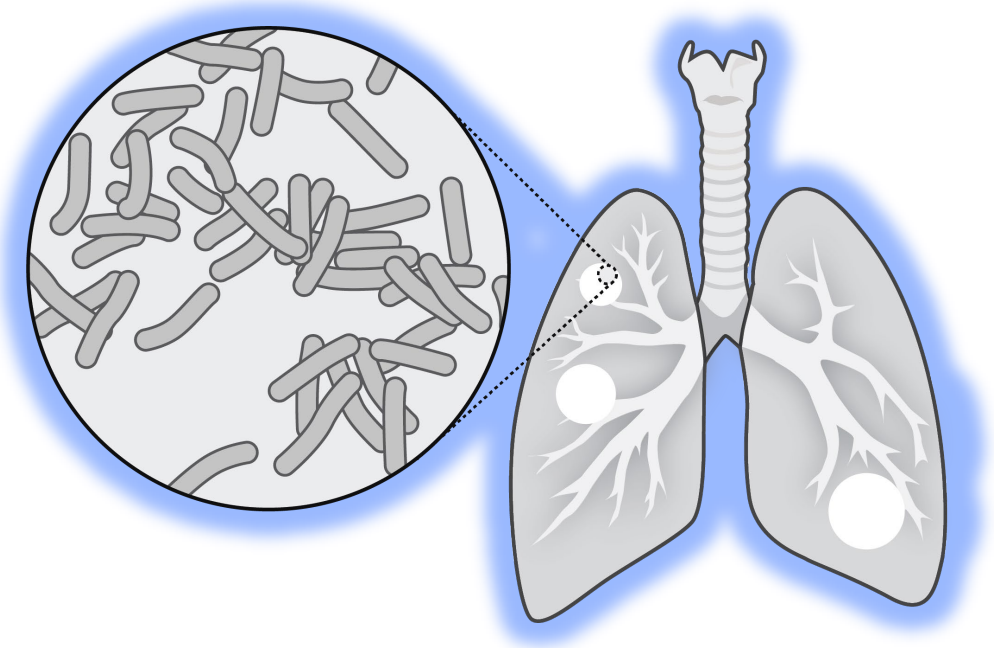
CDC Laboratory Updates

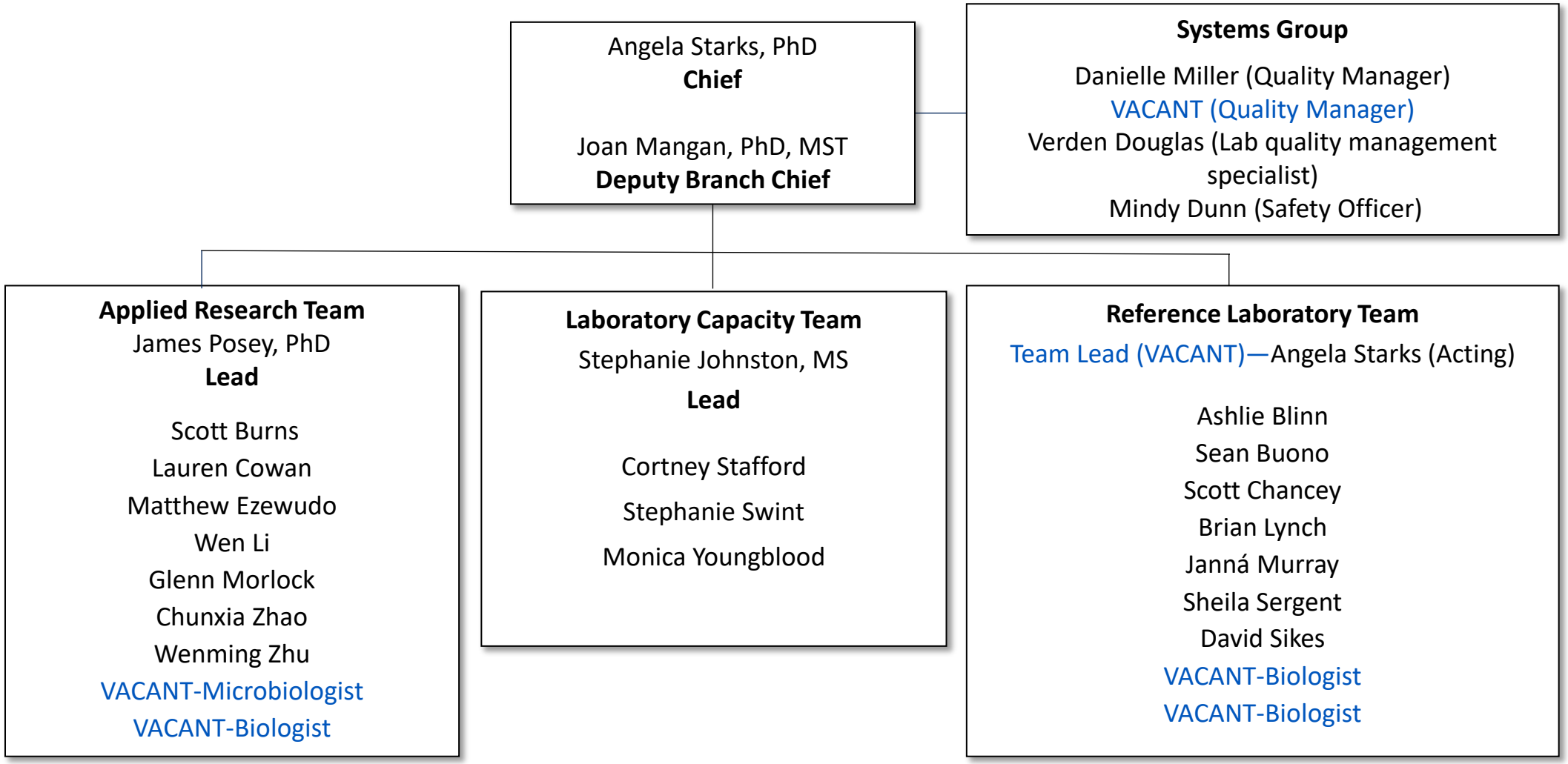


Angela M. Starks, PhD
Chief, Laboratory Branch
Division of Tuberculosis Elimination
National Center for HIV, Viral Hepatitis,
STD, and TB Prevention
March 10, 2026

