Washington State Tuberculosis Services and Standards Manual

Chapter 12:

Lab Services

Washington State Department of HEALTH

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About the Washington State Tuberculosis Services and Standards Manual

Purpose

In Washington State, tuberculosis (TB) care and prevention is governed by state law and rule. The purpose of the TB Services and Standards manual is to provide information and guidance to aid local health jurisdictions (LHJs) in fulfilling the requirements detailed in the Revised Code of Washington (RCW) 70.28.005 and the Washington Administrative Code (WAC) 246-170. This manual includes information and links to CDC guidelines and TB Centers of Excellence materials with key steps and information needed to fulfill these required TB care and prevention tasks.

Audience

The most likely readers of this manual are people working in the health field. This may include, but is not limited to: nurses, physicians, Health Officers, Regional Medical Officers, epidemiologists, disease intervention specialists and outreach workers from local and state TB programs, Indian Health Services, clinics and hospitals.

Eliminating Stigmatizing Language

Judgmental terms and negative connotations of words such as 'defaulter' and 'suspect' may be perceived to place blame for the disease and responsibility for adverse treatment outcomes on the patient. To assist in implementing a change in the use of stigmatizing language the Heartland TB Center of Excellence, the International Union Against TB and Lung Disease, the National Society of TB Clinicians, the global TB community and the Treatment Action Group developed the Stop the Stigma: Eliminating Stigmatizing Language reference tool to aid in identifying suggested replacement language as a reminder of how our words may affect others.

Use This….	Not that….	Use This….	Not that….
Adherence / Non-adherence	Compliance / Non-compliance	Undocumented	Illegal; Illegal alien
Person lost to follow up	Defaulter	Person with TB disease	TB case
TB Prevention and Care	TB Control	Treatment failed	Treatment failure
Person to be evaluated for TB	TB Suspect	Missed doses/ Non-adherent	Delinquent
HIV-Positive	HIV-infected	Contact Analysis; Contact Elicitation; Contact Identification	Investigation; Investigate
Immigrant	Alien	Exposed to TB	TB Contact
Lack of housing; Under-housed; People experiencing homelessness	Homeless/ Homelessness	Tuberculosis	Consumption; White Plague

Adapted from: https://www.heartlandntbc.org/wpcontent/uploads/2021/12/FactSheet_Final_5_19_16.pdf

Stop TB Partnership's Words Matter Language Guide is an additional resource available to encourage positive change, sensitize, promote appropriate language, end the stigmatization, and empower people affected by TB.

How to Use This Manual

Icons

Throughout the manual, these icons quickly cue you about important information and other resources:

This warns about high-consequence information you must understand when performing the task.

This signals when you should call to report or to consult on the task.

This highlights special considerations for pediatric patients.

This suggests another relevant area in the manual or another resource that you may want to review.

This alerts you that a form is available for the task.

Chapter 12: Laboratory Services

Introduction

Purpose

Use this section to:

- Get contact information for Washington State Public Health Lab (WAPHL) and some private laboratories.
- Determine which tests are available and the turnaround times.
- Identify which laboratory can perform a specific test.

The diagnosis of tuberculosis (TB), management of patients with the disease, and public health TB prevention and elimination services rely on accurate laboratory tests. Laboratory services are an essential component of effective TB control, providing key information to clinicians (for patient care) and public health agencies (for control services).

Policy

Public health laboratories should ensure that clinicians and public health agencies within their jurisdictions have ready access to reliable laboratory tests for diagnosis and treatment of TB. This may come from the WAPHL, private laboratories and reference or core laboratories.

Effective TB care requires:

- timely, complete, and accurate communication among the laboratory system, TB program, and healthcare provider, and.
- good quality specimens that are packaged and transported in a timely manner.

In the WAC, see Chapter 246-101 (Notifiable Conditions) in the Title 246 (Department of Health).

For unfamiliar terms and acronyms refer to *Chapter 18: Glossary*.

TB Laboratories in Washington State

Washington State Public Health Laboratory (WAPHL)

As the state's primary reference laboratory, the Washington State Public Health Lab (WAPHL) provides LHJs, hospitals, clinics and specialty laboratories with a wide range of services including identification, confirmation, susceptibility testing of pathogenic organisms, consultation and training in laboratory methodologies. Here are some other important details about WAPHL services. The WAPHL

- Receives and processes *Mycobacterium tuberculosis* (MTB) specimens five days a week, 8 am to 5 pm.
- Accepts primary specimens and referral isolates from Reference (Core) labs for identification and susceptibility testing of MTB.
- Coordinates genotyping of positive isolates.
- Serves as a consultant for questions involving mycobacterium laboratory testing.
- Coordinates whole genome sequencing of positive isolates.

Contact Information

Washington State Public Health Laboratory

1610 NE 150th ST

Shoreline, WA 98155

WAPHL website: https://doh.wa.gov/public-health-healthcare-providers/public-health-laboratories

WAPHL email: StateTBLab@doh.wa.gov

TB Lab Lead, Phone: 206-418-5473. The TB Lab Lead is the subject matter expert that specializes on the day to day operations of the lab.

TB Lab Supervisor, Phone: 206-418-5474. The TB Lab Supervisor is a resource for customer service answers if the lab is busy.

See the **Lab Test Menu** for TB related testing, requisition forms and turnaround times (TAT)

Tuberculosis Laboratory Diagnostics Summary (wa.gov)

For information on submitting sputum samples for TB Testing to WAPHL see: Washington State Public Health Lab TB Specimen Submission Instructions

For information on collecting and submitting all types of AFB samples see: SCSI-TB-AFB-Cx-V1-Public Health Laboratories Instructions for Collecting and Submitting Specimens (wa.gov)

Community Based Clinical Laboratories

Private laboratories may be found as part of a hospital or hospital system, such as Harborview/UW Medicine Laboratories and King County Lab, or they may be commercial facilities such as LabCorp or Quest Diagnostics. Most laboratories provide Interferon Gamma Release Assay (IGRA) testing, either QuantiFERON or T-Spot as well as primary specimen smear and culture testing for mycobacteria. However, for the next steps, specimen identification and susceptibility testing many of these labs refer isolates either to a Core Lab (reference Lab) or to the WAPHL. Contact your local laboratory to find out what tests and services they offer.

Core / Reference Laboratories (Public and Private)

Contact Information	Testing Provided
National PHL DST Reference Center California Department of Public Health 850 Marina Bay Parkway, E164 Richmond, CA 94804 Tel: (510) 412-3929 Fax: (510) 412-3704	• Pyrosequencing (PSQ) for the molecular detection of drug resistance • Confirmation of first-line drug testing on Mycobacterium tuberculosis (MTB) complex isolates • Second-line drug testing on MTB complex isolates
Centers for Disease Control and Prevention CDC STAT Lab TB Laboratory, Unit 29 1600 Clifton Road, NE Atlanta, Ga. 30333	• DNA sequencing for the molecular detection of drug resistance (MDDR Program) • Confirmation of first-line drug testing on MTB complex isolates • Second-line drug testing on MTB complex isolates
National Jewish Health **Mycobacteriology Reference Laboratory** 1400 Jackson St. Denver, CO 80206 Tel: 800-550-6227 Fax: (303) 398-1953	• Non-tuberculosis mycobacterium susceptibility testing • Confirmation of first-line drug testing on MTB complex isolates • Second-line drug testing on MTB complex isolates

Bacteriology Testing Used in Diagnosing TB Disease

Examinations of clinical specimens (e.g., sputum, urine, or cerebrospinal fluid) are of critical diagnostic importance. The specimens should be examined and cultured in a laboratory that specializes in testing for MTB. Optimal bacteriologic examination has five parts:

1. Specimen collection, transport, and processing
2. Acid Fast Bacilli (AFB) smear classification
3. Direct detection of MTB in clinical specimens using nucleic acid amplification (NAA) and, as applicable, molecular detection of drug resistance (MDDR)
4. Specimen culture and identification of MTB
5. Drug susceptibility testing using growth-based and molecular methods

To confirm the diagnosis of mycobacterial disease, AFB smear and culture and sensitivities must all be ordered:

- The WAPHL automatically performs culture identification on any isolate, and first-line susceptibility testing is automatically performed on all initial MTB complex isolates,
- Many private labs do not do this automatically, so all tests (NAA, smear, culture, sensitivities) must be ordered separately.

