BD BACTEC™ MGIT™ 960 PZA Kit

For the Antimycobacterial Susceptibility Testing of *Mycobacterium tuberculosis*

R_x Only CE IVD

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2019-10

INTENDED USE

The BD BACTEC™ MGIT™ 960 PZA Kit is a rapid qualitative procedure for susceptibility testing of *Mycobacterium tuberculosis*, from culture, to pyrazinamide (PZA). The BD BACTEC MGIT 960 PZA Kit is used with the BD BACTEC MGIT System.

SUMMARY AND EXPLANATION

Antimycobacterial susceptibility testing is valuable in the proper treatment of patients with tuberculosis. The treatment of tuberculosis is commonly through a multiple drug regimen that includes the antimycobacterial drug pyrazinamide. It is important that the antimycobacterial drugs prescribed show appropriate activity against *Mycobacterium tuberculosis*, i.e., susceptibility of the isolate to the drug.

Multidrug resistant *Mycobacterium tuberculosis* (MDR-TB) has recently become a serious public health problem.[1] Resistance to any of the primary drugs, including pyrazinamide, makes the disease more difficult and expensive to treat. The rapid detection of these resistant isolates is critical to effective patient management.

Two methods have been widely used for antimycobacterial susceptibility testing. The first method, known as the Method of Proportion,[2] uses Middlebrook and Cohn 7H10 Agar. It compares colony counts on drug-containing and drug-free media. The testing for pyrazinamide requires some modification from the general methods because the drug is active *in vitro* only at lower pH values.[3] A modification to the method of proportion method was developed using a 7H10 agar medium at pH 5.5, with a drug concentration of 25–50 µg/mL.[4] A limitation of the method is that at a pH of 5.5, many isolates of *M. tuberculosis* either fail to grow or grow poorly. Agar-based methods such as the agar proportion method have not proven to be satisfactory for PZA susceptibility testing because of the failure of many isolates to grow when the agar has been acidified for the PZA test.

The second method, known as the BD BACTEC 460TB radiometric susceptibility method,[5] is based on the production of radioactive ^{14}C-labeled carbon dioxide by the growing mycobacteria, manifested by a Growth Index increase in the system. A modification to the BD BACTEC 460TB susceptibility method was developed using a modified 7H12 radiometric medium, BD BACTEC PZA Test Medium, with a reduced pH of 6.0.[6] At this pH, PZA activity against mycobacteria can be determined without inhibiting the growth of most *M. tuberculosis* isolates. The BD BACTEC 460TB PZA susceptibility test uses a pyrazinamide drug concentration of 100 µg/mL. Susceptibility testing in the BD BACTEC 460TB System has proven to be satisfactory and is presently considered the reference method for PZA susceptibility testing. The Clinical and Laboratory Standards Institute (CLSI) recommends the BD BACTEC 460TB method for PZA susceptibility testing.[2]

Use of the BD BACTEC MGIT instrument in combination with the BD BACTEC MGIT 960 PZA kit is a non-radiometric method of determining antimycobacterial susceptibility to PZA. The BD BACTEC MGIT 960 PZA Kit has been developed to allow susceptibility testing at a pyrazinamide concentration of 100 µg/mL. This concentration correlates with the concentration used in the BD BACTEC 460TB System.

PRINCIPLES OF THE PROCEDURE

BD BACTEC MGIT 960 PZA Medium is a tube containing a modified Middlebrook 7H9 Broth, which supports the growth and detection of mycobacteria. The BD BACTEC MGIT 960 PZA Medium tube contains a fluorescent compound embedded in silicone on the bottom of a 16 x 100 mm round-bottom tube. The fluorescent compound is sensitive to the presence of oxygen dissolved in the broth. The initial concentration of dissolved oxygen quenches the emission from the compound, and little fluorescence can be detected. Later, actively growing and respiring microorganisms consume the oxygen, which allows the compound to fluoresce.

The BD BACTEC MGIT 960 PZA Kit is a 4–21 day qualitative test. The test is based on growth of the *M. tuberculosis* isolate in a drug-containing tube compared to a drug-free tube (Growth Control). The BD BACTEC MGIT instrument monitors tubes for increased fluorescence. Analysis of fluorescence in the drug-containing tube compared to the fluorescence of the Growth Control tube is used by the instrument to determine susceptibility results.

The BD BACTEC MGIT instrument automatically interprets these results and reports a susceptible or resistant result.

REAGENTS

The BD BACTEC MGIT 960 PZA Medium tube contains 110 µL of fluorescent indicator and 7 mL of PZA broth. The indicator contains Tris 4,7 - diphenyl-1, 10 phenanthroline ruthenium chloride pentahydrate in a silicone rubber base. The tubes are capped with a polypropylene cap.

Approximate Formula* Per L of Purified Water:

Modified Middlebrook 7H9 broth	5.9 g
Casein peptone	1.25 g

BD BACTEC MGIT 960 PZA Kit contains two lyophilized vials of pyrazinamide and six vials of PZA Supplement.

Approximate Formula* Per Vial Lyophilized drug: Pyrazinamide	20,000 µg

BD BACTEC MGIT 960 PZA Supplement contains 15 mL of enrichment

Approximate Formula* Per L Purified Water:

Bovine albumin	50.0 g	Catalase	0.03 g
Dextrose	20.0 g	Oleic Acid	0.1 g
Polyoxyethylene stearate (POES)	1.1 g		

**Adjusted and/or supplemented as required to meet performance criteria.*

Storage and reconstitution of reagents:

BD BACTEC MGIT 960 PZA Medium - On receipt, store at 2–25 °C. DO NOT FREEZE. Broth should appear clear and colorless. Do not use if turbid. Minimize exposure to light. Tubes stored as labeled prior to use, may be inoculated up to the expiration date.

BD BACTEC MGIT 960 PZA Drug vials - On receipt, store the lyophilized drug vials at 2–8 °C. Once reconstituted, the antibiotic solution may be frozen and stored at -20 °C or colder up to six months, not to exceed the original expiration date. Once thawed, use immediately. Discard unused portions.

BD BACTEC MGIT 960 PZA Supplement - On receipt, store in the dark at 2–8 °C. Avoid freezing or overheating. Open and use prior to the expiration date. Minimize exposure to light.