The Work of CDC's TB Laboratory

- **Reference laboratory services**
  - Molecular Detection of Drug Resistance (MDDR) Service
  - Phenotypic susceptibility testing
- **Applied research**
  - Improve outbreak detection
  - Identify and characterize drug-resistance mechanisms
  - Optimize use of state-of-the-art technologies
- **Supporting U.S. laboratory capacity**
  - Cooperative agreement funding
  - Technical assistance
  - Education and training

DTBE Laboratory Branch Organizational Chart



Date: 03/03/2026

Updates to CDC Reference Laboratory Testing Services

MDDR Service Updates
(Planned for week of March 16th)

- **Reimplementing MDDR for DNA extracts from CDC's Infectious Diseases Pathology Branch**
  - DNA extracts from formalin-fixed paraffin-embedded (FFPE) tissue samples PCR positive for *M. tuberculosis*
  - Transferred to DTBE/Laboratory Branch
  - Evaluated by Sanger sequencing for rifampin, isoniazid, and fluoroquinolone resistance
    - Also evaluating small region of *pncA*, primarily for *M. bovis* His57Asp
  - Enhancement from previous pyrosequencing assay—only rifampin and isoniazid resistance evaluated
- **Formal communication to public health partners is forthcoming**

MDDR Service Updates (2)
(Tentatively Planned for April)

- **Implementation of minimum inhibitory concentration (MIC) testing**
  - Includes moxifloxacin, levofloxacin, linezolid, clofazimine, and bedaquiline by broth microdilution
  - MIC for pretomanid evaluated by MGIT (0.06 µg/ml–16 µg/ml)

  - Reporting MIC value—no consensus-based breakpoints for many drugs with method used
  - Established quality control range for each drug

SENSITITRE CUSTOM PLATE FORMAT

2011140914

Plate Code: **CML1FCMY** Date: **10-Jun-19**

	1	2	3	4	5	6	7	8	9	10	11	12
A	BDQ 0.008	BDQ 0.015	BDQ 0.03	BDQ 0.06	BDQ 0.12	BDQ 0.25	BDQ 0.5	BDQ 1	BDQ 2	BDQ 4	RIF 0.06	RIF 0.12
B	RIF 0.25	RIF 0.5	RIF 1	RIF 2	RIF 4	INH 0.03	INH 0.06	INH 0.12	INH 0.25	INH 0.5	INH 1	INH 2
C	INH 4	INH 8	INH 16	OFL 0.12	OFL 0.25	OFL 0.5	OFL 1	OFL 2	OFL 4	OFL 8	LEVO 0.12	LEVO 0.25
D	LEVO 0.5	LEVO 1	LEVO 2	LEVO 4	MXF 0.06	MXF 0.12	MXF 0.25	MXF 0.5	MXF 1	MXF 2	MXF 4	KAN 0.12
E	KAN 0.25	KAN 0.5	KAN 1	KAN 2	KAN 4	KAN 8	KAN 16	AMI 0.12	AMI 0.25	AMI 0.5	AMI 1	AMI 2
F	AMI 4	AMI 8	AMI 16	CAP 0.12	CAP 0.25	CAP 0.5	CAP 1	CAP 2	CAP 4	CAP 8	CAP 16	LZD 0.12
G	LZD 0.25	LZD 0.5	LZD 1	LZD 2	LZD 4	LZD 8	CFZ 0.015	CFZ 0.03	CFZ 0.06	CFZ 0.12	CFZ 0.25	POS
H	CFZ 0.5	CFZ 1	CFZ 2	CFZ 4	EMB 0.25	EMB 0.5	EMB 1	EMB 2	EMB 4	EMB 8	EMB 16	NEG

ANTIMICROBICS

BDQ	Bedaquiline
RIF	Rifampin
INH	Isoniazid
LEVO	Levofloxacin
KAN	Kanamycin
AMI	Amikacin
LZD	Linezolid
CFZ	Clofazimine
OFL	Ofloxacin
CAP	Capreomycin
MXF	Moxifloxacin
EMB	Ethambutol
POS	Positive Control
NEG	Negative Control

Example MIC Report Format

MTBC MIC by Broth Microdilution*	Result
Rifampin	0.12 µg/mL
Isoniazid	>16 µg/mL
Ethambutol	≤0.25 µg/mL
Ofloxacin	8 µg/mL
Levofloxacin	1 µg/mL
Moxifloxacin	≤0.06 µg/mL
Amikacin	2 µg/mL
Capreomycin	8 µg/mL
Linezolid	>8 µg/mL
Clofazimine	0.06 µg/mL
Bedaquiline	0.5 µg/mL

Comments and Disclaimers

*Testing method: Minimum inhibitory concentration (MIC) determination by broth microdilution. This test has not been cleared or approved by the FDA. The performance characteristics have been established by the DTBE Reference Laboratory.

Breakpoints for drugs using the specific method performed have not been established.
Additional information may be found at https://journals.asm.org/doi/pdf/10.1128/jcm.02919-20.

When will MIC testing be performed?

- **Test order code CDC-10186—Preapproval will be required through use of revised MDDR request form**
- **Resources to perform MIC testing are constrained—not universally performed for all isolates**
- **Rifampin resistance/multidrug resistance (MDR) detected by:**
  - Submitting laboratory (preapproval through MDDR request form)
  - In-house through MDDR service (automatically reflexed)
- **On request due to clinical need (e.g., use of BPaL/BPalM)**

Revised MDDR request form

Section 4. Minimum Inhibitory Concentration (MIC) testing

Note: *MIC testing (includes levofloxacin, moxifloxacin, linezolid, clofazimine, bedaquiline, and pretomanid) only performed for RIF-R/MDR or by special request due to clinical need. Please indicate request below and reason for request. Pre-approval is required prior to shipment of sample.*

☐ **Requesting MIC testing for new/repurposed drugs**

Reason for request:

☐ **Use of BPaL/ BPaLM**

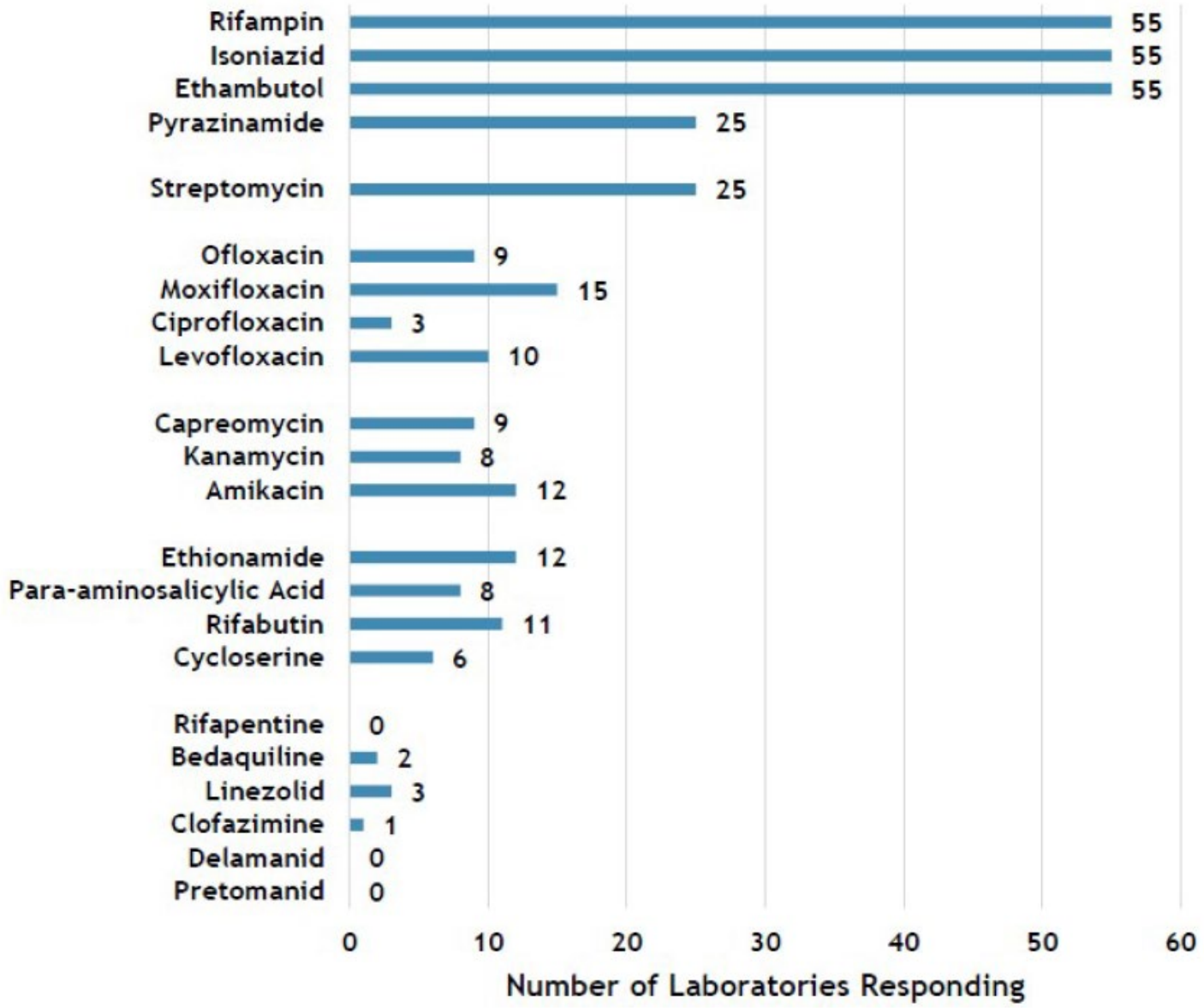
☐ **Use of other regimen containing new/repurposed drugs (Please specify)**

☐ **Clinical need (Please provide justification)**

Status of TB Susceptibility Testing in United States

Data from CDC's March 2025 Model Performance Evaluation Program (MPEP) Report

Figure 5. Antituberculosis Drugs Tested by Growth-based Method by Participating Laboratories



Limited Access to Susceptibility Testing for New and Repurposed Drugs

- No FDA approved, commercial assay for this purpose - requires validation as a laboratory developed test
- Knowledge base for optimal growth-based and molecular testing continuing to grow
- Testing recommended before initiating use of BPaL/BPaLM
- Currently limited to a few U.S. laboratories

MDDR Service Updates (3)
(Tentatively Planned for June)

- **Eliminating test order (CDC-10185) request for drug susceptibility testing only by agar proportion (i.e., no request for molecular results)**
  - Low volume test order from small number of public health laboratories (PHLs)
  - Corresponded with public health laboratories to gauge impacts—no concerns expressed
- **After eliminating CDC-10185, all requests would have molecular AND phenotypic testing (at least agar proportion)**
  - Helpful for internal evaluation of results
  - Streamlines workflow, especially with addition of new service offerings like MIC testing