Test	Description	Typical Laboratory Turnaround Times
AFB Smear	• Provides the physician with a preliminary confirmation of the diagnosis. • It usually is the first bacteriologic evidence of the presence of mycobacteria in a clinical specimen. • If positive, gives a semiquantitative estimate of the number of bacilli being excreted (which is of vital clinical and epidemiologic importance in assessing the patient's infectiousness). • Does not differentiate between live and dead mycobacterium. • Performed in most laboratories.	**WAPHL:** within 24 hours from lab receiving the specimen. **Typical hospital or private lab:** within 24 hours from laboratory receipt of specimen (time from specimen collection to laboratory receipt should be 24 hours or less).
Culture and Identification (ID) **Nucleic Acid Amplification (NAA) Test**	• Usually necessary for species identification of all clinical specimens suspected of containing mycobacteria through molecular testing. • Is required for drug susceptibility testing and genotyping. • Gold standard for diagnosing TB. • Only detects live mycobacterium.	**WAPHL:** Mycobacterial growth detection: if positive is within 2-6 weeks after receiving. (May take up to 6 weeks if the bacterial load is low.) ID are performed automatically on positive cultures to determine the type of mycobacterium present. WAPHL uses NAA test to identify MTBC or MAC. **Typical hospital or private lab:** (Performed at Harborview, SKC PHL, PAML, UW, and commercial labs.)

		Identification is reported out 1-2 days after culture (usually calling submitters and releasing reports
GeneXpert® Xpert® MTB/RIF Assay	• A test done on clinical specimens for the direct and rapid identification of the MTB. • Allows for the amplification of specific target sequences of nucleic acids that will be detected by a nucleic acid probe. • **Does not replace the need for routine AFB smear and culture.** • Detects MTBC and rpoB mutations. • Performed on decontaminated/concentrated samples (1x per new patient, second by request). **Only sputum samples are validated for GeneXpert.** • Performed after AFB smear, if ordered (more sensitive on smear positive specimens). • A positive GeneXpert is considered a diagnosed case of TB. • **A negative GeneXpert does not rule out TB.** • Does not differentiate between live and dead mycobacterium. • Two methods for NAA testing include: 1. Real-Time Polymerase Chain Reaction (RT-PCR) performed at WAPHL. 2. Hsp65 Sequencing performed at UW for NTM.	**WAPHL**: within 24-48 hours from lab receiving the specimen. **Typical hospital or private lab:** within 24-48 hours from laboratory receipt of specimen
Drug Sensitivity Testing (DST)	For first-line drugs: Is performed on initial isolates of all patients to identify an effective anti-TB regimen. For both first-line and second-line drugs: Is repeated on interim isolates when a patient remains culture-positive after 3 months of treatment. Performed at Harborview, PAML, or WAPHL. Second-line performed at WAPHL or CDC using plate or Agar Proportion Method, if first-line resistance detected (except PZA) or as requested.	**WAPHL:** Performed when requested on NAAT or culture positive specimens. First-line drugs DST, available within 30 days of culture positive result, or 17 days from receiving specimens for reference specimens. First-line (SIRE and PZA) performed automatically, using MGIT instrument, on culture positive specimens. **Reference lab:** Second-line DST usually reported 4 weeks from request or when identified resistant in first-line DST.

Drug Resistance Mutation Detection	Detects common mutations located within specific regions of TB DNA associated with drug resistance. Performed when requested on NAAT or culture positive specimens. Molecular Detection of Drug Resistance (MDDR) is performed at CDC for detecting mutations. Detected mutation does not always mean total resistance to the drug(s).	MDDR turnaround time is 5 weeks from date received at CDC (sequencing results usually within 1-2 weeks, and phenotypic DST up to 5 weeks).
Genotyping	• Performed automatically on culture positive specimens. • Determines the strain of TB and whether it matches other strains of TB.	Performed by a CDC contracted lab in Michigan. Results are returned in approximately 14 days
Acronyms: Washington State Public Health Lab (WAPHL), Seattle and King County Public Health Lab (SKC PHL), Pathology Associates Medical Laboratory (PAML), University of Washington (UW), Non-tuberculosis mycobacteria (NTM), Mycobacterium Tuberculosis Complex (MTBC), Mycobacterium Avium Complex (MAC), Centers for Disease Control (CDC), Streptomycin, Isoniazid, Rifampin, Ethambutol (SIRE), Pyrazinamide (PZA).		
Adapted from: ATS, CDC, IDSA. Controlling tuberculosis in the United States: recommendations from the American Thoracic Society, CDC, and the Infectious Diseases Society of America. MMWR 2005;54(No. RR-12):19; and Tenover, R., et al. The resurgence of tuberculosis: is your laboratory ready? Journal of Clinical Microbiology 1993:767–770 and Tuberculosis Laboratory Diagnostics Summary (wa.gov)		

For more detailed information on Bacteriology Testing for TB see: CDC. *Chapter 3. Diagnosis of Tuberculosis Disease*. Core Curriculum on Tuberculosis: What the Clinician Should Know. Seventh Edition 2021 and

Practical Guidance for Clinical Microbiology Laboratories: Mycobacteria. ASM Journals, Clinical Microbiology Reviews, Vol. 31, No. 2

For more detailed information on Bacteriology Testing for TB at WAPHL see: Tuberculosis Laboratory Diagnostics Summary (wa.gov)

When confirming the diagnosis of mycobacterial disease, AFB smear and culture and sensitivities must be ordered.

Bacteriologic Examination of Clinical Specimens

1. Specimen collection for clinical samples, respiratory and extrapulmonary TB

TB disease can occur in almost any anatomical site; thus, a variety of clinical specimens, sputum as well as other samples such as urine, cerebrospinal fluid, pleural, synovial or peritoneal fluids, pus, or biopsy specimens may be submitted for examination in the case of presumptive extrapulmonary TB disease. Procedures for the expeditious and proper handling of the specimen must be in place or assured before the specialist performs an invasive procedure to obtain the specimen. It is especially important to ensure rapid transportation of specimens to the laboratory according to the laboratory's instructions.

For more information on: Collection of Respiratory Samples and Patient Instructions and (18)Instructions for sputum collection.pdf (TB Partners SharePoint)

During procedures in which aerosols may be produced, such as **induced sputum induction**, use appropriate respiratory protection and environmental controls. For more information, refer to the CDC's Guidelines for Preventing the Transmission of Mycobacterium tuberculosis in Health-care Settings, 2005 (MMWR 2005;54[No. RR-17])

Alaska PHL will run GeneXpert on both gastric aspirate and tissue specimens for WA State TB Program.

- Unprocessed gastric aspirate samples need 5 – 10 mL of gastric aspirate in a tube with some sodium carbonate preservative to neutralize the pH.
- Tissue samples - a visible amount in a tube with sterile saline to keep it moist. The lab cannot accept tissues in formalin, fixative, preservative, or wrapped in gauze. After the samples have been decontaminated/digested they can be run on the GeneXpert.
- If the samples have been processed/decontaminated at WAPHL then Alaska PHL needs 1 mL of the sample sediment to run on the GeneXpert.
- Samples should remain refrigerated and shipped cool (but not frozen).
- Complete the Alaska PHL requisition then contact WAPHL at StateTBLab@doh.wa.gov and they will have you send them the requisition and specimen to process as needed and send to Alaska PHL.