Directions For Use:

Reconstitute each BD BACTEC MGIT 960 PZA lyophilized drug vial with **2.5 mL** of sterile distilled/deionized water to make a stock solution of 8000 µg/mL.

POTENTIALLY INFECTIOUS TEST SPECIMEN: Pathogenic microorganisms, including hepatitis viruses and Human Immunodeficiency Virus, may be present in clinical specimens. “Standard Precautions”[7-10] and institutional guidelines should be followed in handling all items contaminated with blood and other body fluids.

WARNINGS AND PRECAUTIONS: FOR *IN VITRO* DIAGNOSTIC USE.

Working with *M. tuberculosis* growth in culture requires Biosafety Level (BSL) 3 practices, containment equipment and facilities.

Read and follow directions contained in all appropriate package inserts including the BD BBL™ MGIT 7 mL Mycobacteria Growth Indicator Tube.

Prior to use, the user should examine the tubes and vials for evidence of contamination or damage. Discard any tubes or vials if they appear unsuitable. Dropped tubes should be examined carefully. If damage is seen, the tube should be discarded.

In the event of tube breakage: 1) Close the instrument drawers; 2) Turn off the instrument; 3) Vacate the area immediately; 4) Consult your facility/CDC guidelines. An inoculated leaking or broken tube may produce an aerosol of mycobacteria; appropriate handling should be observed.

Autoclave all inoculated MGIT tubes prior to disposal.

INOCULUM PREPARATION

All preparations detailed below must be from pure cultures of *M. tuberculosis*. The laboratory should confirm, by appropriate identification techniques, that the isolate to be tested is a pure culture of *M. tuberculosis*.

Inoculum can be prepared from solid media or from a positive BD BACTEC MGIT 7 mL tube. In addition, cultures grown in liquid and on solid media can be used to prepare a seed MGIT tube, which can then be used to prepare the inoculum. Each of these options is described below.

Preparation of the Inoculum from Solid Media:

NOTE: It is important to prepare the inoculum according to the following instructions to obtain the appropriate organism concentration for the susceptibility test.

1. Add 4 mL of BD BBL Middlebrook 7H9 Broth (or BD BBL MGIT broth) to a 16.5 x 128 mm sterile tube with cap containing 8–10 glass beads.
2. Scrape with a sterile loop as many colonies as possible from growth no more than fourteen days old, trying not to remove any solid medium. Suspend the colonies in the Middlebrook 7H9 Broth.
3. Vortex the suspension for 2–3 minutes to break up the larger clumps. The suspension should exceed a 1.0 McFarland standard in turbidity.
4. Let the suspension sit for 20 minutes without disturbing.
5. Transfer the supernatant fluid to another 16.5 x 128 mm sterile tube with cap (avoid transferring any of the sediment) and let sit for another 15 minutes.
6. Transfer the supernatant fluid (it should be smooth, free of any clumps) to a third 16.5 x 128 mm sterile tube. **NOTE**: The organism suspension should be greater than a 0.5 McFarland standard at this step.
7. Adjust the suspension to a 0.5 McFarland standard by visual comparison to a 0.5 McFarland turbidity standard. Do not adjust below a 0.5 McFarland standard.
8. Dilute 1 mL of the adjusted suspension in 4 mL of sterile saline (1:5 dilution). Use this as the AST inoculum and proceed to “Inoculation Procedure for BD BACTEC MGIT 960 PZA Susceptibility Test.”

Preparation of the Inoculum from a Positive BD BACTEC MGIT 7 mL Tube:

1. The first day of an instrument positive BD BACTEC MGIT tube is considered Day 0.
2. For the preparation of the test inoculum, a positive 7 mL MGIT tube should be used the day after it first becomes positive on the BD BACTEC MGIT instrument (Day 1), up to and including the fifth day (Day 5) after instrument positivity. A tube which has been positive longer than five days should be subcultured to a fresh 7 mL MGIT tube containing BD BACTEC MGIT Growth Supplement and tested on the BD BACTEC MGIT instrument until positive, and used from one to five days following positivity. See "Preparation of a Seed MGIT Tube from Liquid Media."
3. If the tube is a Day 1 or Day 2 positive, no dilution is required. Use this as the AST inoculum and proceed to "Inoculation Procedure for BD BACTEC MGIT 960 PZA Susceptibility Test."
4. If the tube is a Day 3, Day 4, or Day 5 positive, then dilute 1 mL of the positive broth in 4 mL of sterile saline (1:5 dilution). Mix tube thoroughly. Use this as the AST inoculum and proceed to "Inoculation Procedure for BD BACTEC MGIT 960 PZA Susceptibility Test."

Preparation of a Seed MGIT Tube from Liquid Media

1. Mix the tube by inversion or vortexing.
2. Make a 1:100 dilution by adding 0.1 mL of the culture into 10 mL of BD BBL Middlebrook 7H9 Broth or BD BBL MGIT Broth. Mix well.
3. Add 0.5 mL of this suspension into a 7 mL MGIT tube supplemented with 0.8 mL of BD BACTEC MGIT Growth Supplement.
4. Cap tightly and gently mix by inverting 2–3 times.
5. Enter the tube into a BD BACTEC MGIT instrument and test until positive.

   NOTE: Time to positivity **must** be ≥ 4 days for use as AST inoculum. If tube becomes positive in < 4 days, return to step 1 and prepare a new seed tube.
6. This tube may now be used from one to five days following positivity. Proceed to "Preparation of the Inoculum from a Positive BD BACTEC MGIT 7 mL Tube" above.

Preparation of a Seed MGIT Tube from Solid Media

1. Using a sterile loop, scrape growth from a slant and add to a 7 mL MGIT tube supplemented with 0.8 mL of BD BACTEC MGIT Growth Supplement.
2. Cap tightly and gently mix by inverting 2–3 times.
3. Enter the tube into a BD BACTEC MGIT instrument and test until positive.

   NOTE: Time to positivity **must** be ≥ 4 days for use as AST inoculum. If tube becomes positive in < 4 days, return to step 1 and prepare a new seed tube.
4. This tube may now be used from one to five days following positivity. Proceed to "Preparation of the Inoculum from a Positive BD BACTEC MGIT 7 mL Tube" above.