Laboratory Capacity Team Updates

Stephanie Johnston

Cortney Stafford

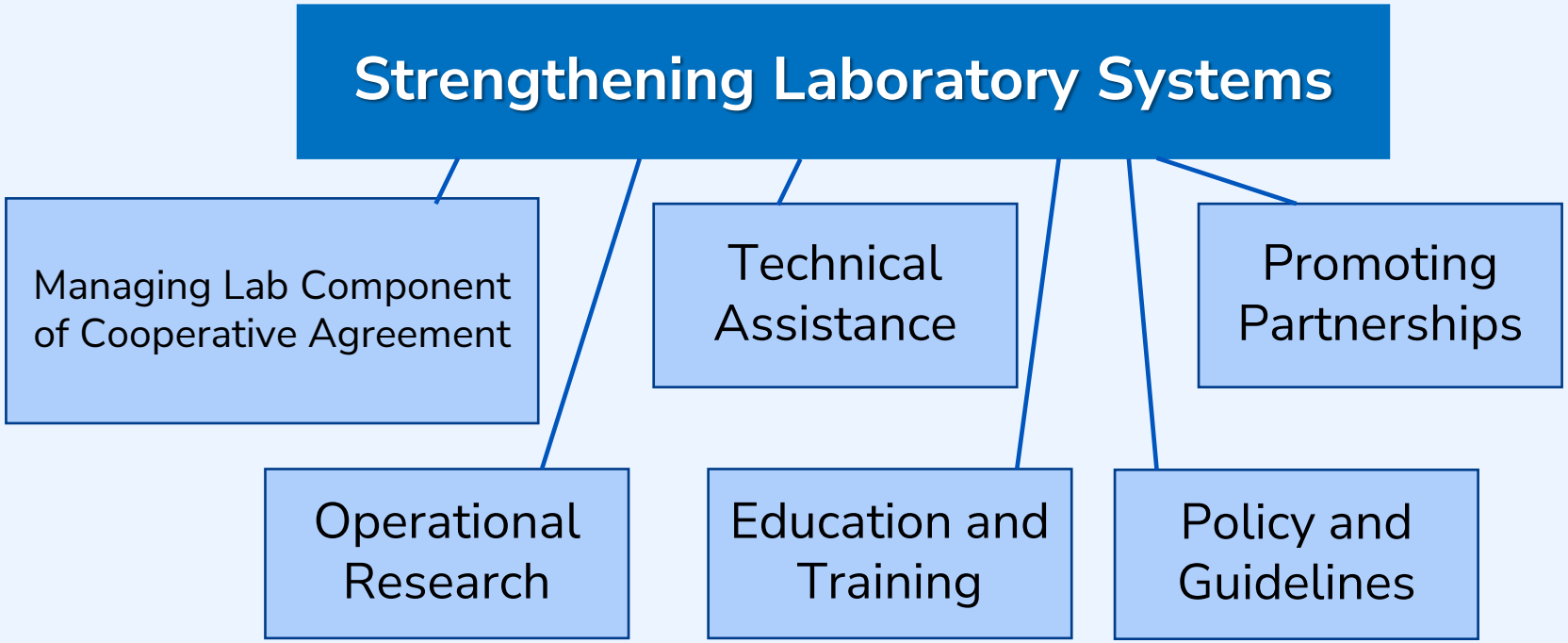
Monica Youngblood

Stephanie Swint

Laboratory Capacity Team

Laboratory Capacity Team

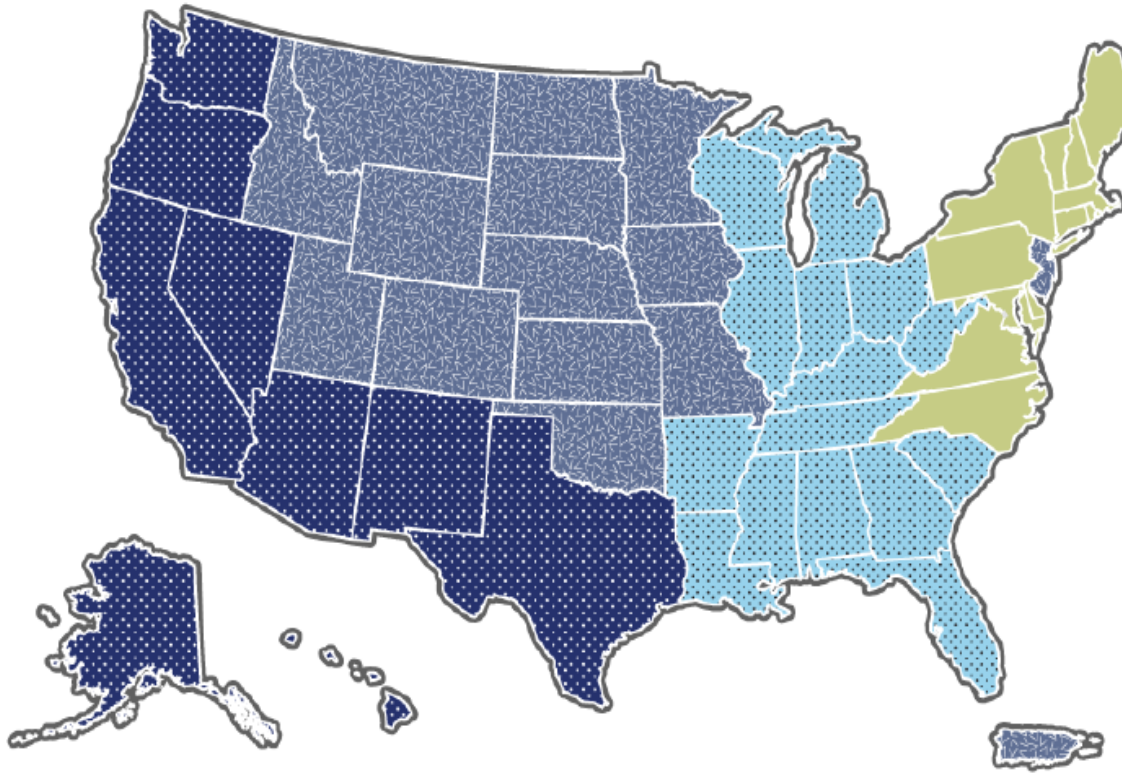
- Focus on consultancy for strengthening laboratory systems primarily in the United States
- Currently 4 team members



CDC Cooperative Agreement Supporting TB Testing

DTBE Elimination and Laboratory Strengthening Component

- 58 awardees (~$6.7M)
  - 50 state public health laboratories
  - 6 large cities (Houston, Los Angeles, New York City, Philadelphia, San Diego, San Francisco)
  - Washington, DC and Puerto Rico