For additional information on collection of gastric aspirates and preparation of the specimen for transport, see the guide and Francis J. Curry International Tuberculosis Center's online tool Pediatric Tuberculosis: A Guide to the Gastric Aspirate Procedure | Curry International Tuberculosis Center (ucsf.edu)

A portion of any biopsy specimen should be set aside WITHOUT FIXATION and sent to the laboratory specifically for mycobacteriology (e.g., PCR, AFB culture), and the remaining portion of the biopsy can then be placed in formalin for histologic examination**. Once in formalin, tissue cannot be used for culture and the sensitivity of PCR testing is greatly reduced.**

2. AFB Smear Classification and Results

Microscopic detection of AFB in smears may provide the initial bacteriologic evidence of the presence of mycobacteria in a clinical specimen. Smear microscopy is the quickest and easiest procedure that can be performed. 5,000–10,000 bacilli per ml of specimen must be present to allow the detection of bacteria in stained smears. However, smear examination permits only the presumptive diagnosis of TB disease because the:

- AFB in a smear may be acid-fast organisms other than MTB
- sample may not be large enough or may be saliva rather than sputum
- sample may not have been stored or transported in an appropriate manner

See: (18)Instructions for sputum collection.pdf (TB Partners SharePoint)

Many TB patients also have negative AFB smears with a subsequent positive culture. **Negative smears do not exclude TB disease.**

3. Direct Detection of MTB in Clinical Specimens using NAAT

Nucleic acid amplification tests (NAATs) are used to amplify DNA and RNA segments to rapidly identify the microorganisms in a specimen. NAAT testing can reliably detect MTB DNA in specimens in just hours, compared to a week or more for detection of MTB organisms in culture. A single negative NAAT test result should not be used as a definitive result to exclude TB disease, especially when the clinical suspicion of TB disease is moderate to high.

The **Xpert MTB/RIF** is a NAAT assay that simultaneously detects MTB complex and resistance mutations to rifampin (RIF), one of the most effective drugs used to treat TB. As with other NAAT assays, the Xpert MTB/RIF assay should be interpreted along with clinical, radiographic, and other laboratory findings. To conduct the Xpert MTB/RIF assay, a sputum sample is mixed with a decontaminating reagent provided with the assay, and a cartridge containing the mixture is placed in the GeneXpert machine.

GENEXPERT® XPERT® MTB/RIF ASSAY RESULT INTERPRETATION

Smear Result	MTB/RIF Assay Result	Interpretation
Smear Positive for AFB	MTB DETECTED	MTB target is detected within the sample. Use clinical judgment to determine whether to begin therapy while awaiting culture results. A positive NAAT test does not necessarily indicate the presence of viable organisms.
	MTB Not Detected	MTB target is not detected within the sample. Use clinical judgment to determine whether to begin therapy while awaiting culture results. A patient is presumed to have an infection with nontuberculous mycobacteria, pending culture results. A negative MTB result on the Xpert MTB/RIF assay does not rule out pulmonary TB.

Smear Negative for AFB	MTB DETECTED	MTB target is detected within the sample. Use clinical judgment to determine whether to begin therapy while awaiting culture results. A positive NAAT test does not necessarily indicate the presence of viable organisms.
	MTB Not Detected	Use clinical judgment to determine whether to begin therapy while awaiting results of culture and other diagnostic tests. A negative MTB result on the Xpert MTB/RIF assay does not rule out pulmonary TB.

GENEXPERT® XPERT® RIFAMPIN RESULT INTERPRETATION

Rifampin Result	Interpretation
RIF Resistance NOT DETECTED	No rpoB mutation detected; likely rifampin susceptible.
RIF Resistance DETECTED	rpoB mutation detected; likely rifampin resistant. Confirmatory testing in progress.
RIF Resistance INDETERMINATE	Insufficient MTB in the sample to allow determination of the rpoB mutation result.

CDC and Washington State TB Program recommend **NAAT testing be performed on at least one respiratory specimen from each patient with signs and symptoms of pulmonary TB for whom a diagnosis of TB is being considered but has not yet been established**, and for whom the test result would alter case management or TB control activities, such as contact investigations.

The Xpert MTB/ RIF assay does not replace the need for AFB smear microscopy or culture for mycobacteria, growth-based drug susceptibility testing, and genotyping. Providers and laboratories need to ensure that patient specimens are available for all recommended mycobacterial testing.

4. Specimen Culture and Identification

Culture remains the gold standard for laboratory confirmation of TB disease, and growing bacteria are required to perform drug susceptibility testing and genotyping. In accordance with current recommendations, sufficient numbers and portions of specimens should always be reserved for culture.

Mycobacterial growth can usually be detected within 2-4 weeks after the lab receives the specimen (if it is smear positive). It may take up to 6 weeks to finalize results if the bacterial load is low (i.e., smear negative). Identification is then usually reported out 1-2 days after culture growth.

Positive cultures for MTB confirm the diagnosis of TB disease; however, in the absence of a positive culture, TB disease may also be diagnosed on the basis of clinical signs and symptoms alone.

Culture examinations should be performed on all diagnostic specimens, regardless of AFB smear or NAAT results.

5. Drug Susceptibility Testing (DST)

In Chapter 3: Laboratory, Table 4 of the document, Drug Resistant Tuberculosis: A Survival Guide for Clinicians 3rd Edition/2022 Updates, a summary of genes associated with drug resistance and the predominant mutations found in clinical isolates is provided as a reference to better understand genotypic (molecular) drug susceptibility test results.

- Although major genes associated with drug resistance have been identified, the understanding of drug resistance at the genetic level remains variable and incomplete. Therefore, 100% sensitivity for detecting all drug resistance is not currently achievable.
- Specificity for resistance detection by molecular methods for certain drugs is not 100% (using growth-based DST as the gold standard)

There are 3 ways in which drug susceptibility testing (DST) is done:

1. Xpert MTB/RIF assay
2. Molecular Detection of Drug Resistance (MDDR) (Genotypic)
3. Growth-based/ culture-based (Phenotypic) Drug Susceptibility Testing

1. The Xpert MTB/RIF assay

See the tables above in the section: Direct Detection of MTB in Clinical Specimens using NAAT: **GENEXPERT® XPERT® MTB/RIF ASSAY RESULT INTERPRETATION** and **GENEXPERT® XPERT® RIFAMPIN RESULT INTERPRETATION**

Positive results for MTB complex and RIF resistance indicate that the bacteria have a high probability of resistance to RIF which in most cases is accompanied by resistance to isoniazid (MDR-TB). This result should be confirmed by DNA sequencing as applicable to identify the specific mutation present. If RIF resistance is confirmed, rapid molecular testing for drug resistance to both first and second-line drugs should be performed so that an effective treatment regimen can be selected.

Positive results for MTB complex but negative for RIF resistance mean that the bacteria are probably susceptible to RIF. **However, all tests that are positive for MTB complex should have growth-based drug susceptibility testing to first-line TB drugs.**

Positive results for MTB complex and indeterminate for RIF resistance mean that the test could not accurately determine if the bacteria are resistant. Growth-based susceptibility testing to first-line TB drugs should be performed and consider requesting rapid molecular testing for drug resistance (MDDR).

For more information on XPERT Interpretation see:
APHL. **Laboratory Considerations for Use of Cepheid Xpert® MTB/RIF Assay**. November 2013. and CDC. **TB Diagnostic Tool: Xpert MTB/RIF Assay Fact Sheet**. May 4, 2016.

2. Molecular Detection of Drug Resistance (MDDR)

This testing should be done for patients with risk factors for drug-resistant TB who have AFB smear positive and/ or NAAT test positive respiratory specimens. Some of the assays can be performed directly on patient specimens prior to cultures turning positive; others currently require an isolate cultured from patient specimens.

CDC's MDDR service is available nationally, and it is free of charge through state public health laboratories. Other services for molecular detection are available through some public health, clinical, or commercial laboratories. To request MDDR service, complete the MMDR Request Form, and submit to StateTBLab@doh.wa.gov and Ryan.Ortiguerra@doh.wa.gov.

Since February 2023, the CDC has implemented a new targeted **next generation sequencing (tNGS) assay** as the primary method for MDDR service. The new assay enhances early detection of mutations associated with drug resistance and allows for examination of genetic loci associated with resistance to rifampin, isoniazid, ethambutol, pyrazinamide, fluoroquinolones, second-line injectables, clofazimine, linezolid, and bedaquiline. Growth-based drug susceptibility testing will be performed concurrently, but will not yet include testing for clofazimine, linezolid, and bedaquiline.

