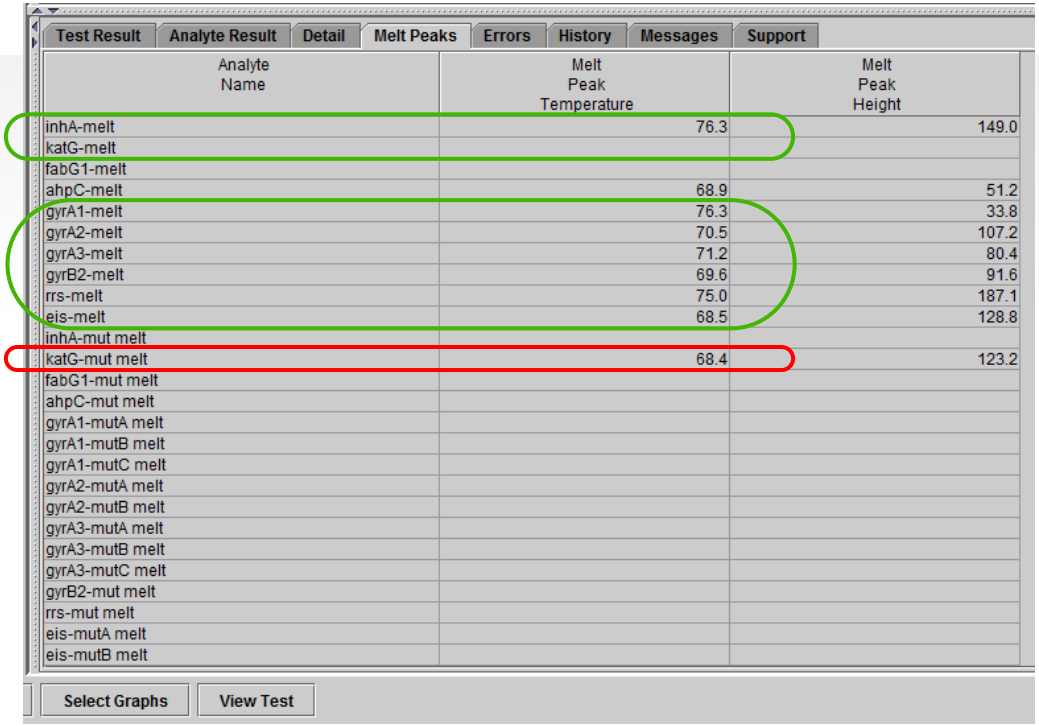
INH Resistance



Analyte Name	Melt Peak Temperature	Melt Peak Height
inhA-melt	76.3	149.0
katG-melt		
fabG1-melt		
ahpC-melt	68.9	51.2
gyrA1-melt	76.3	33.8
gyrA2-melt	70.5	107.2
gyrA3-melt	71.2	80.4
gyrB2-melt	69.6	91.6
rrs-melt	75.0	187.1
eis-melt	68.5	128.8
inhA-mut melt		
katG-mut melt	68.4	123.2
fabG1-mut melt		
ahpC-mut melt		
gyrA1-mutA melt		
gyrA1-mutB melt		
gyrA1-mutC melt		
gyrA2-mutA melt		
gyrA2-mutB melt		
gyrA3-mutA melt		
gyrA3-mutB melt		
gyrA3-mutC melt		
gyrB2-mut melt		
rrs-mut melt		
eis-mutA melt		
eis-mutB melt		