PROCEDURE

Materials Provided: BD BACTEC MGIT 960 PZA Kit containing two vials each lyophilized drug and six vials of PZA Supplement (approximately 50 tests per kit).

Materials Required But Not Provided: BD BACTEC MGIT 960 PZA Medium (25 tubes per carton), ancillary culture media, reagents, quality control organisms and laboratory equipment as required for this procedure.

Inoculation Procedure for BD BACTEC MGIT 960 PZA Susceptibility Test:

Important considerations when preparing the PZA AST Set are the proper reconstitution of the lyophilized drug, use of pure culture and the proper dilution of the organism for the Growth Control and PZA tube. It is important to add drug only to the corresponding MGIT tube labeled "PZA." Use only the BD BACTEC MGIT 960 PZA Supplement supplied with the kit and BD BACTEC MGIT 960 PZA Medium tubes when performing the PZA AST set.

1. Label two 7 mL BD BACTEC MGIT 960 PZA Medium tubes for each test isolate. Label one as GC (Growth Control), one as PZA. Place the tubes in the correct sequence in the two tube AST set carrier (see BD BACTEC MGIT Instrument User's Manual).
2. Aseptically add 0.8 mL of BD BACTEC MGIT 960 PZA Supplement to each tube.
3. Using a micropipet, aseptically pipet 100 µL of the 8000 µg/mL BD BACTEC MGIT 960 PZA drug solution to the appropriately labeled MGIT PZA tube. No PZA drug solution should be added to the appropriately labeled MGIT GC tube.

Drug	Concentration of Drug after Reconstitution*	Volume Added to MGIT Tubes for Test	Final Concentration in MGIT Tubes
BD BACTEC MGIT PZA	8000 µg/mL	100 µL	100 µg/mL*

*PZA must be reconstituted using 2.5 mL sterile/deionized water to achieve the concentration indicated.

4. **Growth Control tube preparation and inoculation:** Aseptically pipet 0.5 mL of the AST inoculum (see "INOCULUM PREPARATION") into 4.5 mL of sterile saline to prepare the **1:10** Growth Control suspension. Mix the Growth Control suspension thoroughly. Inoculate 0.5 mL of the **1:10** Growth Control suspension into the MGIT tube labeled "GC."

   NOTE: It is important to use an appropriately prepared **1:10** dilution for the "GC" tube to ensure accurate AST results and avoid PZA AST set errors.
5. **Drug-containing tube inoculation:** Aseptically pipet 0.5 mL of the AST inoculum (see "INOCULUM PREPARATION") into the MGIT tube labeled "PZA."

6. Tightly recap the tubes. Mix tubes thoroughly by gentle inversion three to four times.
7. Enter the PZA set into the BD BACTEC MGIT instrument using the AST set entry feature (refer to the BD BACTEC MGIT Instrument User's Manual). Ensure that the Growth Control tube is in the first left tube position. Select PZA as the drug in the 2 tube AST set carrier definition when performing the AST set entry.
8. Streak 0.1 mL of the organism suspension to a BD Trypticase™ Soy Agar with 5% Sheep Blood (TSA II) plate. Enclose in a plastic bag. Incubate at 35–37 °C.
9. Check the blood agar plate at 48 hours for bacterial contamination. If the blood agar plate shows no growth, then allow PZA testing to proceed. If the blood agar plate shows growth, discard the PZA set (refer to the BD BACTEC MGIT Instrument User's Manual) and repeat testing with a pure culture of *Mycobacterium tuberculosis*.

User Quality Control: Upon receipt of a new shipment or lot number of BD BACTEC MGIT 960 PZA Kit vials or BD BACTEC MGIT 960 PZA Medium, it is recommended that the control organism shown below be tested. The control organism should be a pure culture and the culture should be prepared according to "INOCULUM PREPARATION" instructions.

The quality control (QC) AST Set should be prepared according to the "Inoculation Procedure for BD BACTEC MGIT 960 PZA Susceptiblity Test" instructions. Important considerations when preparing the QC AST Set are the proper reconstitution of the lyophilized drug, use of pure culture and the proper dilution of the QC organism for the Growth Control and PZA tubes. It is important to add drug only to the corresponding MGIT tube labeled "PZA."

The same control organism should be run as batch QC once each week when susceptibility testing is performed. Observation of the proper results, as shown below, within 4–20 days indicates that the BD BACTEC MGIT 960 PZA reagents are ready for use in testing patient isolates.

If the proper results are not observed, do not report patient results. Repeat QC and any patient isolates affected by the initial QC failure. If the repeat QC does not perform as expected, do not report patient results. Do not use the product until you have contacted Technical Services at 1.800.638.8663 (United States Only).

Strains	GC	BD BACTEC MGIT PZA
M. tuberculosis ATCC® 27294	Positive	Susceptible

During the external evaluation of the BD BACTEC MGIT 960 PZA Kit the average time to result for the control organism was seven days with a range of four to eleven days. The most common causes of QC failures during the external evaluation were over-inoculated PZA Sets and contaminated QC cultures.

RESULTS

The BD BACTEC MGIT instrument will monitor AST sets until a susceptible or resistant determination is made. Once the set testing is completed, the results are reported by the BD BACTEC MGIT instrument (refer to the BD BACTEC MGIT Instrument User's Manual). The BD BACTEC MGIT instrument will report an AST Set result as an Error ("X"), no susceptibility interpretation, when certain conditions occur that may affect the test results. Conditions that may result in an Error ("X") result are described in Section 7–Troubleshooting of the BD BACTEC MGIT Instrument User's Manual.

It is important to include the test method, drug name and concentration when reporting results. The Pulmonary and/or Infectious Disease specialist in TB control should be consulted concerning the appropriate therapeutic regimen and dosages.

Mono-resistance to pyrazinamide is uncommon, therefore in the event of unexpected resistant results, verify purity and identification of the isolate tested as *M. tuberculosis*. Guidelines for mycobacterial purity checks can be found in the CLSI M24 standard.[2]

BD BACTEC MGIT 960 PZA result reporting

Drug (concentration)	BD BACTEC MGIT System result	Recommended Report	Action
PZA (100 µg/mL)	Susceptible	Isolate tested with BD BACTEC MGIT System [PZA/100 µg/mL] and result is susceptible.	No action.
	Resistant	Isolate tested with BD BACTEC MGIT System [PZA/100 µg/mL] and result is resistant.	If isolate is mono-resistant to PZA, confirm that isolate tested is a pure culture of *Mycobacterium tuberculosis*.
	Error "X"	No report.	Repeat test.