Currently, the tNGS assay examines 24 amplicons across 16 genes (12 anti-tuberculosis drugs). The tNGS testing panel includes:

Drug	Genetic loci tested	Upstream region[1]	Nucleotide position in rRNA[2]	Codons[3]	Rubric for Lab Reporting[4]
Rifampin	*rpoB* rifampin-resistance-determining region (RRDR)			Gly426 to Leu452	All mutations in the RRDR and codons 170 and 491 reported
	rpoB-170			Val170	
	rpoB-491			Ile491	
Isoniazid	*katG*			Val1 to 741*	All mutations except lineage markers and synonymous mutations at positions other than codon 1
	fabG1-inhA promoter	-140 to -1			All mutations upstream of *fabG1* start codon and mutations at codon 203 only
	fabG1-203			Leu203	
Ethambutol	*embB* (partial)			Thr277 to Thr437	All mutations except lineage markers and synonymous mutations
Pyrazinamide	*pncA*	-40 to -1		Met1 to 187*	All mutations upstream of the *pncA* start codon and all mutations in the open reading frame5 except synonymous mutations

Fluroquinolones	*gyrA* quinolone-resistance–determining region (QRDR)			Gly88 to Asp94	All mutations at codons 88 to 94 except synonymous mutations
	gyrB			Arg446 to Gly537	All mutations except synonymous mutations
Amikacin, Kanamycin, Capreomycin	*rrs* (partial)		1177 to 1537		Mutations at nucleotides 1401, 1402, and 1484 only
Kanamycin	*eis* promoter	-127 to -1			All mutations
Bedaquiline	*atpE*	-48 to -1		Met1 to 82*	All mutations upstream of the *atpE* start codon and non-synonymous mutations in the open reading frame[5]
	rv0678	-84 to -1		Val1 to 166*	All mutations upstream of the *rv0678* start codon and non- synonymous mutations in the open reading frame[5]
	pepQ	-33 to --1		Val1 to 373*	All mutations upstream of the *pepQ* start codon and non-synonymous mutations in the open reading frame[5]
Clofazimine	*rv0678*	-84 to -1		Val1 to 166*	All mutations upstream of the *rv0678* start codon and non- synonymous mutations in the open reading frame[5]
	pepQ	-33 to --1		Val1 to 373*	All mutations upstream of the *pepQ* start codon and non-synonymous mutations in the open reading frame[5]
Linezolid	*rplC*	-18 to -1		Met1 to 217*	All mutations upstream of the *rplC* start codon and non-synonymous mutations in the open reading frame[5]
	rrl (partial)		2003 to 2367 and 2449 to 3056		All mutations

[1] Coordinates are relative to the predicted start codon.

[2] Nucleotide positions are indicated for *rrs* and *rrl* because a promoter region and codon numbering are not applicable for these rRNA genes.

[3] Codon numbers define amino acid position in the translated protein.

[4] When present in the open reading frame, mutations will be reported as indicated with the exclusion criteria defined. When absent, the report will indicate no mutation detected. Mutations are identified by comparing sequencing data for each sample to the sequence of the H37Rv reference isolate. The minimum reportable alternate allele frequency threshold for the analytic pipeline results is 10%.

[5] Open reading frame is the genetic sequence that is transcribed into mRNA and ultimately translated into protein corresponding with the codon position defined for some of the genetic loci examined in the tNGS assay.

* Indicates a STOP codon.

For more information about CDC's MDDR service, see the MDDR User Guide.

For more information, see CDC MDDR service using targeted next generation sequencing (tNGS) assay.pdf (TB Partners SharePoint)

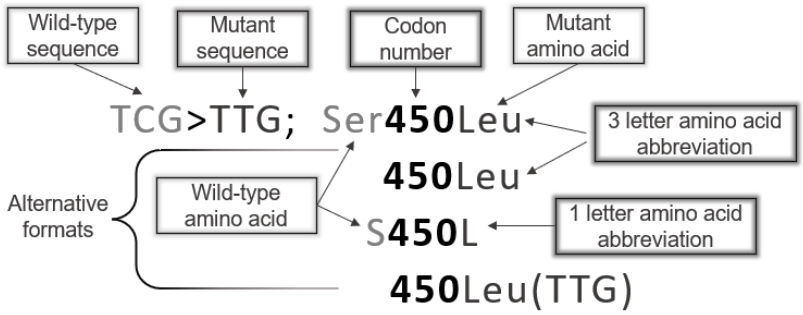
There are other terms and items you may see on a laboratory report. The table below has a few detailed definitions associated with mutations.

Definitions/Detailed Information about Genotypic/Molecular DST

Single nucleotide polymorphism (SNP)	A change in a single nucleotide in the DNA sequence, an A, T, C, or G from what is commonly observed (i.e., wild type). Multiple point mutations can occur within the same locus.
Deletion	A mutation that can occur when a single nucleotide or set of nucleotides is removed from a DNA sequence. A deletion can be small (i.e., one to few nucleotides) or large (i.e., a whole segment of the chromosome) and the effect of the deletion on viability of the organism or antibiotic resistance will depend on the location of the deletion and how the deletion affects protein synthesis.
Insertion	A mutation that can occur when a single nucleotide or set of nucleotides is inserted within a DNA sequence. An insertion can be small (i.e., one to few nucleotides) or large (i.e., a whole segment of the chromosome). Note: Insertions and deletions are often referred to as indels. Also, insertions and deletions can result in what is known as a frameshift mutation (also called frameshift change or FSC). Therefore, if "frameshift" or "FSC" is listed as the result on the laboratory report, mark the gene name, the result of mutation, and the test type.
Note: Insertions and deletions are often referred to as **indels**. Also, insertions and deletions can result in what is known as a frameshift mutation (also called frameshift change or FSC). Therefore, if "frameshift" or "FSC" is listed as the result on the laboratory report, mark the gene name, the result of mutation, and the test type.	
Nucleic acid change	A change in a single nucleic acid usually is a gene-level mutation, as only specific gene(s) are affected. There are three types of gene-level mutations: base substitutions, insertions and deletions. Base substitution is the simplest type of gene-level mutation, and is also referred to as single nucleotide polymorphism (SNP). Since only one nucleotide is changed, only one codon is affected. A codon is a DNA (or RNA) sequence of three nucleotides that represents one unit of genomic information to encode one specific amino acid (or a codon can instruct the termination of protein synthesis and referred to as stop codon). A base substitution can result in three subcategories of mutations: missense mutations, nonsense mutations, or silent mutation. In a missense mutation, a change in a nucleic acid results in a different amino acid being encoded into the translated protein. Some missense mutations can alter the shape and function of the resulting protein. In nonsense mutations, a change in a nucleic acid results in a stop codon rather than a codon encoding a particular amino acid. The new stop codon results in a premature termination of a protein. Missense and nonsense mutations are nonsynonymous mutation resulting in a change in amino acid sequence. A silent mutation is a synonymous mutation in which the altered codon does not result in a different amino acid. Synonymous mutations occur because multiple codons can encode the same amino acid.

	Insertions or deletions, as described above, can lead to a frameshift mutation. Frameshift mutations occur if the number of nucleotide bases inserted or removed from the DNA segment is not a multiple of three. Consequently, amino acids encoded at and after the frameshift mutation result in an entirely different protein. Results from molecular assays based on sequencing target genes will report the detected specific mutations. See figure below for guide to understanding sequence-based molecular test reports. The examples below show commonly detected mutations in drug resistant TB. For example, TCG>TTG nucleic acid change in the rpoB gene represents the wild-type DNA sequence (TCG) followed by the three letters of the mutant sequence (TTG). This nucleic acid change may be reported as TCG 531 TTG, in which 531 represents the codon position. Below is a guide to understanding sequence-based molecular test report using *rpoB* mutation reporting as an example. Note that since February 2023, the CDC MDDR report no longer provides the nucleotide mutation, but only provides the amino acid change (nucleotide mutation is provided if in non-coding region of the gene). Also, mutations in the *rpoB* gene are reported using the *M. tuberculosis* numbering system (prior to Feb 2023, the *E. coli* numbering system was used) If a nucleic acid mutation is detected in a promoter region, the mutation and its location relative to the start codon will be reported. For example, nucleic acid change G-15T detected for *inhA* indicates change from C (cytosine) to T (thymine), and -15 indicates that the mutation is located 10 base pairs upstream of *inhA* gene's start codon.