MTB DETECTED

INH Resistance DETECTED

FLQ Resistance NOT DETECTED

AMK Resistance NOT DETECTED

KAN Resistance NOT DETECTED

CAP Resistance NOT DETECTED

ETH Resistance NOT DETECTED

- *katG* in the mutant window

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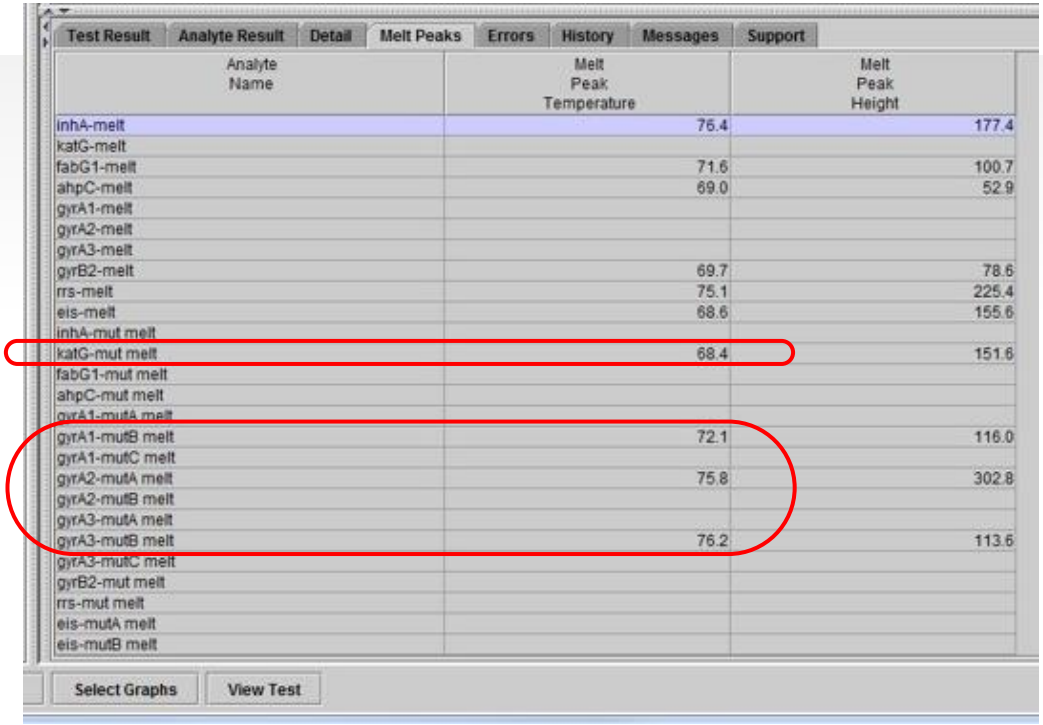
INH Resistance, Low FLQ Resistance



MTB DETECTED

INH Resistance DETECTED

Low FLQ DETECTED

AMK Resistance NOT DETECTED

KAN Resistance NOT DETECTED

CAP Resistance NOT DETECTED

ETH Resistance NOT DETECTED

- *katG* in the mutant window
- Specific pattern, indicating low Fluoroquinolone resistance

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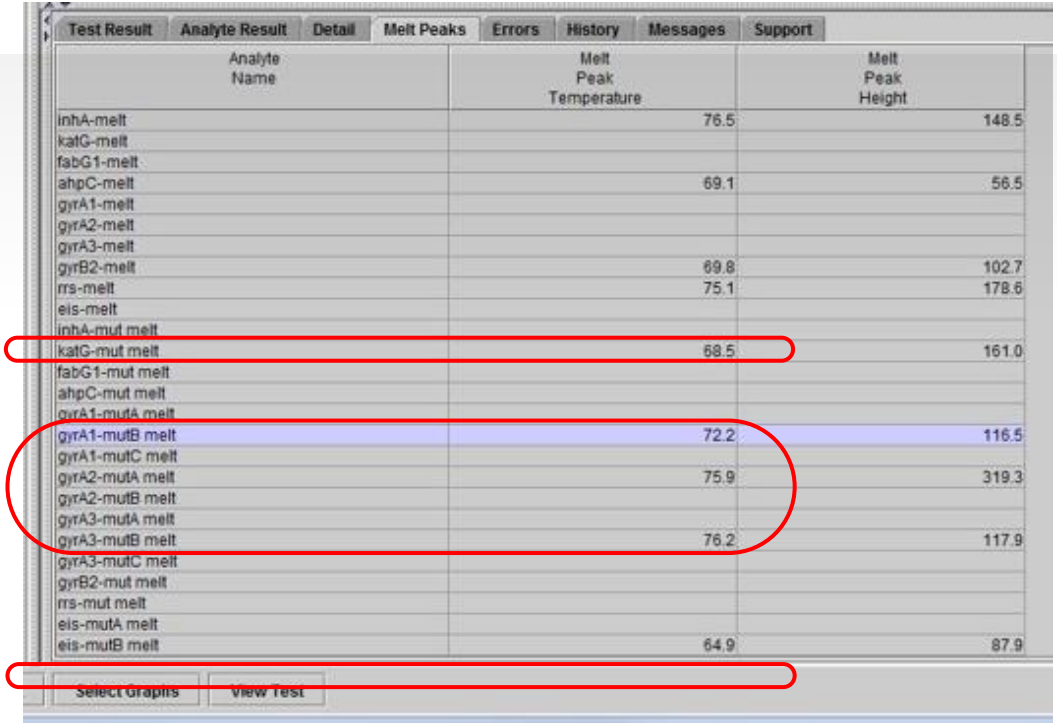
INH + Low FLQ + KAN Resistance