LIMITATIONS OF THE PROCEDURE

The BD BACTEC MGIT 960 PZA susceptibility test does not interpret the degree of susceptibility of the isolate being tested. Results are reported as either susceptible or resistant.

The BD BACTEC MGIT 960 PZA susceptibility test can only be performed using a BD BACTEC MGIT instrument. The PZA Sets cannot be read manually.

Use only pure cultures of *M. tuberculosis*. Cultures that are contaminated or that may contain multiple species of mycobacteria may give erroneous results and should not be tested. Direct testing from clinical specimens is not recommended.

Suspensions made from solid media must be allowed to settle for the prescribed times prior to standardization. Inoculum preparations made from solid media should be visually compared to a 0.5 McFarland turbidity standard; failure to do so may give inaccurate results or cause an AST Set error.

Failure to use the 1:5 dilution of the organism suspension, when indicated, to inoculate the drug containing tubes may give inaccurate results.

Failure to use a 1:10 dilution of the organism suspension for the inoculation of the Growth Control tube may give inaccurate results or cause an AST Set error.

Failure to reconstitute the PZA drug with the appropriate volume of sterile distilled / deionized water may give inaccurate results.

Thorough mixing of inoculated tubes is important. Failure to mix the tubes adequately may lead to false resistant results.

Failure to load the tubes of the AST Set into the AST Set Carrier in the proper sequence may give inaccurate results. Failure to select the appropriate set carrier drug definition may result in invalid or inaccurate results.

Failure to load the AST Set into the instrument correctly will result in an anonymous condition that must be resolved within eight hours. If condition is not resolved within eight hours, the AST Set must be discarded and set up again.

Failure to use the BD BACTEC MGIT 960 PZA Supplement in the PZA AST set may give inaccurate results. DO NOT add BD BACTEC MGIT 960 SIRE Supplement or BD BACTEC MGIT Growth Supplement to the PZA AST set.

Failure to use BD BACTEC MGIT 960 PZA Medium for the PZA AST set may give inaccurate results. DO NOT substitute BD BBL MGIT 7 mL Mycobacteria Growth Indicator Tubes for BD BACTEC MGIT 960 PZA Medium.

EXPECTED VALUES

A total of 118 clinical isolates of *M. tuberculosis* were tested with the BD BACTEC MGIT 960 PZA susceptibility test at four geographically diverse sites. The testing included both fresh clinical and subcultured isolates from both liquid and solid culture sources. A total of 228 PZA susceptibility tests (liquid and solid) were performed.

During the external evaluation of the BD BACTEC MGIT 960 PZA Kit, there were nine PZA tests from clinical isolates that required repeat testing due to contamination (six isolates) or overinoculation/procedural errors (three isolates).

The average time-to-result for the BD BACTEC MGIT 960 PZA susceptibility test is seven days with a range from four to seventeen days. The data are shown in Figure 1 at end of insert.

PERFORMANCE CHARACTERISTICS

Analytical Studies

Liquid and Solid Media AST Inoculum Ranges:

Liquid media - The recommended procedure for preparing a PZA Set from a positive MGIT 7 mL tube uses a direct inoculum on Day 1 and Day 2 post-positivity and a dilute (1:5) inoculum on Day 3 to Day 5 post-positivity. Internal studies show that inocula prepared from a Day 1 to Day 5 positive MGIT 7 mL tube range between 2.0×10^4 to 7.5×10^6 CFU/mL.

Solid media - The recommended procedure for preparing a PZA Set from growth on solid media (up to 14 days after first visible growth is seen) uses a 1:5 dilution of an organism suspension equivalent to a 0.5 McFarland Standard. Internal studies show that inocula prepared from solid medium culture range between 2.1×10^5 to 3.9×10^6 CFU/mL.

Lot Reproducibility:

Lot reproducibility was evaluated using twenty-five *M. tuberculosis* strains (including three ATCC strains). Each strain was tested in triplicate with the BD BACTEC MGIT 960 PZA susceptibility test. Each replicate represented a separate test condition differentiated by lot of PZA drug, PZA supplement and PZA medium used (three lots each).

Observed results were compared to the expected results. The overall reproducibility for the BD BACTEC MGIT 960 PZA susceptibility test is 96.8%.

CDC Challenge Panel Testing:

The performance of the BD BACTEC MGIT 960 PZA susceptibility test was evaluated using a panel of challenge strains obtained from the Centers for Disease Control and Prevention (CDC), Atlanta, GA, USA. The panel consisted of nine strains of *M. tuberculosis* with known susceptibility patterns (using BD BACTEC 460TB). The panel was tested in triplicate with the BD BACTEC MGIT 960 PZA susceptibility test. The BD BACTEC MGIT 960 PZA results were compared to the CDC expected results. The overall agreement with CDC expected results for the BD BACTEC MGIT 960 PZA susceptibility test is 98.7%.

Clinical Evaluation

The BD BACTEC MGIT 960 PZA susceptibility test was evaluated at four geographically diverse clinical sites composed of regional reference centers and university hospital-based laboratories, including two ex-US sites. The BD BACTEC MGIT 960 PZA susceptibility test was compared to the BD BACTEC 460TB PZA susceptibility test method.

Reproducibility Testing:

The reproducibility of the BD BACTEC MGIT 960 PZA susceptibility test was evaluated at the clinical sites using a panel of five qualified strains. The BD BACTEC MGIT 960 PZA test results were compared to the expected results. The overall reproducibility for the BD BACTEC MGIT 960 PZA susceptibility test is 94%.

CDC Challenge Panel Testing:

The performance of the BD BACTEC MGIT 960 PZA susceptibility test was evaluated at each of the four clinical sites using a panel of challenge strains obtained from the Centers for Disease Control and Prevention (CDC), Atlanta, GA, USA. The panel consisted of nine strains of *M. tuberculosis* with known susceptibility patterns (using BD BACTEC 460TB). Of the thirty-six PZA results collected with the BD BACTEC MGIT 960 PZA susceptibility test, thirty-three agreed with the CDC expected results. The calculated percent agreement to the CDC expected results for the BD BACTEC MGIT 960 PZA susceptibility test is 91.7%.