Guide to understanding sequence-based molecular test report: *rpoB* mutation* as example



*using *M. tuberculosis* numbering system for reporting *rpoB* mutation

Amino acid change	For missense mutations, in which a change in a nucleic-acid results in a different amino acid being encoded into the translated protein, the amino acid change is reported. For example, the TCG>TTG nucleic acid change in the *rpoB* gene, Ser450Leu indicates a change from the wild-type amino acid Ser (serine) at position 531 to Leu (leucine). Ser450Leu can also be reported as S450L by using a one letter amino acid abbreviation.

Adapted from: Curry International Tuberculosis Center and California Department of Public Health, Chapter 3, Laboratory, Drug-Resistant Tuberculosis: A Survival Guide for Clinicians, Third Edition /2022 Updates

3. Phenotypic (Growth-based) Drug Susceptibility Testing

The initial MTB isolate from a patient should be tested for resistance to the first-line anti-TB drugs: isoniazid, rifampin, ethambutol, and pyrazinamide. The results of both growth-based and molecular drug susceptibility tests should inform the clinicians' choices of the appropriate drugs for treating each patient.

If there is a high clinical suspicion or lab confirmation that the patient has TB disease, they should be started on treatment without delay as DST results can take weeks to become available. **Call the WA State TB Program for consultation on what medications to use initially.**

Results

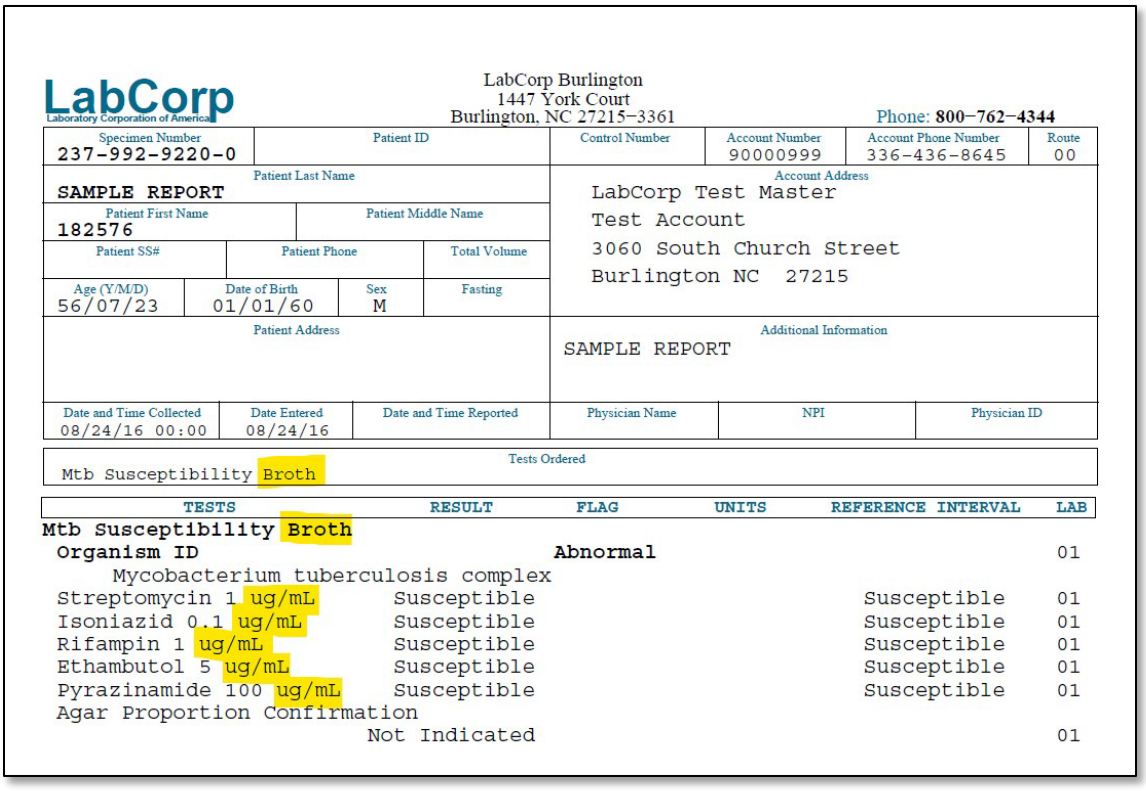
The examples on the pages below show both phenotypic and genotypic results that an LHJ will receive from the lab. The highlighted parts are clues to help identify genotypic from phenotypic results.

Examples of Phenotypic/Growth-Based DST Lab Results (Notice results are referring to concentrations of drugs and growth medium used.)

Sample Result from Florida Lab: Sensititre MIC Phenotypic DST Report

Test	Result	Reference Range	Date Approved
Rifabutin Interpretation	**Resistant**	Susceptible: ≤0.25 Resistant: ≥0.5	
Ofloxacin Interpretation	**Not Tested**	Susceptible: ≤1 Resistant: ≥2	
Ethionamide Interpretation	**Not Tested**	Susceptible: ≤1.2 Resistant: ≥2.5	
Amikacin MIC	16 µg/mL		
Amikacin Interpretation	**No Interpretation**	Susceptible: ≤2 Resistant: Breakpoint not established	
Moxifloxacin MIC	0.25 µg/mL		
Moxifloxacin Interpretation	**No Interpretation**	Susceptible: ≤0.12 Resistant: Breakpoint not established	
Para-Aminosalicylic Acid MIC	<0.5 µg/mL		
Para-Aminosalicylic Acid Interpretation	Susceptible	Susceptible: ≤0.5 Resistant:Breakpoint not established	
Cycloserine MIC	4 µg/mL		
Cycloserine Interpretation	Susceptible	Susceptible: ≤8.0 Resistant: Breakpoint not established	
Capreomycin MIC	5 µg/mL		
Capreomycin Interpretation	Susceptible	Susceptible: ≤5 Resistant: Breakpoint not established	
Levofloxacin MIC	0.5 µg/mL		
Levofloxacin Interpretation	Susceptible	Susceptible: ≤0.5 Resistant: Breakpoint not established	
Linezolid MIC	0.25 µg/mL		
Linezolid Interpretation	Susceptible	Susceptible: ≤1.0; Resistant: Breakpoint	

Sample Result from LabCorp: Liquid (Broth) Medium Phenotypic DST Report



LabCorp
Laboratory Corporation of America

LabCorp Burlington
1447 York Court
Burlington, NC 27215-3361
Phone: 800-762-4344

Specimen Number	Patient ID	Control Number	Account Number	Account Phone Number	Route
237-992-9220-0			90000999	336-436-8645	00

Patient Last Name: SAMPLE REPORT
Patient First Name: 182576
Patient Middle Name:
Patient SS#:
Patient Phone:
Total Volume:
Age (Y/M/D): 56/07/23
Date of Birth: 01/01/60
Sex: M
Fasting:
Patient Address:

Account Address:
LabCorp Test Master
Test Account
3060 South Church Street
Burlington NC 27215