MTB DETECTED

INH Resistance DETECTED

Low FLQ DETECTED

AMK Resistance NOT DETECTED

KAN Resistance DETECTED

CAP Resistance NOT DETECTED

ETH Resistance NOT DETECTED

- *katG* in the mutant window
- Specific pattern, indicating low FLQ resistance
- *eis- mutB* melt + *rrs* wild type – KAN resistance

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INH + KAN Resistance, AMK and CAP Resistance Indeterminate

Test Result | Analyte Result | Detail | Melt Peaks | Errors | History | Support

Analyte Name	Melt Peak Temperature	Melt Peak Height
inhA-melt	76.3	265.9
katG-melt		
fabG1-melt	71.5	183.2
ahpC-melt	68.9	50.6
gyrA1-melt	76.3	83.8
gyrA2-melt	70.3	63.8
gyrA3-melt	71.2	84.2
gyrB2-melt	69.5	100.1
rrs-melt		
eis-melt		
inhA-mut melt		
katG-mut melt	68.3	168.7
fabG1-mut melt		
ahpC-mut melt		
gyrA1-mutA melt		
gyrA1-mutB melt		
gyrA1-mutC melt		
gyrA2-mutA melt		
gyrA2-mutB melt		
gyrA3-mutA melt		
gyrA3-mutB melt		
gyrA3-mutC melt		
gyrB2-mut melt		
rrs-mut melt		
eis-mutA melt		
eis-mutB melt	63.7	57.0

MTB DETECTED

INH Resistance DETECTED

FLQ Resistance NOT DETECTED

AMK Resistance INDETERMINATE

KAN Resistance DETECTED

CAP Resistance INDETERMINATE

ETH Resistance NOT DETECTED

- *katG* in the mutant window
- All *gyrA* and *gyrB* targets in wild type
- *eis- mutB* melt peak, no valid peak for *rrs*

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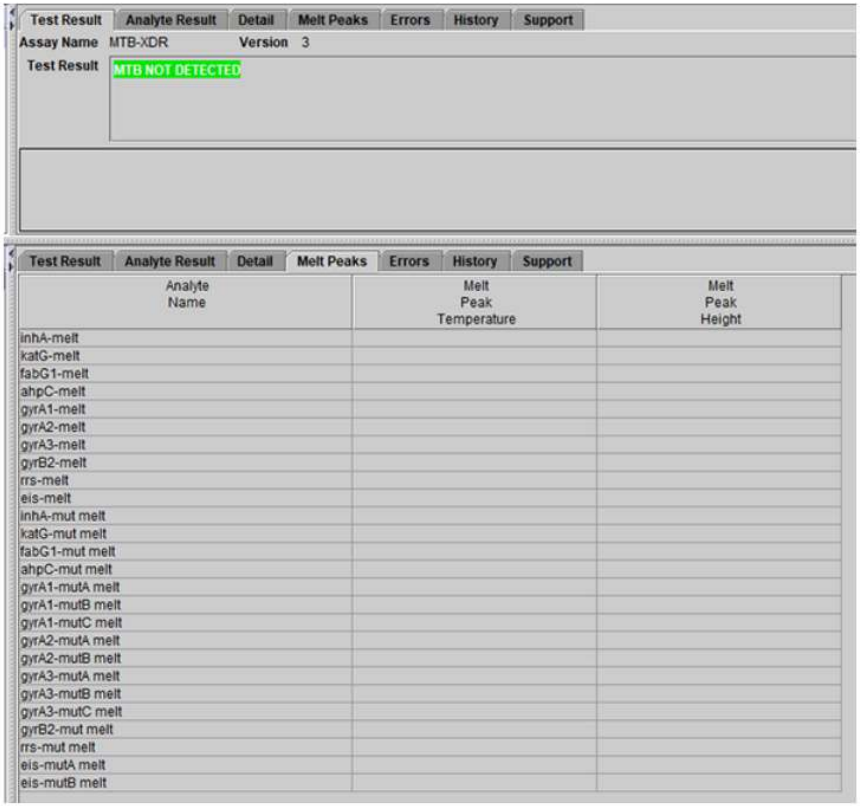
MTB NOT DETECTED