Other Sites:
Stephanie Johnston: Houston, Los Angeles, San Diego, San Francisco, New York City
Stephanie Swint: Philadelphia, District of Columbia
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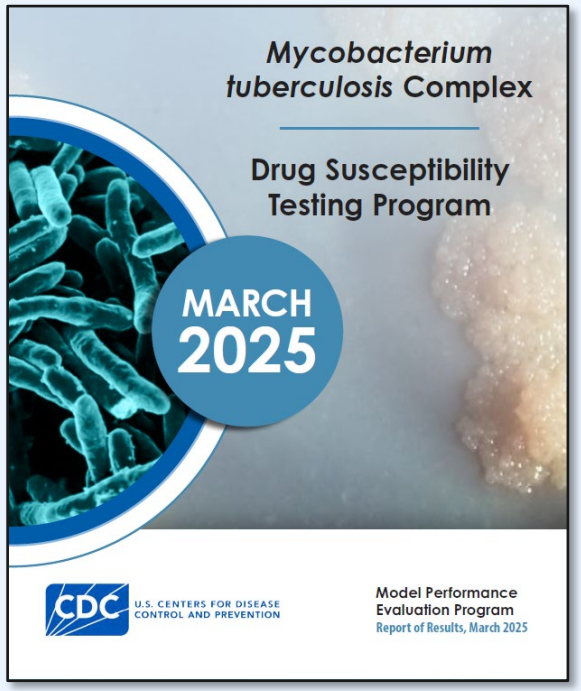
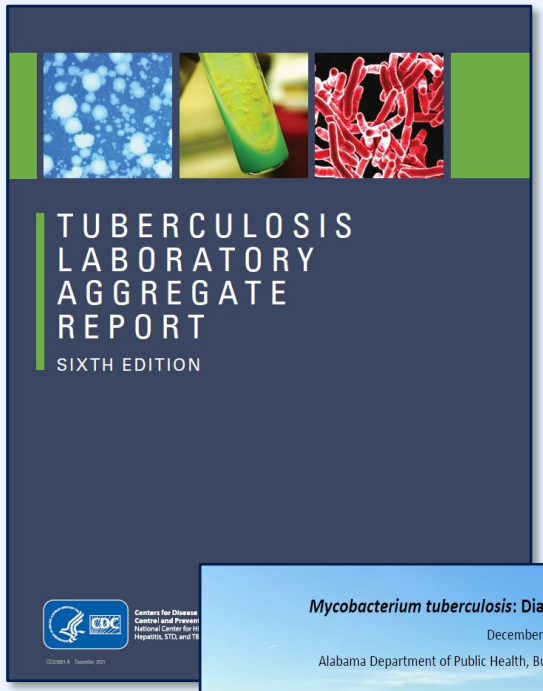
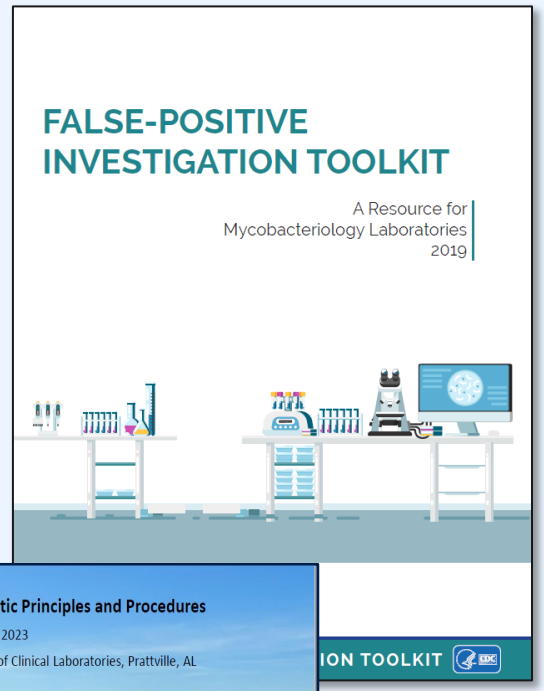
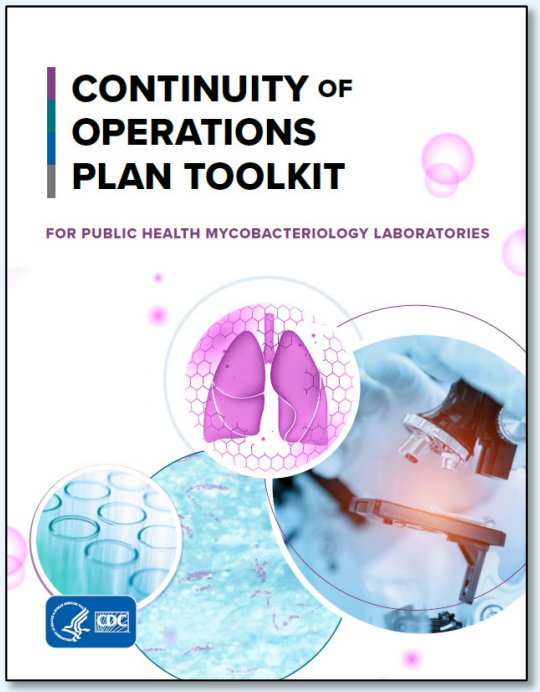
Programs, Resources, & Tools