Clinical Isolate Testing:

A total of 118 clinical isolates of *M. tuberculosis* were tested with the BD BACTEC MGIT 960 PZA susceptibility test and the BD BACTEC 460TB PZA susceptibility test. This included testing of both fresh clinical and subcultured isolates from both liquid and solid culture sources. This generated a total of 228 test results.

Table 1 presents the results from clinical isolate testing for PZA drug at 100 µg/mL from liquid source cultures, from solid source cultures and both source cultures combined.

Table 1: Clinical Isolate Results – BD BACTEC MGIT 960 PZA susceptibility test compared to BD BACTEC 460TB susceptibility test

		BD BACTEC 460TB System		BD BACTEC MGIT 960 System			
		Expected PZA Results		Susceptible Results		Resistant Results	
Source	# Tests	S	R	# agree	Category agreement % (95% CI)	# agree	Category agreement % (95% CI)
LIQUID	112	89	23	88	98.9% (93.9–100)	22	95.7% (78.1–99.9)
SOLID	113*	90	23	88	97.8% (92.2–99.7)	20	87.0% (66.4–97.2)
ALL	225*	179	46	176	98.3% (95.2–99.7)	42	91.3% (79.2–97.6)

*Three BD BACTEC 460TB borderline results are not included in this table.

All isolates with discordant BD BACTEC MGIT 960 PZA test results were tested using the BD BACTEC 460TB PZA susceptibility test at two independent sites. Discordant results were those strains where the BD BACTEC MGIT 960 PZA test result differed from the BD BACTEC 460TB PZA test result. Borderline results are not included in the performance calculations for the BD BACTEC MGIT 960 PZA Kit.

Of the four discordant PZA susceptible (S-BACTEC MGIT 960, R-BACTEC 460TB) isolates tested, one had susceptible results from both independent sites and the other three had resistant results from both independent sites. Of the three discordant PZA resistant (R-BACTEC MGIT 960, S-BACTEC 460TB) isolates tested, all isolates had susceptible results from both independent sites.

Two of the three BD BACTEC 460TB borderline PZA results (S-BACTEC MGIT 960, B-BACTEC 460TB) had susceptible results from both independent sites. One of the three BD BACTEC 460TB borderline PZA results (R-BACTEC MGIT 960, B-BACTEC 460TB) had one independent site determine a susceptible result. The other independent site determined a borderline result.

AVAILABILITY

Cat. No.	Description
245128	BD BACTEC™ MGIT™ 960 PZA Kit.
245115	BD BACTEC™ MGIT™ 960 PZA Medium, 25 tests.

REFERENCES

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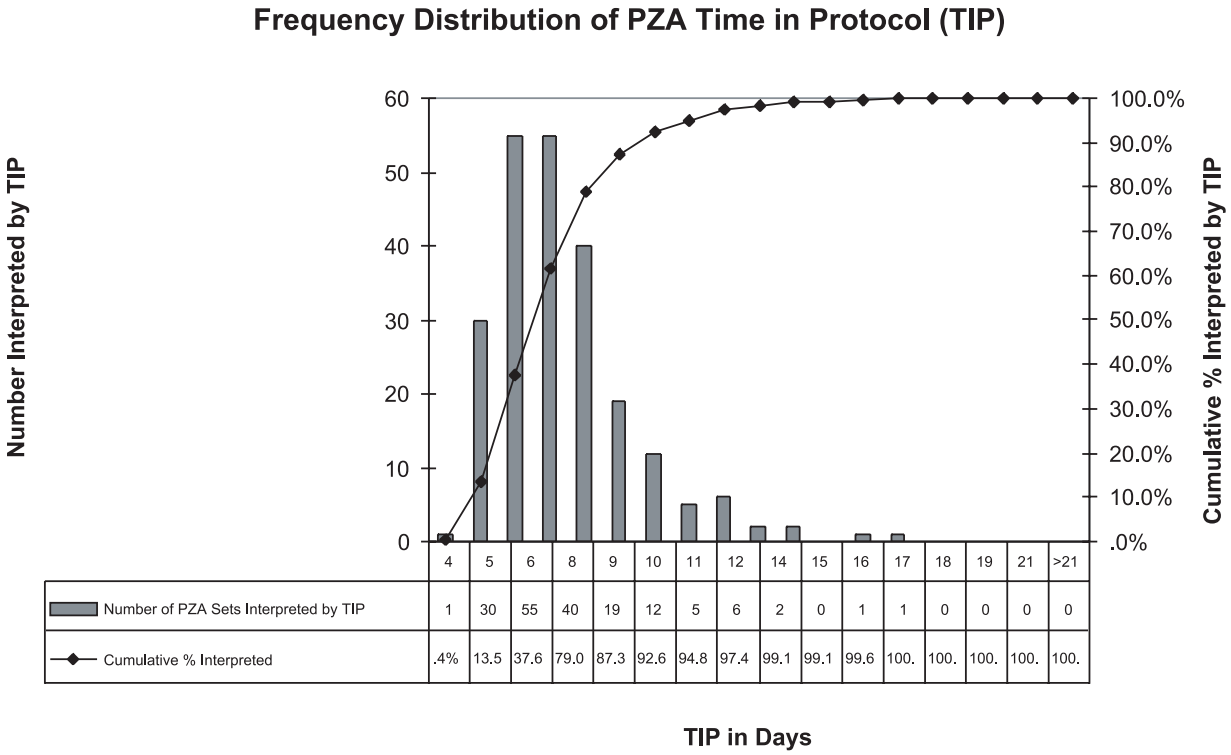
Technical Information: In the United States contact BD Technical Service and Support at 1.800.638.8663 or bd.com.

Figure 1: Distribution of BD BACTEC MGIT 960 PZA AST Time to Result



TIP	4	5	6	8	9	10	11	12	14	15	16	17	18	19	21	>21
Number of PZA Sets Interpreted by TIP	1	30	55	40	19	12	5	6	2	0	1	1	0	0	0	0
Cumulative % Interpreted	.4%	13.5	37.6	79.0	87.3	92.6	94.8	97.4	99.1	99.1	99.6	100.	100.	100.	100.	100.