- *The MTB target is not detected within the sample.*
- SPC:PASS. The SPC met the acceptable
- Probe Check: PASS. All probe check results pass

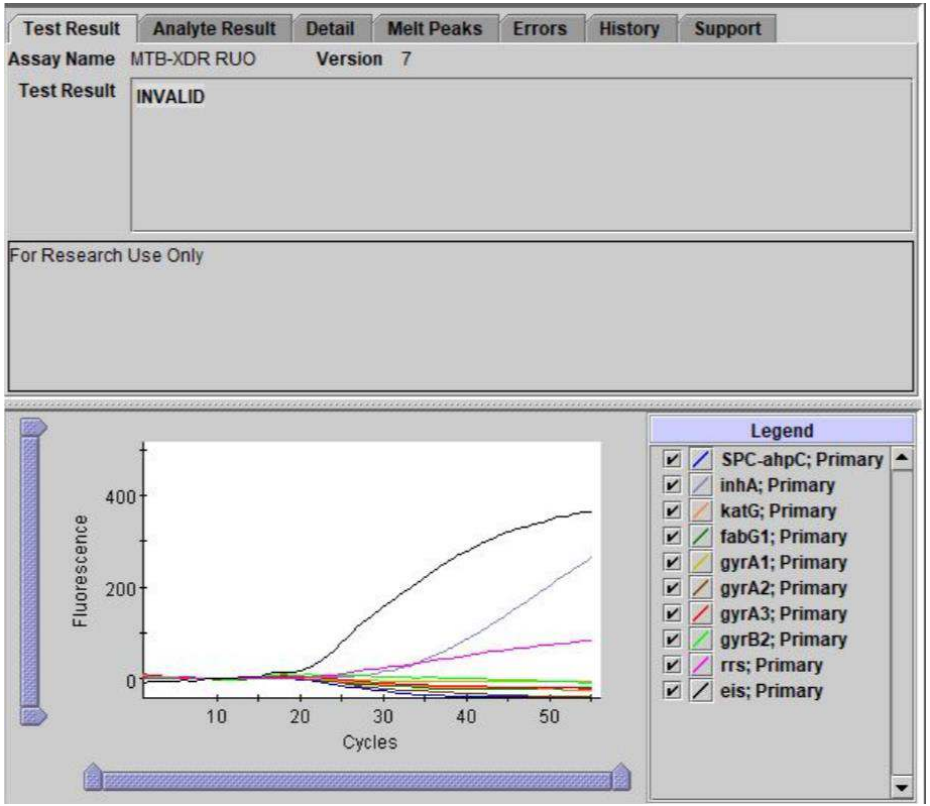
Troubleshooting

Retests

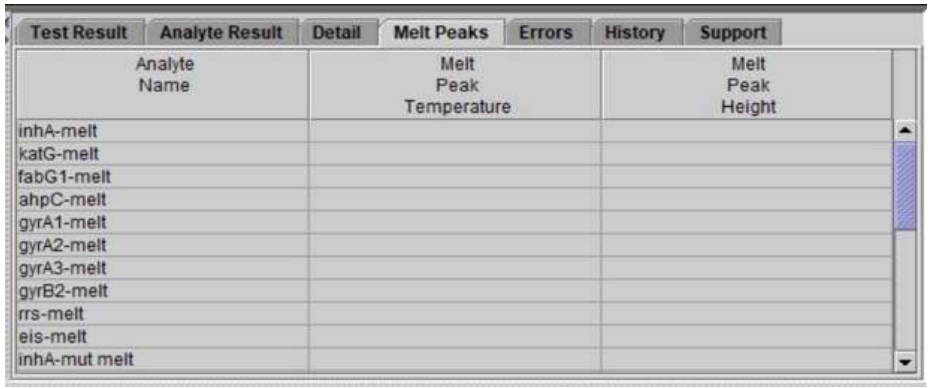
Reasons to Repeat the Test

- If any test results yields the following:
- INVALID
- ERROR
- NO RESULT
- INDETERMINATE