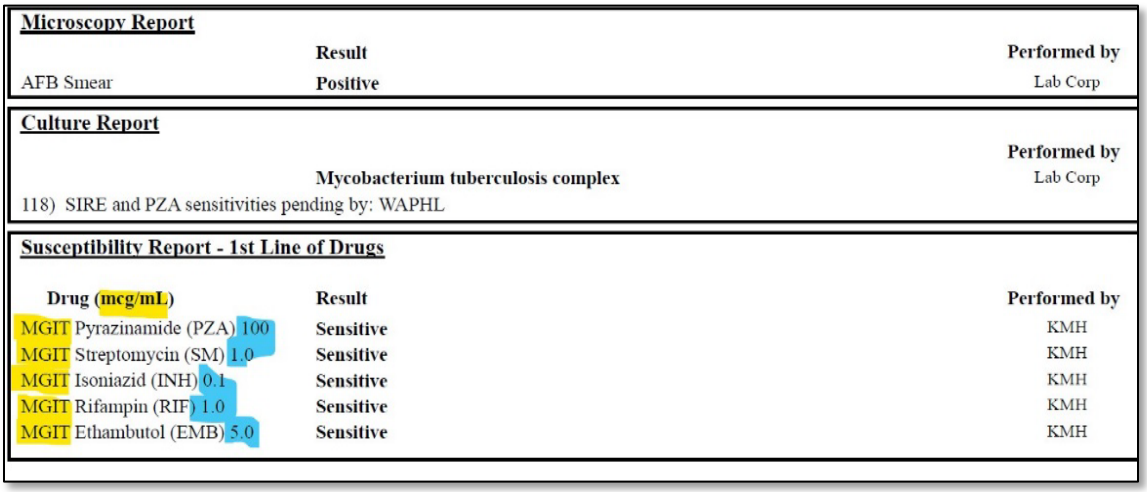
Additional Information: SAMPLE REPORT

Date and Time Collected	Date Entered	Date and Time Reported	Physician Name	NPI	Physician ID
08/24/16 00:00	08/24/16				

Tests Ordered: Mtb Susceptibility Broth

TESTS	RESULT	FLAG	UNITS	REFERENCE INTERVAL	LAB
Mtb Susceptibility Broth					
Organism ID		**Abnormal**			01
Mycobacterium tuberculosis complex					
Streptomycin 1 ug/mL	Susceptible			Susceptible	01
Isoniazid 0.1 ug/mL	Susceptible			Susceptible	01
Rifampin 1 ug/mL	Susceptible			Susceptible	01
Ethambutol 5 ug/mL	Susceptible			Susceptible	01
Pyrazinamide 100 ug/mL	Susceptible			Susceptible	01
Agar Proportion Confirmation					
	Not Indicated				01

Sample Result from WA Public Health Laboratory: MGIT Phenotypic DST Report



Microscopy Report

	Result	Performed by
AFB Smear	**Positive**	Lab Corp

Culture Report

		Performed by
	Mycobacterium tuberculosis complex	Lab Corp

118) SIRE and PZA sensitivities pending by: WAPHL

Susceptibility Report - 1st Line of Drugs

Drug (mcg/mL)	Result	Performed by
MGIT Pyrazinamide (PZA) 100	**Sensitive**	KMH
MGIT Streptomycin (SM) 1.0	**Sensitive**	KMH
MGIT Isoniazid (INH) 0.1	**Sensitive**	KMH
MGIT Rifampin (RIF) 1.0	**Sensitive**	KMH
MGIT Ethambutol (EMB) 5.0	**Sensitive**	KMH

Sample Result from CDC: Solid (Agar) Medium Phenotypic DST Report

MTBC Agar Proportion Susceptibility*	% Resistant	Interpretation
Isoniazid 0.2 µg/mL	0 %	Susceptible
Isoniazid 1.0 µg/mL	0 %	Susceptible
Isoniazid 5.0 µg/mL	0 %	Susceptible
Rifampin 1.0 µg/mL	0 %	Susceptible
Ethambutol 5.0 µg/mL	0 %	Susceptible
Streptomycin 2.0 µg/mL	0 %	Susceptible
Streptomycin 10.0 µg/mL	0 %	Susceptible
Rifabutin 2.0 µg/mL	0 %	Susceptible
Ciprofloxacin 2.0 µg/mL	0 %	Susceptible
Kanamycin 5.0 µg/mL	0 %	Susceptible
Ethionamide 10.0 µg/mL	0 %	Susceptible
Capreomycin 10.0 µg/mL	0 %	Susceptible
PAS 2.0 µg/mL	0 %	Susceptible
Ofloxacin 2.0 µg/mL	0 %	Susceptible
Amikacin 4.0 µg/mL	0 %	Susceptible

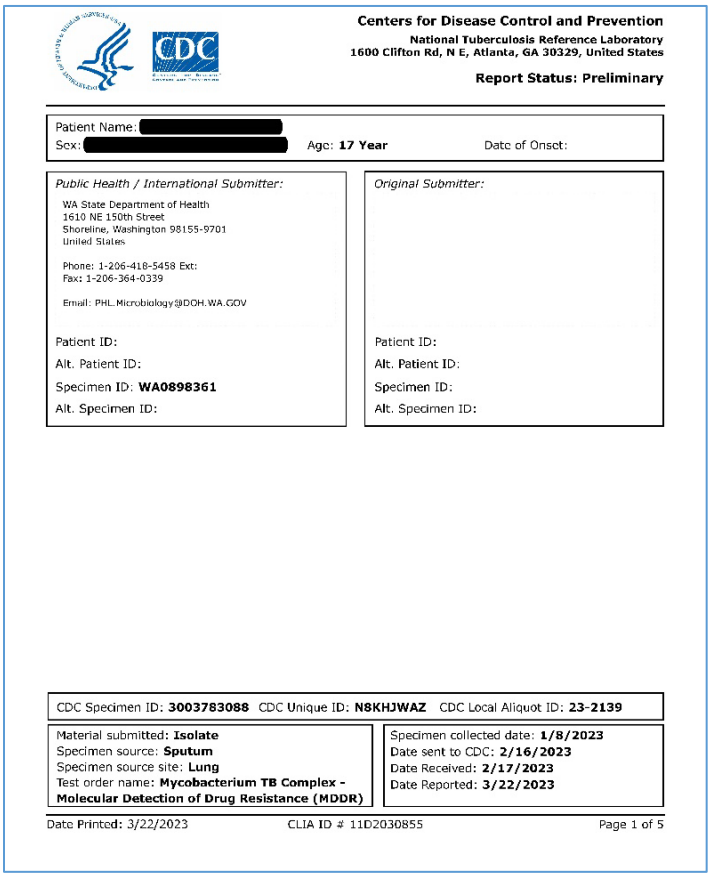
Comments and Disclaimers

* Susceptibility testing method: Indirect agar proportion, 7H10 medium. Resistance is defined as >1% (growth on drug-containing medium compared to drug-free medium).

For more information on testing for drug resistance see Chapter 3: Laboratory in Drug-Resistant Tuberculosis: A Survival Guide for Clinicians, 3rd edition/2022 Updates

Example CDC MDDR and Phenotypic DST Report* (report format current as of February, 2023) Report

- Page 1 = Patient, submitter, and sample information
- Page 2 = Phenotypic DST results
- Page 3-4 = Molecular sequencing results (first-line drugs, floroquinolones, second-line injectables, bedaquiline, clofazimine, and linezolid)
- Page 5 = Report comments, disclaimers, and contact information



Centers for Disease Control and Prevention
National Tuberculosis Reference Laboratory
1600 Clifton Rd, N E, Atlanta, GA 30329, United States

Report Status: Preliminary

Patient Name: [redacted]
Sex: [redacted] Age: **17 Year** Date of Onset:

Public Health / International Submitter:

WA State Department of Health
1610 NE 150th Street
Shoreline, Washington 98155-9701
United States

Phone: 1-206-418-5458 Ext:
Fax: 1-206-364-0339

Email: PHL.Microbiology@DOH.WA.GOV

Patient ID:
Alt. Patient ID:
Specimen ID: **WA0898361**
Alt. Specimen ID:

Original Submitter:

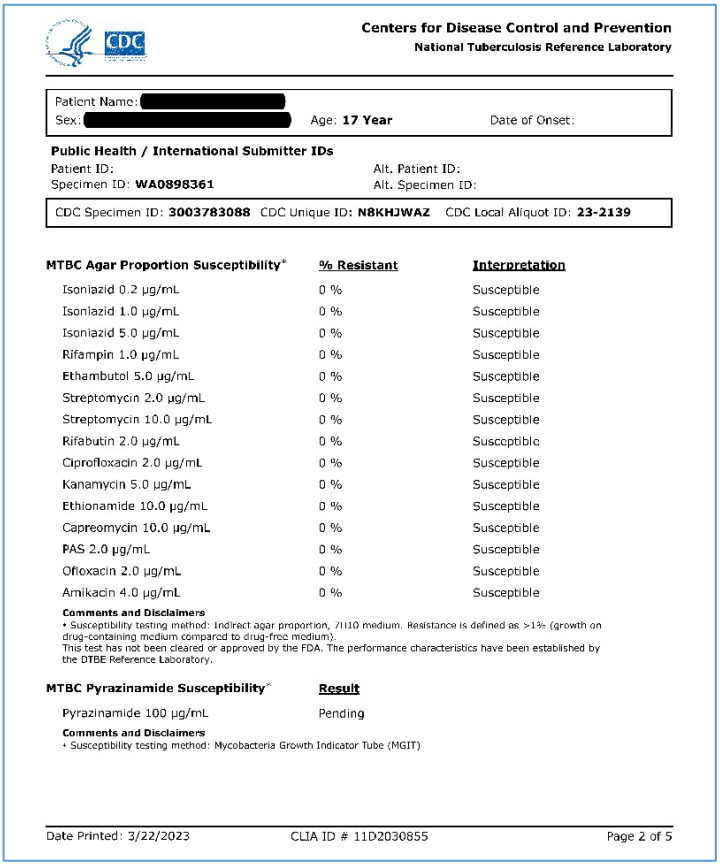
Patient ID:
Alt. Patient ID:
Specimen ID:
Alt. Specimen ID:

CDC Specimen ID: **3003783088** CDC Unique ID: **N8KHJWAZ** CDC Local Aliquot ID: **23-2139**

Material submitted: **Isolate**
Specimen source: **Sputum**
Specimen source site: **Lung**
Test order name: **Mycobacterium TB Complex - Molecular Detection of Drug Resistance (MDDR)**

Specimen collected date: **1/8/2023**
Date sent to CDC: **2/16/2023**
Date Received: **2/17/2023**
Date Reported: **3/22/2023**

Date Printed: 3/22/2023 CLIA ID # 11D2030855 Page 1 of 5



Centers for Disease Control and Prevention
National Tuberculosis Reference Laboratory

Patient Name: [redacted]
Sex: [redacted] Age: **17 Year** Date of Onset:

Public Health / International Submitter IDs
Patient ID:
Specimen ID: **WA0898361**
Alt. Patient ID:
Alt. Specimen ID:

CDC Specimen ID: **3003783088** CDC Unique ID: **N8KHJWAZ** CDC Local Aliquot ID: **23-2139**

MTBC Agar Proportion Susceptibility*	**% Resistant**	**Interpretation**
Isoniazid 0.2 µg/mL	0 %	Susceptible
Isoniazid 1.0 µg/mL	0 %	Susceptible
Isoniazid 5.0 µg/mL	0 %	Susceptible
Rifampin 1.0 µg/mL	0 %	Susceptible
Ethambutol 5.0 µg/mL	0 %	Susceptible
Streptomycin 2.0 µg/mL	0 %	Susceptible
Streptomycin 10.0 µg/mL	0 %	Susceptible
Rifabutin 2.0 µg/mL	0 %	Susceptible
Ciprofloxacin 2.0 µg/mL	0 %	Susceptible
Kanamycin 5.0 µg/mL	0 %	Susceptible
Ethionamide 10.0 µg/mL	0 %	Susceptible
Capreomycin 10.0 µg/mL	0 %	Susceptible
PAS 2.0 µg/mL	0 %	Susceptible
Ofloxacin 2.0 µg/mL	0 %	Susceptible
Amikacin 4.0 µg/mL	0 %	Susceptible

Comments and Disclaimers
• Susceptibility testing method: Indirect agar proportion, 7H10 medium. Resistance is defined as >1% (growth on drug-containing medium compared to drug-free medium).
This test has not been cleared or approved by the FDA. The performance characteristics have been established by the DTBE Reference Laboratory.

MTBC Pyrazinamide Susceptibility^	**Result**
Pyrazinamide 100 µg/mL	Pending

Comments and Disclaimers
• Susceptibility testing method: Mycobacteria Growth Indicator Tube (MGIT)

Date Printed: 3/22/2023 CLIA ID # 11D2030855 Page 2 of 5

Patient Name: [redacted]
Sex: [redacted] Age: **17 Year** Date of Onset:

Public Health / International Submitter IDs
Patient ID: Alt. Patient ID:
Specimen ID: **WA0898361** Alt. Specimen ID:

CDC Specimen ID: **3003783088** CDC Unique ID: **N8KHJWAZ** CDC Local Aliquot ID: **23-2139**

Rifampin (RIF)	**Result**	**Interpretation**
RIF interpretation		RIF susceptible
rpoB	No mutations	

Isoniazid (INH)	**Result**	**Interpretation**
INH interpretation		Cannot rule out INH resistance.
inhA	No mutations	
fabG1	No mutations	
katG	No mutations	

Ethambutol (EMB)	**Result**	**Interpretation**
EMB interpretation		Cannot rule out EMB resistance.
embB	No mutations	

Pyrazinamide (PZA)	**Result**	**Interpretation**
PZA interpretation		Cannot rule out PZA resistance.
pncA	No mutations	

Fluoroquinolones (FQ)	**Result**	**Interpretation**
FQ interpretation		Cannot rule out FQ resistance.
gyrA	No mutations	
gyrB	No mutations	

Centers for Disease Control and Prevention
National Tuberculosis Reference Laboratory

Patient Name: [redacted]
Sex: [redacted] Age: **17 Year** Date of Onset:

Public Health / International Submitter IDs
Patient ID: Alt. Patient ID:
Specimen ID: **WA0898361** Alt. Specimen ID:

CDC Specimen ID: **3003783088** CDC Unique ID: **N8KHJWAZ** CDC Local Aliquot ID: **23-2139**

Amikacin, Capreomycin, and Kanamycin (AMK, CAP, and KAN)	**Result**	**Interpretation**
AMK CAP and KAN interpretation		Cannot rule out resistance to AMK, CAP, and KAN.
rrs	No mutations	
eis	No mutations	

Bedaquiline (BDQ)	**Result**	**Interpretation**
BDQ interpretation		Cannot rule out BDQ resistance.
atpE	No mutations	
rv0678	No mutations	
pepQ	No mutations	

Clofazimine (CFZ)	**Result**	**Interpretation**
CFZ interpretation		Cannot rule out CFZ resistance.
pepQ	No mutations	
rv0678	No mutations	

Linezolid (LZD)	**Result**	**Interpretation**
LZD interpretation		Cannot rule out LZD resistance.
rplC	No mutations	
rrl	No mutations	

Centers for Disease Control and Prevention
National Tuberculosis Reference Laboratory

Patient Name: [redacted]
Sex: [redacted] Age: **17 Year** Date of Onset:

Public Health / International Submitter IDs
Patient ID: Alt. Patient ID:
Specimen ID: **WA0898361** Alt. Specimen ID:

CDC Specimen ID: **3003783088** CDC Unique ID: **N8KHJWAZ** CDC Local Aliquot ID: **23-2139**

Report Comments and Disclaimers
Results for molecular detection of drug resistance (MDDR) service determined by targeted next generation sequencing assay.

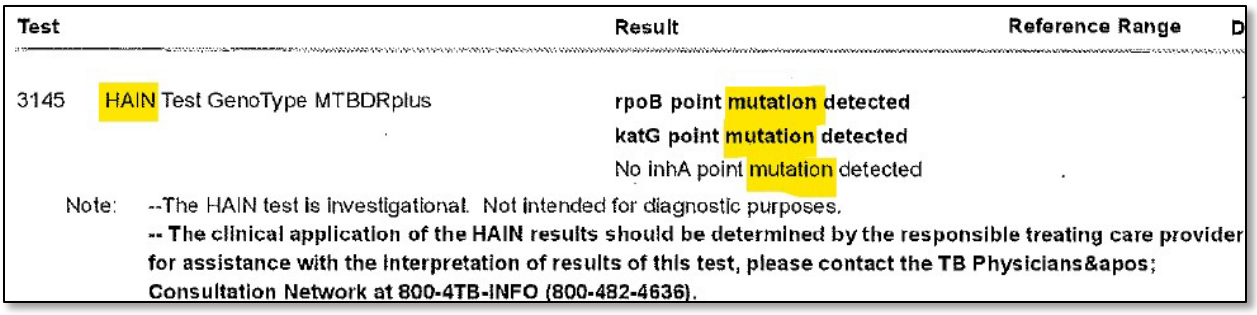
Results for MDDR assays were developed, and the performance characteristics determined by the DTBE Reference Laboratory. They have not been cleared or approved by the Food and Drug Administration.