Change History

Revision	Date	Change Summary
(04)	2019-09	Converted printed instructions for use to electronic format and added access information to obtain the document from bd.com/e-labeling.
(05)	2019-10	Added Chart of Frequency Distribution of PZA Time in Protocol (TIP), inadvertently not included in the previously undistributed version.

US Customers only: For symbol glossary, refer to bd.com/symbols-glossary

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RRRR-MM-DD / RRRR-MM (MM = konec měsíce)
ÅÅÅÅ-MM-DD / ÅÅÅÅ-MM (MM = slutning af måned)
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AAAA-MM-DD / AAAA-MM (MM = fin del mes)
AAAA-KK-PP / AAAA-KK (KK = kuu lõpp)
AAAA-MM-JJ / AAAA-MM (MM = fin du mois)
GGGG-MM-DD / GGGG-MM (MM = kraj mjeseca)
ÉÉÉÉ-HH-NN / ÉÉÉÉ-HH (HH = hónap utolsó napja)
AAAA-MM-GG / AAAA-MM (MM = fine mese)
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MMMM-MM-DD / MMMM-MM (MM = mėnesio pabaiga)
GGGG-MM-DD/GGGG-MM (MM = mēneša beigas)
JJJJ-MM-DD / JJJJ-MM (MM = einde maand)
ÅÅÅÅ-MM-DD / ÅÅÅÅ-MM (MM = slutten av måneden)
RRRR-MM-DD / RRRR-MM (MM = koniec miesiąca)
AAAA-MM-DD / AAAA-MM (MM = fim do mês)
AAAA-LL-ZZ / AAAA-LL (LL = sfârşitul lunii)
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GGGG-MM-DD / GGGG-MM (MM = kraj meseca)
ÅÅÅÅ-MM-DD / ÅÅÅÅ-MM (MM = slutet av månaden)
YYYY-AA-GG / YYYY-AA (AA = ayın sonu)
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In Vitro Diagnostic Medical Device / Медицински уред за диагностика ин витро / Lékařské zařízení určené pro diagnostiku in vitro / In vitro diagnostisk medicinsk anordning / Medizinisches In-vitro-Diagnostikum / In vitro διαγνωστική ιατρική συσκευή / Dispositivo médico para diagnóstico in vitro / In vitro diagnostika meditsiiniaparatuur / Dispositif médical de diagnostic in vitro / Medicinska pomagala za In Vitro Dijagnostiku / In vitro diagnosztikai orvosi eszköz / Dispositivo medicale per diagnostica in vitro / Жасанды жағдайда жүргізетін медициналық диагностика аспабы / In Vitro Diagnostic 의료 기기 / In vitro diagnostikos prietaisas / Medicīnas ierīces, ko lieto in vitro diagnostikā / Medisch hulpmiddel voor in-vitro diagnostiek / In vitro diagnostisk medisinsk utstyr / Urządzenie medyczne do diagnostyki in vitro / Dispositivo médico para diagnóstico in vitro / Dispozitiv medical pentru diagnostic in vitro / Медицинский прибор для диагностики in vitro / Medicínska pomôcka na diagnostiku in vitro / Medicinski uređaj za in vitro dijagnostiku / Medicinteknisk produkt för in vitro-diagnostik / İn Vitro Diyagnostik Tıbbi Cihaz / Медичний пристрій для діагностики in vitro / 体外诊断医疗设备

Temperature limitation / Температурни ограничения / Teplotní omezení / Temperaturbegrænsning / Temperaturbegrenzung / Περιορισμοί θερμοκρασίας / Limitación de temperatura / Temperatuuri piirang / Limites de température / Dozvoljena temperatura / Hőmérsékleti határ / Limiti di temperatura / Температураны шектеу /온도 제한 / Laikymo temperatūra / Temperatūras ierobežojumi / Temperatuurlimiet / Temperaturbegrensning / Ograniczenie temperatury / Limites de temperatura / Limite de temperatură / Ограничение температуры / Ohraničenie teploty / Ograničenje temperature / Temperaturgräns / Sıcaklık sınırlaması / Обмеження температури / 温度限制

Batch Code (Lot) / Код на партидата / Kód (číslo) šarže / Batch-kode (lot) / Batch-Code (Charge) / Κωδικός παρτίδας (παρτίδα) / Código de lote (lote) / Partii kood / Numéro de lot / Lot (kod) / Tétel száma (Lot) / Codice batch (lotto) / Топтама коды / 배치 코드(로트) / Partijos numeris (LOT) / Partijas kods (laidiens) / Lot nummer / Batch-kode (parti) / Kod partii (seria) / Código do lote / Cod de serie (Lot) / Код партии (лот) / Kód série (šarža) / Kod serije / Partinummer (Lot) / Parti Kodu (Lot) / Код партії / 批号（亚批）

Contains sufficient for <n> tests / Съдържанието е достатъчно за <n> теста / Dostatečné množství pro <n> testů / Indeholder tilstrækkeligt til <n> tests / Ausreichend für <n> Tests / Περιέχει επαρκή ποσότητα για <n> εξετάσεις / Contenido suficiente para <n> pruebas / Küllaldane <n> testide jaoks / Contenu suffisant pour <n> tests / Sadržaj za <n> testova / <n> teszthez elegendő / Contenuto sufficiente per <n> test / <n> тесттері үшін жеткілікті / <n> 테스트가 충분히 포함됨 / Pakankamas kiekis atlikti <n> testų / Satur pietiekami <n> pārbaudēm / Inhoud voldoende voor “n” testen / Innholder tilstrekkelig til <n> tester / Zawiera ilość wystarczającą do <n> testów / Conteúdo suficiente para <n> testes / Conţinut suficient pentru <n> teste / Достаточно для <n> тестов(а) / Obsah vystačí na <n> testov / Sadržaj dovoljan za <n> testova / Innehåller tillräckligt för <n> analyser / <n> test için yeterli malzeme içerir / Вистачить для аналізів: <n> / 足够进行 <n> 次检测