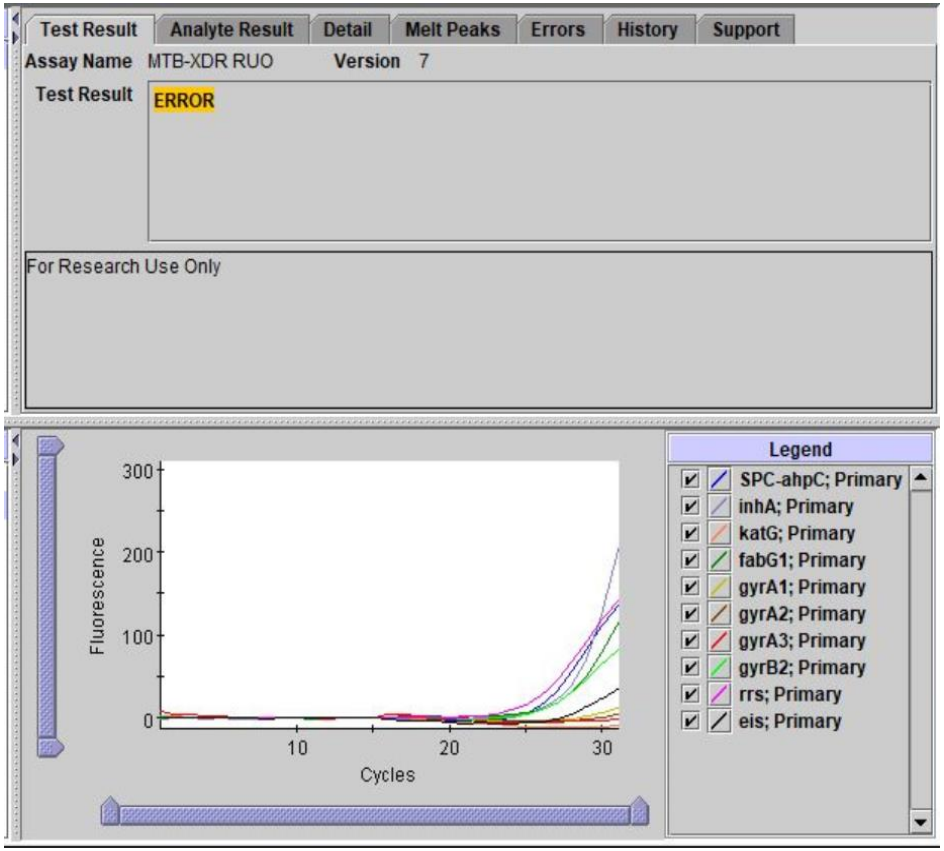
Invalid Result



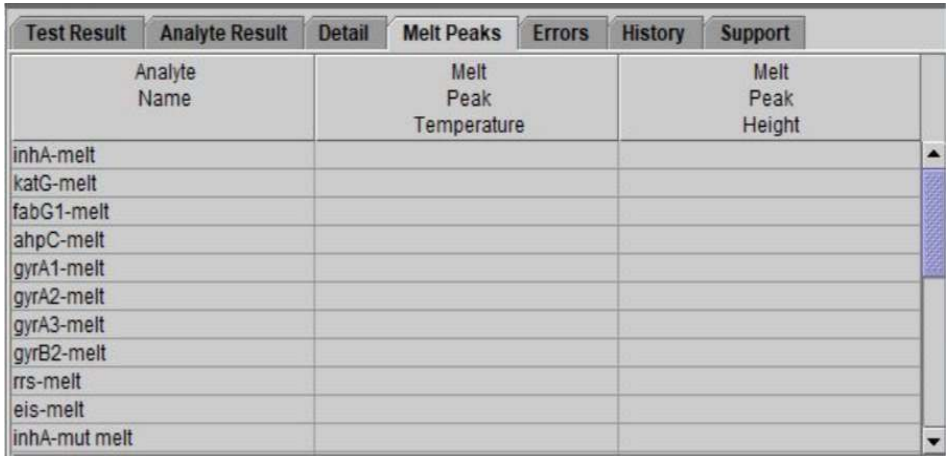
- INVALID result indicates that the SPC failed.
- The sample was not properly processed, or PCR is inhibited or the sample was not properly collected.