A negative result (e.g., no mutations) does not rule out contributory mutations present elsewhere in the genome.

Additional resources for medical consultation are available from your state TB program (https://www.cdc.gov/tb/links/tboffices.htm) or the TB Centers of Excellence for Training, Education, and Medical Consultation [(877)-390-6682 / https://www.cdc.gov/tb/education/tb_coe/default.htm].

Approved by: David Sikes
Ph: 404-639-2455
Fax: 404-639-5491
E-mail: ZRG5@cdc.gov

Sample Result from Florida Lab: HAIN (MTBDRplus) Genotypic DST Report



Test		Result	Reference Range	D
3145	HAIN Test GenoType MTBDRplus	**rpoB point mutation detected** **katG point mutation detected** No inhA point mutation detected		

Note: --The HAIN test is investigational. Not intended for diagnostic purposes.
-- The clinical application of the HAIN results should be determined by the responsible treating care provider for assistance with the interpretation of results of this test, please contact the TB Physicians' Consultation Network at 800-4TB-INFO (800-482-4636).

Follow-up Bacteriologic Examination

Follow-up bacteriologic examinations are important for assessing the patient's infectiousness and response to therapy. Culture conversion is the most important objective measure of response to treatment. Specimens should be obtained at least monthly until two consecutive specimens sent for culture are reported as negative.

The Culture conversion date is documented by the first negative culture that is collected in a series of previously positive cultures, and where all subsequent culture results negative.

Legal Requirements for Lab Reporting

Laboratories should report positive MTB cultures, and positive NAAT results and drug susceptibilities (culture based and molecular) within 2 days (either by phone or electronically) to the ordering health care provider and LHJ as required by statute or regulation. (WAC 246-101-201)

Out-of-state laboratories that receive referral specimens must contact the health care provider and health department in the patient's state of origin. Follow-up results should be reported.

TB Case Managers should follow up with laboratories if anticipated results are not received within expected time frames!

Prompt reporting to public health authorities ensures that the person with TB disease can be adequately treated, interrupting the potential for ongoing transmission. It also ensures that contact investigations can be initiated quickly to find contacts of the patient who may have LTBI or TB disease.

For more information on reporting requirements see *Chapter 2: Surveillance*

Genotyping

Genotyping is a laboratory-based approach used to describe, classify, compare and cluster strains of MTB by analyzing their genetic makeup (i.e., DNA). The information that genotyping provides is uniquely valuable to numerous aspects of TB prevention and control. Among the most widespread and frequent uses of genotyping data are the identification and monitoring of TB case clusters, along with aiding the detection of recent, ongoing disease transmission.

Current CDC whole-genome technologies first compare the genetic makeup of TB strains at the level of individual genes using what is referred to as whole-genome multi-locus sequence typing (wgMLST). Strains that match at this level of comparison are assigned a whole-genome multi-locus sequence type (wgMLSType) used to identify and monitor clusters of TB case isolates. Strains clustered by wgMLSType do not necessarily indicate direct transmission of disease between cases of that cluster.

Within a given wgMLSType cluster of TB strains, closer comparison at the level of individual nucleotides (i.e., single nucleotide polymorphisms or SNPs) allows the identification of TB strains that are more closely related genetically. So-called wgSNP comparison is performed by reflex for isolates in a cluster growing at a rate greater than expected, or by request of the WA DOH TB program. Strains showing few SNP differences *may* indicate TB cases related in ongoing transmission. While of immense value in the investigation of disease transmission within a cluster of TB cases, genotyping data cannot by itself prove the occurrence or direction of disease transmission between TB cases and should always be evaluated considering corresponding epidemiologic link data.

In addition to informing the identification and investigation of TB case clusters, genotyping plays a vital role in many other aspects of TB work, including:

- identifying strains of M.bovis, including those that are not reportable (i.e., M.bovis-BCG),
- discerning reinfection by a completely different strain versus from recurrence of the same or similar strain,
- detecting potential cross-contamination between TB isolates, and
- detecting outbreaks of TB disease, individual cases that may not have been previously recognized as related

Genotyping is performed on isolates from all culture-positive TB cases. Currently, WAPHL sends isolates out to a partner state lab in Michigan commissioned by the CDC to perform genotyping. Batches of isolates for genotyping are sent routinely (typically on a weekly basis).

For more information on genotyping see:
Lee R.S., Behr M.A. The implications of whole-genome sequencing in the control of tuberculosis. *Ther Adv Infect Dis*. 2016; 3(2): 47-62.
and
CDC. **Chapter 3. Diagnosis of Tuberculosis Disease**. Core Curriculum on Tuberculosis: What the Clinician Should Know. Seventh Edition 2021.

Shipping your Specimens

There are three main categories of transportation methods: medical couriers, ground transportation, and air transportation.

Shipping Instructions for using PHL Courier Service (free for LHJs).

- Call Delivery Express Logistics (DEL) Customer Service at 425.251.3533 and select option 1.
- Provide Account number 114099 and identify which LHJ you are calling from.
- Provide any weekend LHJ-specific instructions for things such as: LHJ site access, LHJ hours of operation, or other relevant collection instructions.
- Provide LHJ contact name and contact phone number.
- DEL will provide a tracking number for your specific collection and delivery request.
- Weekday pickup (Mon-Fri): LHJ must call before 5pm on the current business day for next day collection. If DEL receives the request early in the day and if time permits DEL will attempt to collect and deliver the same day.
- Weekend and Holiday pickup: LHJ must call before 5 pm Friday or before 5 pm prior to a holiday. For example:
  - Holiday is on Friday: call before end of business day on Thursday (5 PM).
  - Holiday is on Monday: call before end of business day on Friday (5 PM).

SHIP TO: State of Washington Department of Health

- Public Health Laboratories Mycobacteriology Unit
- 1610 NE 150th Street
- Shoreline, WA 98155-9701
- (206) 418-5473

Ground and Air Shipping

While the WAPHL courier service is the best option for most LHJs, Category B Infectious Substances (raw diagnostic specimens, such as sputum, blood, or tissue) can be transported via air or ground using other services, here are some common examples (in order of preference):

- Medical courier
- Air shipped by private carrier (e.g., Federal Express, United Parcel Service, etc.)
- Greyhound bus
- US Postal Service (USPS)

Cultures of MTB (not raw diagnostic specimens) are considered "infectious substances" according to regulations of the U.S. Department of Transportation (DOT) and the International Air Transport Association (IATA). Shipping of infectious substances must follow regulations established by both organizations.

- US Department of Transportation regulations may be found at:.
- For shipments by private carriers, diagnostic specimens must be packaged according to International Air Transport Association (IATA) Packing Instruction 650.

Washington State Public Health Lab TB Specimen Submission Instructions

National Jewish Health, Specimen Submission Policy (2022).

Mailing Standards of the United States Postal Service: Domestic Mail Manual.pdf

Pipeline and Hazardous Materials Safety Administration (PHMSA): Transporting Infectious Substances Safely.pdf.

US Department of Transportation Regulations.

International Air Transport Association (IATA) Packing Instruction 650.

Resources

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Francis J. Curry International Tuberculosis Center. **Drug-Resistant Tuberculosis: A Survival Guide for Clinicians, 3rd edition/2022 Updates**. Available at: https://www.currytbcenter.ucsf.edu/products/cover-pages/drug-resistant-tuberculosis-survival-guide-clinicians-3rd-edition

- **Chapter 3: Laboratory**. Available at: https://www.currytbcenter.ucsf.edu/products/page/chapter-3-laboratory

Francis J. Curry International Tuberculosis Center. **Pediatric TB: A Guide to the Gastric Aspirate (GA) Procedure**. Available at: https://www.currytbcenter.ucsf.edu/product/guide/pediatric-tuberculosis-a-guide-to-the-gastric-aspirate-procedure

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