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Control / Контролно / Kontrola / Kontrol / Kontrolle / Μάρτυρας / Kontroll / Contrôle / Controllo / Бақылау / 컨트롤 / Kontrolė / Kontrole / Controle / Controlo / Контроль / kontroll / Контроль / 对照

Positive control / Положителен контрол / Pozitivní kontrola / Positiv kontrol / Positive Kontrolle / Θετικός μάρτυρας / Control positivo / Positiivne kontroll / Contrôle positif / Pozitivna kontrola / Pozitív kontroll / Controllo positivo / Оң бақылау / 양성 컨트롤 / Teigiama kontrolė / Pozitīvā kontrole / Positieve controle / Kontrola dodatnia / Controlo positivo / Control pozitiv / Положительный контроль / Pozitif kontrol / Позитивний контроль / 阳性对照试剂

Negative control / Отрицателен контрол / Negativní kontrola / Negativ kontrol / Negative Kontrolle / Αρνητικός μάρτυρας / Control negativo / Negatiivne kontroll / Contrôle négatif / Negativna kontrola / Negatív kontroll / Controllo negativo / Неративтік бақылау / 음성 컨트롤 / Neigiama kontrolė / Negatīvā kontrole / Negatieve controle / Kontrola ujemna / Controlo negativo / Control negativ / Отрицательный контроль / Negatif kontrol / Негативний контроль / 阴性对照试剂

Method of sterilization: ethylene oxide / Метод на стерилизация: етиленов оксид / Způsob sterilizace: etylenoxid / Steriliseringsmetode: ethylenoxid / Sterilisationsmethode: Ethylenoxid / Μέθοδος αποστείρωσης: αιθυλενοξείδιο / Método de esterilización: óxido de etileno / Steriliseerimismeetod: etüleenoksiid / Méthode de stérilisation : oxyde d'éthylène / Metoda sterilizacije: etilen oksid / Sterilizálás módszere: etilén-oxid / Metodo di sterilizzazione: ossido di etilene / Стерилизация әдісі – этилен тотығы / 소독 방법: 에틸렌옥사이드 / Sterilizavimo būdas: etileno oksidas / Sterilizēšanas metode: etilēnoksīds / Gesteriliseerd met behulp van ethyleenoxide / Steriliseringsmetode: etylenoksid / Metoda sterylizacji: tlenek etylu / Método de esterilização: óxido de etileno / Metodă de sterilizare: oxid de etilenă / Метод стерилизации: этиленоксид / Metóda sterilizácie: etylénoxid / Metoda sterilizacije: etilen oksid / Steriliseringsmetod: etenoxid / Sterilizasyon yöntemi: etilen oksit / Метод стерилізації: етиленоксидом / 灭菌方法：环氧乙烷

Method of sterilization: irradiation / Метод на стерилизация: ирадиация / Způsob sterilizace: záření / Steriliseringsmetode: bestråling / Sterilisationsmethode: Bestrahlung / Μέθοδος αποστείρωσης: ακτινοβολία / Método de esterilización: irradiación / Steriliseerimismeetod: kiirgus / Méthode de stérilisation : irradiation / Metoda sterilizacije: zračenje / Sterilizálás módszere: besugárzás / Metodo di sterilizzazione: irradiazione / Стерилизация әдісі – сәуле түсіру / 소독 방법: 방사 / Sterilizavimo būdas: radiacija / Sterilizēšanas metode: apstarošana / Gesteriliseerd met behulp van bestraling / Steriliseringsmetode: bestråling / Metoda sterylizacji: napromienianie / Método de esterilização: irradiação / Metodă de sterilizare: iradiere / Метод стерилизации: облучение / Metóda sterilizácie: ožiarenie / Metoda sterilizacije: ozračavanje / Steriliseringsmetod: strålning / Sterilizasyon yöntemi: irradyasyon / Метод стерилізації: опроміненням / 灭菌方法：辐射

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Upper limit of temperature / Горен лимит на температурата / Horní hranice teploty / Øvre temperaturgrænse / Temperaturobergrenze / Ανώτερο όριο θερμοκρασίας / Límite superior de temperatura / Ülemine temperatuuripiir / Limite supérieure de température / Gornja dozvoljena temperatura / Felső hőmérsékleti határ / Limite superiore di temperatura / Температураның руқсат етілген жоғарғы шеги / 상한 온도 / Aukščiausia laikymo temperatūra / Augšējā temperatūras robeža / Hoogste temperatuurlimiet / Øvre temperaturgrense / Górna granica temperatury / Limite máximo de temperatura / Limită maximă de temperatură / Верхний предел температуры / Horná hranica teploty / Gornja granica temperature / Övre temperaturgräns / Sıcaklık üst sınırı / Максимальна температура / 温度上限

Keep dry / Пазете сухо / Skladujte v suchém prostředí / Opbevares tørt / Trocklagern / Φυλάξτε το στεγνό / Mantener seco / Hoida kuivas / Conserver au sec / Držati na suhom / Száraz helyen tartandó / Tenere all'asciutto / Құрғақ күйінде ұста / 건조 상태 유지 / Laikykite sausai / Uzglabāt sausu / Droog houden / Holdes tørt / Przechowywać w stanie suchym / Manter seco / A se feri de umezeală / Не допускать попадания влаги / Uchovávajte v suchu / Držite na suvom mestu / Förvaras torrt / Kuru bir şekilde muhafaza edin / Берегти від вологи / 请保持干燥

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Perforation / Перфорация / Perforace / Perforering / Διάτρηση / Perforación / Perforatsioon / Perforacija / Perforálás / Perforazione / Тесік тесу / 절취선 / Perforacija / Perforācija / Perforatie / Perforacja / Perfuração / Perforare / Перфорация / Perforácia / Perforasyon / Перфорація / 穿孔