Error Result



- *An ERROR result could be due to, but not limited to:*
- *Probe Check Control failed, or the maximum pressure limits were exceeded.*



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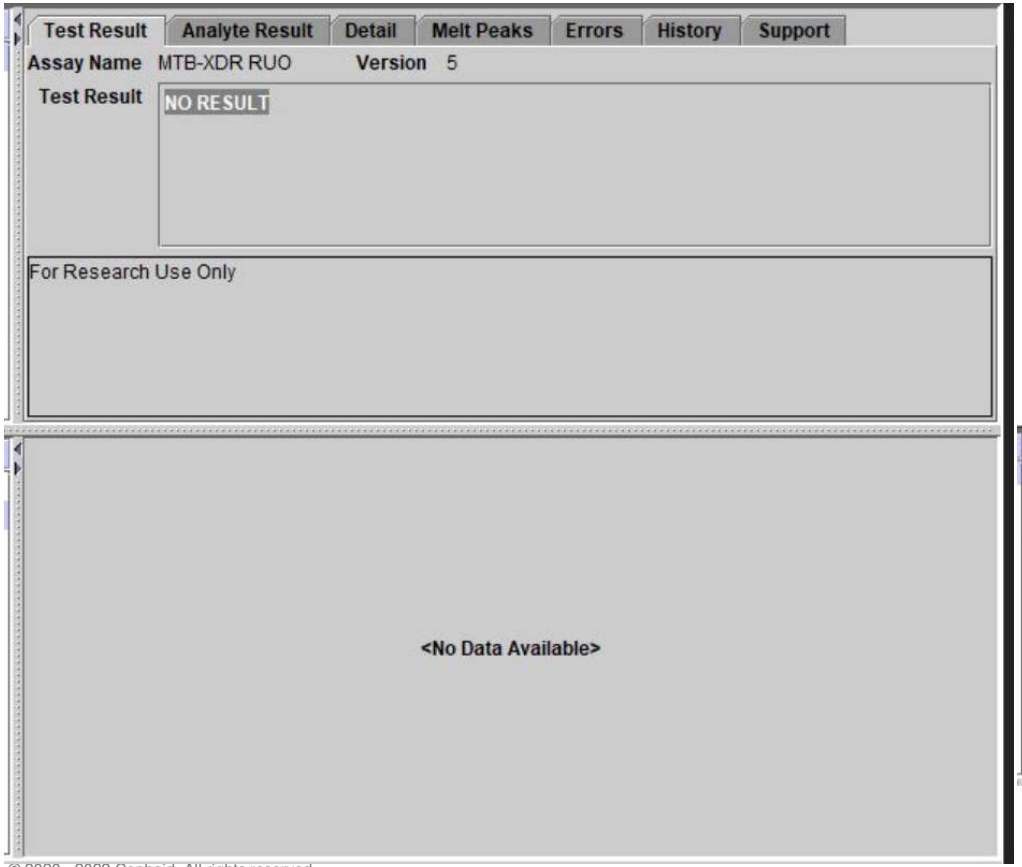
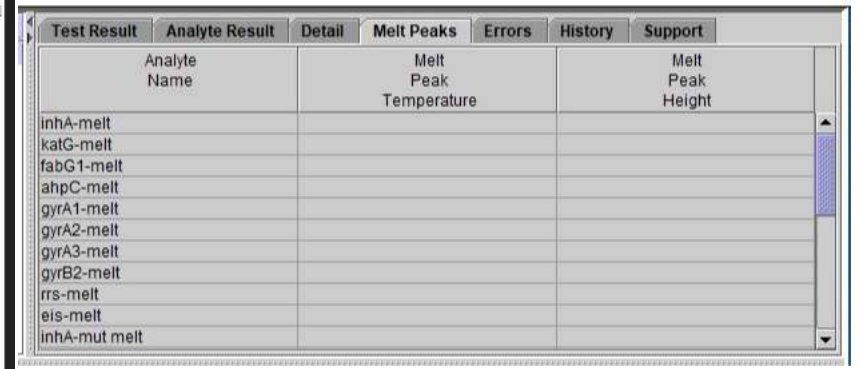
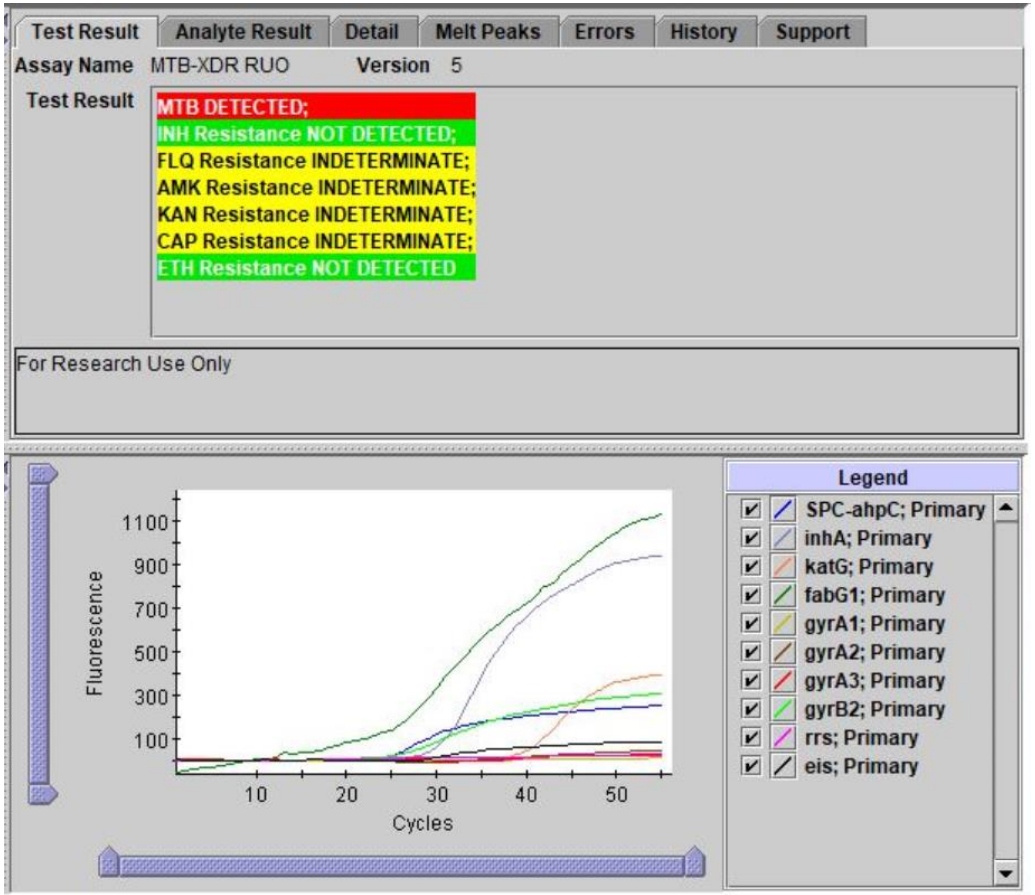
No Result