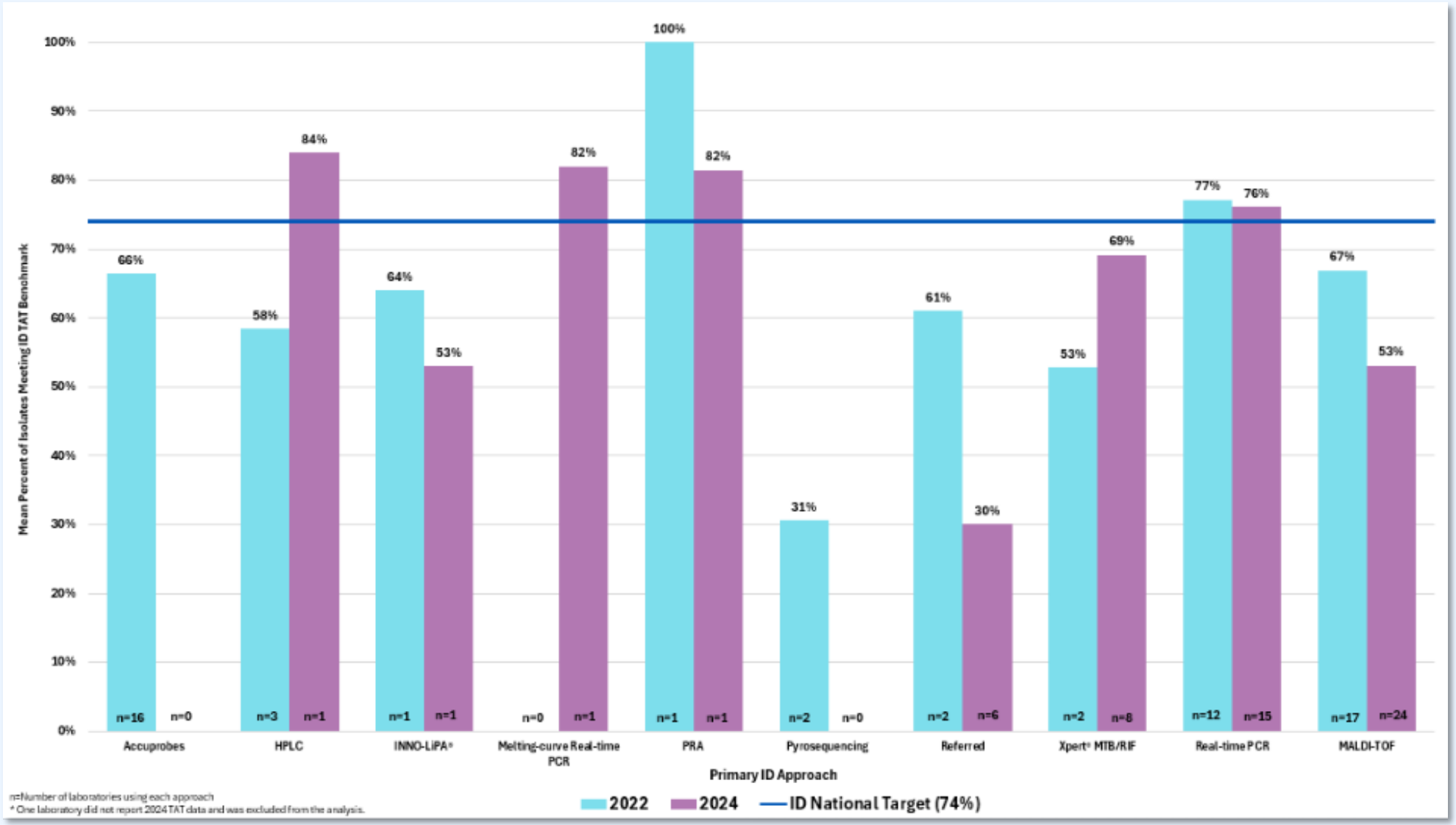
TB Laboratory Aggregate Report

8th Edition in development, spring 2026 release date

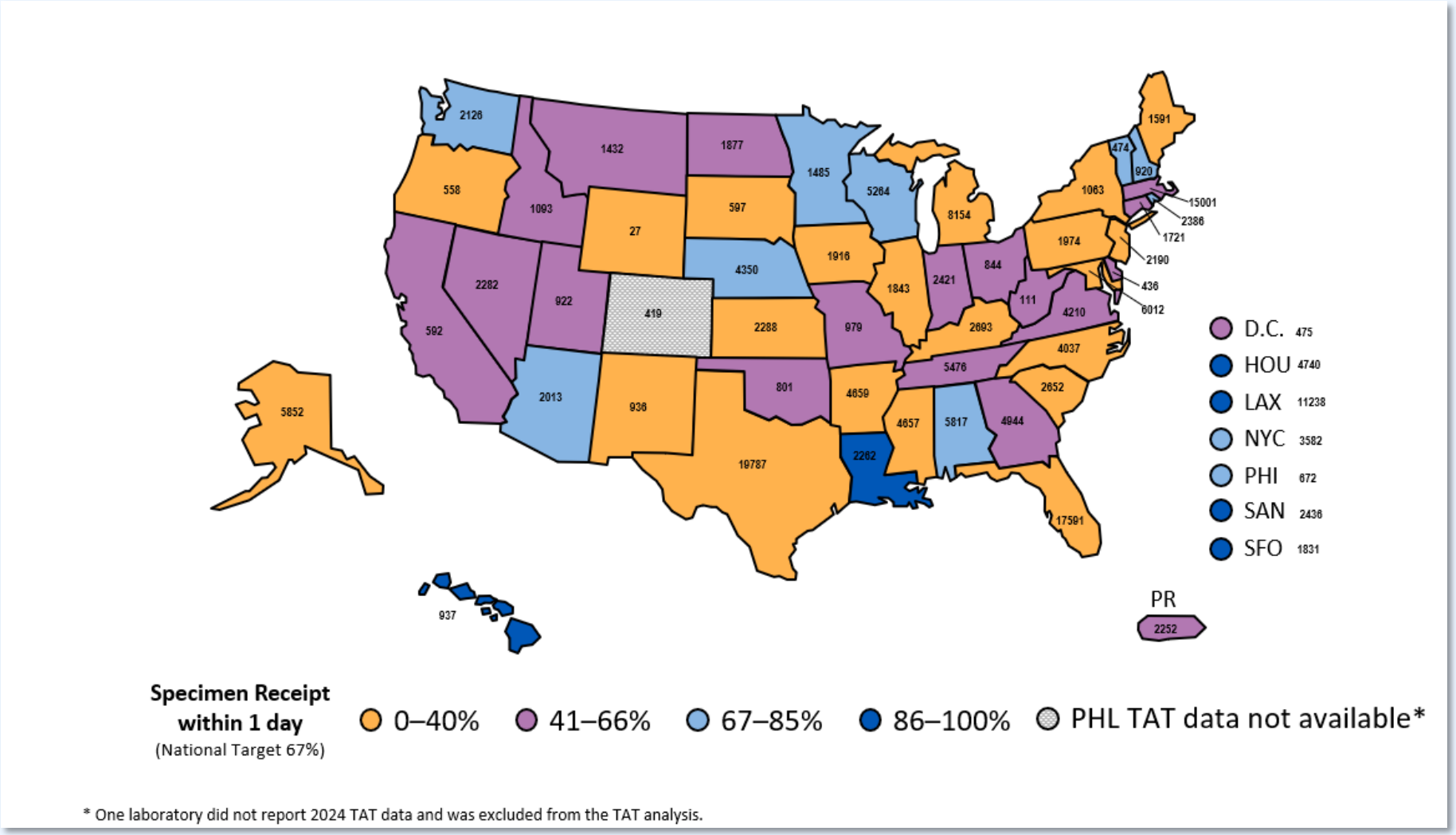
- Between 2022 and 2024:
  - Number of MTBC culture-positive patients increased by 24%
  - NAAT workload volume increased sharply, with a 44.3% increase in patients tested and a 24.3% increase in NAAT-positive patients

- From 2022 to 2024, in-house sequencing/ molecular DST workload volume:
  - Number of patient samples tested increased by 115.3%
    - ➢ Reflecting expanded PHL sequencing capacity and integration into routine workflows

Additional ID methods implemented between 2022 and 2024 after the transition from using AccuProbe® and pyrosequencing; turnaround times were affected



Map of Percent of Specimens Received within 1 Day from Specimen Collection, with Total Number of Specimens Received by PHL, 2024