Do not use if package damaged / Не използвайте, ако опаковката е повредена / Nepoužívejte, je-li obal poškozený / Må ikke anvendes hvis emballagen er beskadiget / Inhal beschädigter Packungnicht verwenden / Μη χρησιμοποιείτε εάν η συσκευασία έχει υποστεί ζημιά. / No usar si el paquete está dañado / Mitte kasutada, kui pakend on kahjustatud / Ne pas l'utiliser si l'emballage est endommagé / Ne koristiti ako je oštećeno pakiranje / Ne használja, ha a csomagolás sérült / Non usare se la confezione è danneggiata / Ерер пакет бұзылған болса, пайдаланба / 패키지가 손상된 경우 사용 금지 / Jei pakuotė pažeista, nenaudoti / Nelietot, ja iepakojums bojāts / Niet gebruiken indien de verpakking beschadigd is / Må ikke brukes hvis pakke er skadet / Nie używać, jeśli opakowanie jest uszkodzone / Não usar se a embalagem estiver danificada / A nu se folosi dacă pachetul este deteriorat / Не использовать при повреждении упаковки / Nepoužívajte, ak je obal poškodený / Ne koristite ako je pakovanje oštećeno / Använd ej om förpackningen är skadad / Ambalaj hasar görmüşse kullanmayın / Не використовувати за пошкодженої упаковки / 如果包装破损，请勿使用

Keep away from heat / Пазете от топлина / Nevystavujte přílišnému teplu / Må ikke udsættes for varme / Vor Wärme schützen / Κρατήστε το μακριά από τη θερμότητα / Mantener alejado de fuentes de calor / Hoida eemal valgusest / Protéger de la chaleur / Držati dalje od izvora topline / Óvja a melegtől / Tenere lontano dal calore / Салқын жерде сақта / 열을 피해야 함 / Laikyti atokiau nuo šilumos šaltinių / Sargāt no karstuma / Beschermen tegen warmte / Må ikke utsettes for varme / Przechowywać z dala od źródeł ciepła / Manter ao abrigo do calor / A se feri de căldură / Не нагревать / Uchovávajte mimo zdroja tepla / Držite dalje od toplote / Får ej utsättas för värme / Isıdan uzak tutun / Берегти від дії тепла / 请远离热源

Cut / Срежете / Odstřihněte / Klip / Schneiden / Κόψτε / Cortar / Lõigata / Découper / Reži / Vágja ki / Tagliare / Кесіңіз / 잘라내기 / Kirpti / Nogriezt / Knippen / Kutt / Odciąć / Cortar / Decupați / Отрезать / Odstrihnite / Iseći / Klipp / Kesme / Розрізати / 剪下

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µL/test / µL/тест / µL/Test / µL/εξέταση / µL/prueba / µL/teszt / µL/테스트 / мкл/тест / µL/tyrimas / µL/pārbaude / µL/teste / мкл/аналіз / µL/检测

Keep away from light / Пазете от светлина / Nevystavujte světlu / Må ikke udsættes for lys / Vor Licht schützen / Κρατήστε το μακριά από το φως / Mantener alejado de la luz / Hoida eemal valgusest / Conserver à l'abri de la lumière / Držati dalje od svjetla / Fény nem érheti / Tenere al riparo dalla luce / Қараңғыланған жерде ұста / 빛을 피해야 함 / Laikyti atokiau nuo šilumos šaltinių / Sargāt no gaismas / Niet blootstellen aan zonlicht / Må ikke utsettes for lys / Przechowywać z dala od źródeł światła / Manter ao abrigo da luz / Feriți de lumină / Хранить в темноте / Uchovávajte mimo dosahu svetla / Držite dalje od svetlosti / Får ej utsättas för ljus / Işıktan uzak tutun / Берегти від дії світла / 请远离光线

Hydrogen gas generated / Образуван е водород газ / Možnost úniku plynného vodíku / Frembringer hydrogengas / Wasserstoffgas erzeugt / Δημιουργία αερίου υδρογόνου / Producción de gas de hidrógeno / Vesinikgaasi tekitatud / Produit de l'hydrogène gazeux / Sadrži hydrogen vodik / Hidrogén gázt fejleszt / Produzione di gas idrogeno / Газтектес сутегі пайда болды / 수소 가스 생성됨 / Išskiria vandenilio dujas / Rodas ūdeņradis / Waterstofgas gegenereerd / Hydrogengass generert / Powoduje powstawanie wodoru / Produção de gás de hidrogénio / Generare gaz de hidrogen / Выделение водорода / Vyrobené použitím vodíka / Oslobađa se vodonik / Genererad vätgas / Açığa çıkan hidrojen gazı / Реакція з виділенням водню / 会产生氢气

Patient ID number / ИД номер на пациента / ID pacienta / Patientens ID-nummer / Patienten-ID / Αριθμός αναγνώρισης ασθενούς / Número de ID del paciente / Patsiendi ID / No d'identification du patient / Identifikacijski broj pacijenta / Beteg azonosító száma / Numero ID paziente / Пациенттің идентификациялық нөмірі / 환자 ID 번호 / Paciento identifikavimo numeris / Pacienta ID numurs / Identificatienummer van de patiënt / Pasientens ID-nummer / Numer ID pacjenta / Número da ID do doente / Număr ID pacient / Идентификационный номер пациента / Identifikačné číslo pacienta / ID broj pacijenta / Patientnummer / Hasta kimlik numarası / Ідентифікатор пацієнта / 患者标识号

Fragile, Handle with Care / Чупливо, Работете с необходимото внимание. / Křehké. Při manipulaci postupujte opatrně. / Forsigtig, kan gå i stykker. / Zerbrechlich, vorsichtig handhaben. / Εύθραυστο. Χειριστείτε το με προσοχή. / Frágil. Manipular con cuidado. / Õrn, käsitsege ettevaatlikult. / Fragile. Manipuler avec précaution. / Lomljivo, rukujte pažljivo. / Törékeny! Óvatosan kezelendő. / Fragile, maneggiare con cura. / Сынғыш, абайлап пайдаланыңыз. / 조심 깨지기 쉬운 처리 / Trapu, elkitės atsargiai. / Trausls; rīkoties uzmanīgi / Breekbaar, voorzichtig behandelen. / Ømtålig, håndter forsiktig. / Krucha zawartość, przenosić ostrożnie. / Frágil, Manuseie com Cuidado. / Fragil, manipulați cu atenție. / Хрупкое! Обращаться с осторожностью. / Krehké, vyžaduje sa opatrná manipulácia. / Lomljivo - rukujte pažljivo. / Bräckligt. Hantera försiktigt. / Kolay Kırılır, Dikkatli Taşıyın. / Тендітна, звертатися з обережністю / 易碎，小心轻放

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