- *A NO RESULT indicates that insufficient data were collected.*
- *For example, the operator stopped a test that was in progress or*
- *a power failure occurred.*



Indeterminate Result



- *An INDETERMINATE result indicates that resistance to a given drug could not definitively be concluded based on the assay algorithm*
- *Retesting with a different sample may or may not lead to a different result.*

Test Result | Analyte Result | Detail | Melt Peaks | Errors | History | Support

Analyte Name	Melt Peak Temperature	Melt Peak Height
inhA-melt	76.4	206.1
katG-melt	73.8	91.9
fabG1-melt	71.5	100.4
ahpC-melt		
gyrA1-melt		
gyrA2-melt		
gyrA3-melt		
gyrB2-melt	69.6	91.3
rrs-melt		
eis-melt	68.7	117.3
inhA-mut melt		

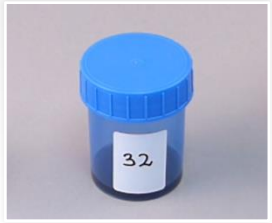
Re-Test Procedure

1

Discard used cartridge.

Follow your institution's safety guidelines for disposal of cartridges.

2



If there is left-over sputum (should be ≥1.0 ml) or reconstituted sediment (should be ≥0.5 ml), use new SR to decontaminate and liquefy the sputum before running the test

If sufficient left-over SR-treated sample is available that has been stored for no longer than 2.5Hrs up to 35 °C or has been stored no longer than 4 hours at 2–8 °C of the initial addition of SR to the sample, the leftover SR treated sample can be processed using a new cartridge.

.

3

Obtain a new cartridge.

Label appropriately as retest on the new cartridge.

Process the sample per the package insert.

4

Run the test on the System.

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Technical Assistance

- Before contacting Cepheid Technical Support, collect the following information:
  - Customer contact details (name and phone number)
  - Product name & kit Lot number
  - GeneXpert Serial number
  - GeneXpert Software version
  - Sample type and collection method used
  - Discrepancy result details / Error messages (if any)

- Log your complaint online using the following link ***http://www.cepheid.com/en/support:*** *Create a Support Case*

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Thank You

www.cepheid.com

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