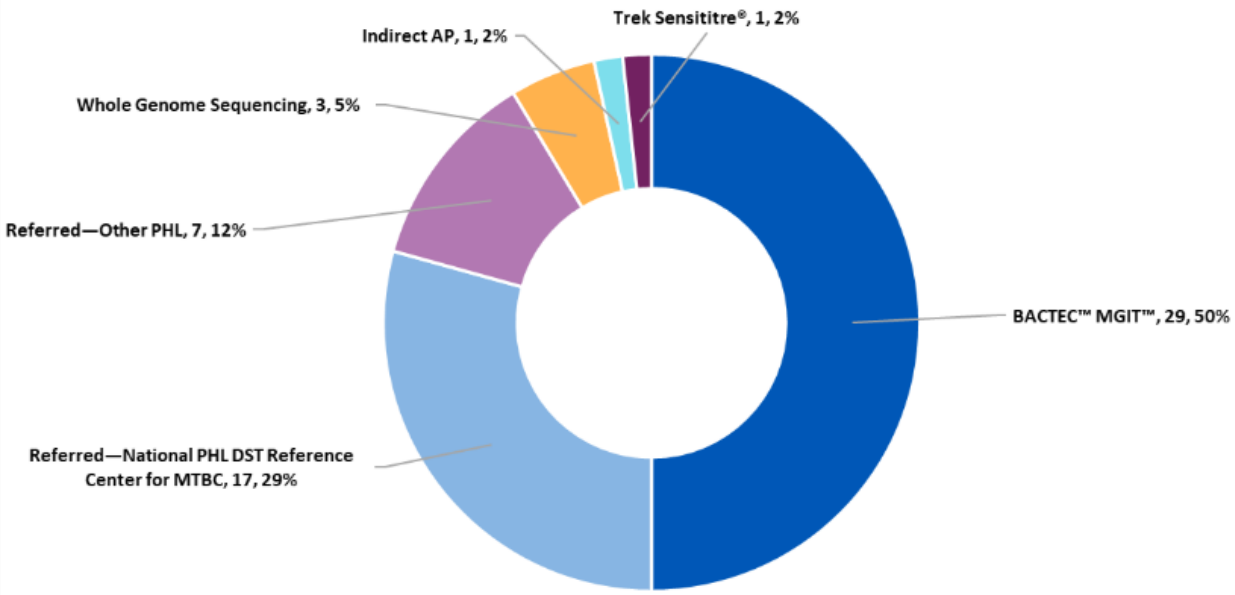


* One laboratory did not report 2024 TAT data and was excluded from the TAT analysis.

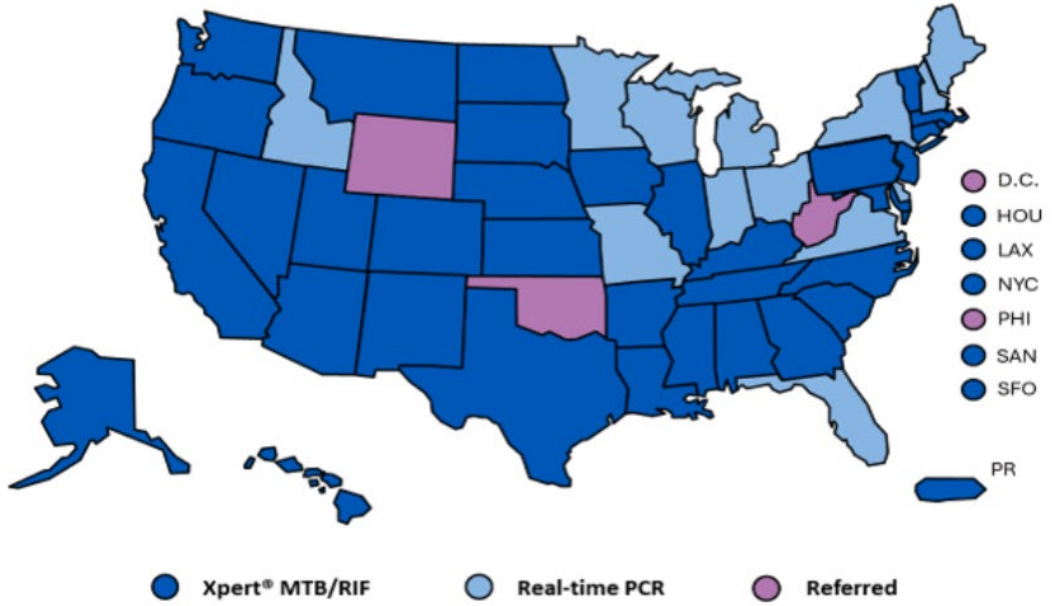
Interferon-Gamma Release Assay (IGRA) Approaches, 2025

IGRA Approach	PHL
Qiagen QuantiFERON® in Another Section of PHL	CO, CT, FL, GA, HI, IA, KS, LAX, ME, MO, MS, MT, ND, NE, NJ, NM, NV, OR, PA, SFO, SC, SD, VT, WY
Qiagen QuantiFERON® in Mycobacteriology Laboratory	DE, HOU, IN, MD, NH, TN
Revvity T-Spot®.TB (referral)	AR, LA

First-line DST Approaches, 2025



Pulmonary NAAT Approaches in 2025



Applied Research Team Updates

National Molecular Surveillance for TB

- **National TB Molecular Surveillance Center (NTMSC) currently at Michigan Bureau of Laboratories**
  - Supports whole genome sequencing (WGS) prospectively on new *M. tuberculosis* isolates
  - WGS data generated at NTMSC available to states for other surveillance or research purposes after consulting with CDC
- **More public health laboratories implementing WGS in-house**
  - Public health laboratories performing WGS in-house (meeting quality criteria) may submit data files in lieu of referral to Michigan
- **CDC deposited deidentified whole genome sequencing data for 28,850 samples (2018–2022) in an NCBI BioProject (PRJNA1237251)**
  - Deidentified data for 2023 will be uploaded soon

Modernized Molecular Surveillance Analytics

- **Modernized and refactored bioinformatic processes**
- **Implemented Nextflow workflow orchestration**
- **Transitioned to the AMD Platform (AMD-P)**
- **Maintained existing wgMLSType cluster names**
- **Added automated communication between TBGIMS and AMD-P**
- **Automated wgSNP comparisons for all new and existing clusters daily when new isolates are added**
- **Added access to GrapeTree**
  - Programs visualize strain comparisons
  - Have ability to add local metadata

Evaluating Susceptibility Testing for Delamanid

- Phenotypic susceptibility testing
  - Delamanid @ 0.06 ug/ml in MGIT
  - To be used for support of clinical trials—not CLIA at this time

Table 1. Critical concentrations and clinical breakpoints for medicines recommended for the treatment of rifampicin-resistant and multidrug-resistant TB.

Drug groups	Drug		LJ	7H10	7H11	MGIT [1]
A. Fluoroquinolones [2]	Levofloxacin (CC) [3]		2.0	1.0	–	1.0
	Moxifloxacin (CC) [3]		1.0	0.5	0.5	0.25
	Moxifloxacin (CB) [4]		–	2.0	–	1.0
	Gatifloxacin (CC) [3, 5]		0.5	–	–	0.25
B. Second-line injectable agents	Amikacin		30.0	2.0	–	1.0
	Capreomycin		40.0	4.0	–	2.5
	Kanamycin [6]		30.0	4.0	–	2.5
	(Streptomycin) [7]		4.0	2.0	2.0	1.0
C. Other second-line agents	Ethionamide [7]		40.0	5.0	10.0	5.0
	Prothionamide [7]		40.0	–	–	2.5
	Cycloserine / terizidone [8]		–	–	–	–
	Linezolid		–	1.0	1.0	1.0
	Clofazimine [9]		–	–	–	1.0
D. Add-on agents (not part of the core MDR-TB regimen)	D1	Pyrazinamide [7]	–	–	–	100.0
		Ethambutol [7]	2.0	5.0	7.5	5.0
	D2	Bedaquiline [9]	–	–	0.25	1.0
		Delamanid [9]	–	–	0.016	0.06
	D3 [10]	p-aminosalicylic acid [7]	–	–	–	–
		Imipenem-cilastatin [7]	–	–	–	–
		Meropenem [7]	–	–	–	–
		Amoxicillin-clavulanate [7]	–	–	–	–
		(Thioacetazone) [7]	–	–	–	–

