



INTROL® TB-XDR Panel M345

INTENDED USE:

The INTROL TB-XDR Panel M345 is intended for use as an external quality control to monitor analytical performance of the extraction, amplification and detection steps of *in vitro* laboratory nucleic acid testing procedures for the qualitative detection of extensively drug resistant (XDR) *Mycobacterium tuberculosis* (MTB) complex by the Xpert® MTB/XDR Assay on Cepheid GeneXpert Instrument Systems. The INTROL TB-XDR Panel M345 drug resistance associated mutations are listed in Table 2.

The World Health Organization (WHO) reports that about 1.7 billion people, 23% of the world's population, are estimated to have a latent TB infection, and are thus at risk of developing active TB disease during their lifetime.¹ Although death rates have fallen steadily since 2000, nevertheless, worldwide, around 7-10 million people still fall ill with the disease each year and half a million new cases of rifampicin-resistant TB were reported in 2018, of which 78% had multi-drug resistant TB (MDR-TB).¹ Highly resistant strains of MDR-TB, which acquired additional resistance to fluoroquinolones and at least one of three injectable second-line drugs (i.e., amikacin, kanamycin, or capreomycin) are termed extensively drug resistant TB (XDR-TB) and are very difficult to treat. Due to resistance to the most potent TB drugs, patients are left with treatment options that are much less effective and early diagnosis becomes crucial.²

PRODUCT SUMMARY and PRINCIPLE:

INTROL TB-XDR Panel M345 consists of non-infectious, synthetic MTB DNA encapsulated in chemically fixed and killed bacterial cells. The MTB DNA is comprised of the following MTB gene segments: *eis* promoter, *fabG1*, *gyrA*, *gyrB*, *inhA* promoter, *katG*, *oxyR-ahpC*, and *rrs*. Drug resistance mutations are incorporated into each of these segments as indicated in Table 2. The controls must undergo a stringent extraction process in order to effectively release the MTB DNA from the cells. INTROL TB-XDR Panel M345 is compatible with the Xpert® MTB/XDR Assay (Cepheid). It does not include the entire MTB genome. Consult with MMQCI for compatibility with other test methods.

Best practice is to establish a quality control program for every assay performed by the laboratory. Routine use of quality controls that are consistent lot to lot and monitor the entire assay assists the laboratory in identifying shifts, trends, and increased frequency of random errors caused by variations in the test system, such as failing reagents and pipetting errors. Early investigation can prevent failed assay runs.

STORAGE and STABILITY:

Upon receipt and after opening, the material should be stored at 2° – 8°C. Do not freeze. Unopened controls are stable through the expiration date printed on the kit label when stored at 2° – 8°C. Discard after use according to your local and federal regulations.

PRECAUTIONS, WARNINGS and LIMITATIONS:

- Do not dilute or transfer to another storage tube.
- This product is intended for *in vitro* analytical testing and is provided for Research Use Only (RUO).
- This product is for use with the Xpert MTB/XDR assay on the GeneXpert Systems. It does not contain the entire MTB genome.
- This product is not intended for use as a substitute for the internal controls provided in the Xpert MTB/XDR assay.
- This product does not contain any biological material of human or animal origin. Universal Precautions are NOT required when handling this product.
- Quality control materials should be used in accordance with local, state, federal regulations and accreditation requirements.
- INTROL TB-XDR Panel M345 cannot be cloned, sold, or transferred without the explicit written consent of MMQCI.

ORDERING INFORMATION:

INTROL TB-XDR Panel M345
 Part Number: M345-5
 Kit Contains: 15 bottles x 1.0 mL
 5 each of INTROL TB-XDR WT, MUT and NEG

COMPOSITION:

The INTROL TB-XDR Panel M345 is comprised of 15 bottles, 5 each of INTROL TB-XDR WT, INTROL TB-XDR MUT and INTROL TB-XDR NEG, 1.0 mL each bottle. INTROL TB-XDR WT and INTROL TB-XDR MUT contain encapsulated MTB DNA. INTROL TB-XDR NEG contains buffer and preservative only. The cells encapsulating the MTB DNA are suspended in buffer with preservative. The presence or absence of drug resistance mutations is specified for each control in Table 1 and Table 2.

INSTRUCTIONS FOR USE:

1. Allow controls to come to room temperature (18° – 25°C).
2. Thoroughly mix controls by vigorously inverting 10 times or vortex for 10 seconds.
3. Before opening bottle, shake down or tap bottle on hard surface to be sure all liquid is out of cap.
4. Pipette 2mL of Sample Reagent directly into the control bottle and re-cap control bottle.
5. Shake control bottle vigorously 10-20 times or vortex for 10 seconds. *Note: One back and forth movement is a single shake.*
6. Incubate at room temperature for 10 minutes, and then shake the control bottle vigorously 10-20 times or vortex for at least 10 seconds. *Note: One back and forth movement is a single shake.*
7. Incubate the sample at room temperature for an additional 5 minutes.
8. Open the cartridge lid. Using the provided transfer pipette, add 2 mL (line on transfer pipette) of the treated control into the open port.
9. Proceed with testing by following the manufacture's test instructions.

For complete Xpert MTB/XDR instructions, refer to the Xpert MTB/XDR package insert provided by Cepheid.

EXPECTED VALUES:

The laboratory should follow Good Laboratory Practice (GLP) and establish its own performance characteristics for INTROL TB-XDR Panel M345 in demonstrating adequate system performance.

Expected results and list of drug resistance mutations when controls are analyzed with the Xpert MTB/XDR Assay on GeneXpert Systems are listed in Tables 1 and 2.

Table 1. Expected Results of INTROL TB-XDR Panel M345 with Xpert MTB/XDR Assay

	INTROL TB-XDR WT	INTROL TB-XDR MUT	INTROL TB-XDR NEG
MTB	Detected	Detected	Not Detected
INH	Resistance Not Detected	Resistance Detected	
FLQ	Resistance Not Detected	Resistance Detected	
AMK	Resistance Not Detected	Resistance Detected	
KAN	Resistance Not Detected	Resistance Detected	
CAP	Resistance Not Detected	Resistance Detected	
ETH	Resistance Not Detected	Resistance Detected	

Table 2. Drug Resistance Mutations* found in INTROL TB-XDR Panel M345

Control	Drug Resistance Mutations
INTROL TB-XDR WT	No mutations/ wildtype
INTROL TB-XDR MUT	<i>eis</i> promoter (-14 C > T), <i>fabG1</i> : L203L (CTg > CTA), <i>gyrA</i> : D94G (GAc > GgC), <i>gyrB</i> : E540D (GAa > GAc), <i>inhA</i> promoter: (-15 C > T), <i>katG</i> : S315T (AgC > AcC), <i>oxyR-ahpC</i> (-39 C > T) and <i>rrs</i> (a1401g)
INTROL TB-XDR NEG	No MTB DNA, no cells

*References citing the mutations can be found at www.tbdreamdb.com.

REFERENCES:

1. WHO Global Tuberculosis Report 2019: https://www.who.int/tb/publications/global_report
2. CDC Division of Tuberculosis Elimination Fact Sheet. May 2012 <https://www.cdc.gov/tb/publications/factsheets/drbb/mdrtb.pdf>