*Table source: Technical manual for drug susceptibility testing of medicines used in the treatment of tuberculosis (who.int)

Delamanid DST Validation

- **Selected 104 strains based on WGS data**
  - 50 resistant and 54 susceptible
  - Most resistant strains had a loss of function variant (*fbiA*, *fbiC*, *fbiD*, *ddn*, or *fgd1*)
- **MGIT 320 with TB eXiST software**
  - Delamanid @ 0.06 mg/mL
- **Determined accuracy**
  - 100% sensitivity and specificity
- **Reproducibility (2/3 completed)**
  - 95%

Pyrazinamide

Status of PZA Susceptibility Testing

- **Communication issued by BD in November 2025 indicating resumption of production of a modified version of the test kit**
  - Change to days post-positivity that inoculum can be prepared (3–5 days only)
  - Adjustment of shelf life from 18 to 13 months

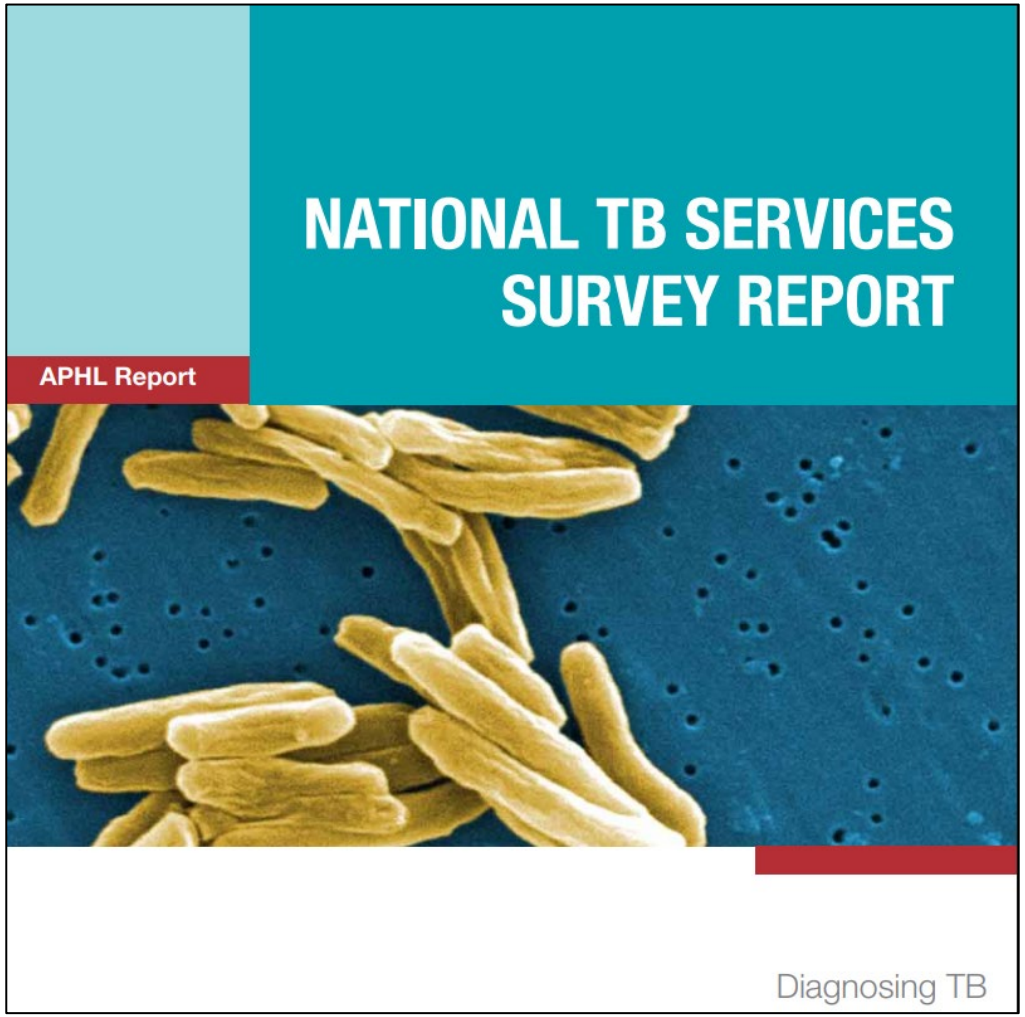
Availability of pncA Sequencing (Interim Solution)

- Submitters to the National PHL DST Reference Center at California Microbial Diseases Laboratory (MDL) will continue to receive services through the reference center
- CDC's Molecular Detection of Drug Resistance (MDDR) service available to all jurisdictions for testing when drug resistance (other than PZA) is suspected or known

Laboratory	States	POC
CA MDL	California, Hawaii, Minnesota, and Nevada + All states currently submitting to National PHL DST Reference Center	cdphtbdst@cdph.ca.gov
DTBE/LB	Alabama, Connecticut, Georgia, Illinois, Indiana, New Jersey, North Dakota, Ohio, Oregon, and Wisconsin	tblab@cdc.gov
FL BPHL	Florida and North Carolina	Patrick.valois@flhealth.gov
TX DSHS	Arizona, Arkansas, Louisiana, Missouri, Tennessee, Texas, Virginia, and West Virginia	Jan.owen@dshs.texas.gov
Wadsworth	Delaware, Maryland, Massachusetts, Michigan, Pennsylvania, New York, Washington (state) and Washington DC	tb_wgs@health.ny.gov

Understanding Current Capacities: APHL National TB Laboratory Services Survey

- **Last completed in 2010**
- **Purpose:**
  - Assess the overall ability of U.S. laboratories to provide quality TB diagnostic services
- **Results:**
  - Useful to identify gaps in capabilities and capacities and identify opportunities to strengthen laboratory systems
- **Release date anticipated mid/late 2026**



Thank you

For more information, contact CDC
1-800-CDC-INFO (232-4636)
TTY: 1-888-232-6348 https://www.cdc.gov/
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