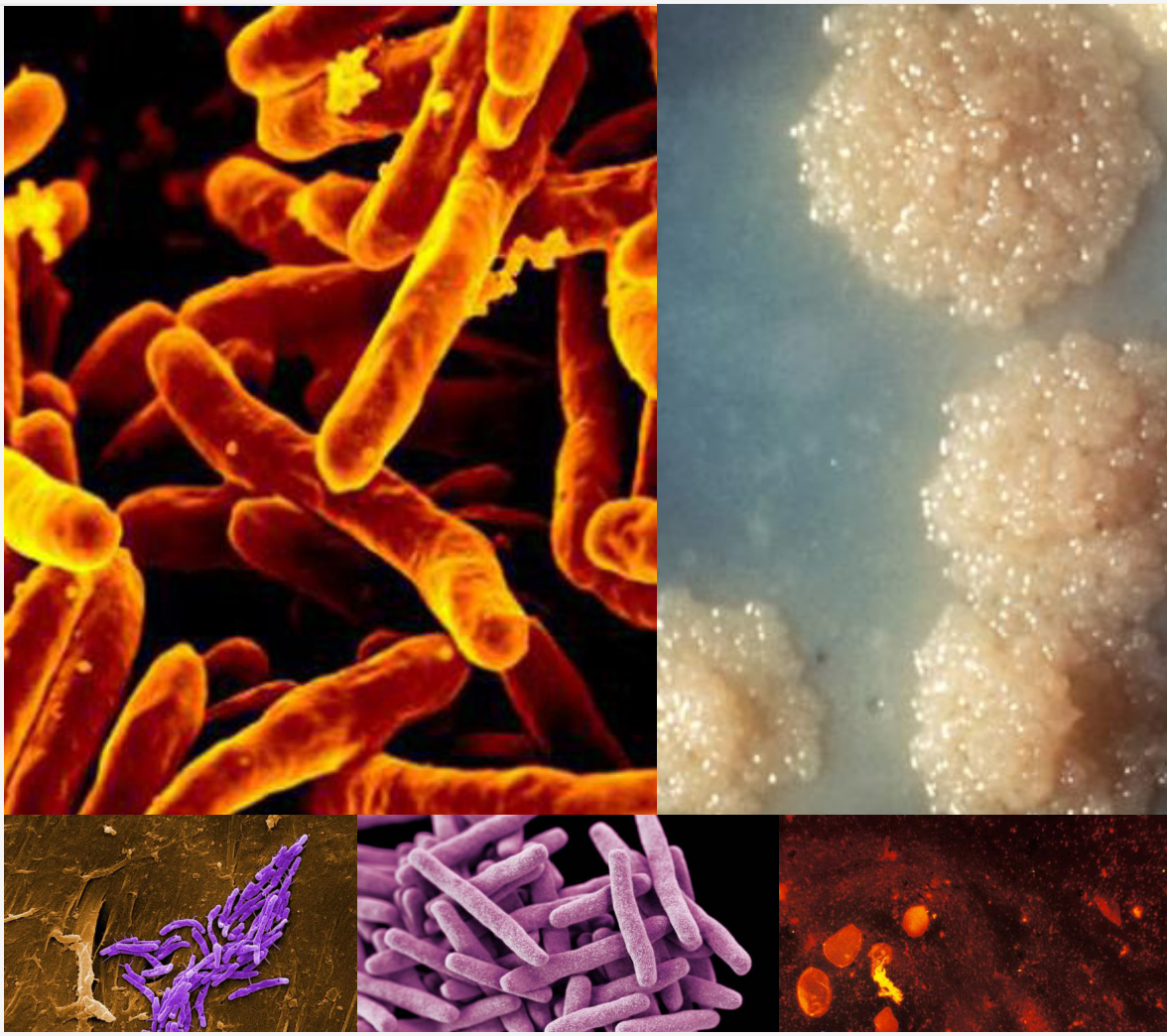
FOURTH EDITION

Tuberculosis Laboratory Aggregate Report



National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention
Division of Tuberculosis Elimination

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Inside This Report

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Introduction

The Laboratory Capacity Team (LCT) in the Laboratory Branch (LB) of the Division of Tuberculosis Elimination (DTBE) at the U.S. Centers for Disease Control and Prevention (CDC) is pleased to present the "Fourth Edition of the Tuberculosis Laboratory Aggregate Report." This report includes a comparison of aggregate workload data for calendar years 2012, 2013, 2014, and 2015, and six-year trends (2010–2015) for turnaround time (TAT). Current public health laboratory (PHL) testing methods and practices for tuberculosis (TB) are also included in this report. Data are self-reported by PHL supported, in part, by the CDC TB Elimination Cooperative Agreement. Data serve as a tool to assess benchmarks and provide peer comparisons. Providing self-reported data back to grantees in a meaningful format is an important mission of LCT.

How to Get the Most from this Report

A key aspect of a quality assurance program is to monitor workload and TAT indicators within a laboratory. By assessing these indicators internally over time, as well as externally against peer data, laboratories can track progress and set realistic goals. The Fourth Edition of the Tuberculosis Laboratory Aggregate Report provides peer data for comparison and serves as a guide to define a laboratory's TAT goals using national averages and trends. For example, if your laboratory is above the national average, continue those efforts. However, if your laboratory is below the national average, focus on efforts for improvement. The Aggregate Report also contains data that is stratified by laboratory volume for a more specific comparison among laboratories. Testing volume and courier service availability are stratified for direct comparison with similar laboratories.

Use the data in this Aggregate Report to your advantage. Information from this report can be used to either document your program's accomplishments or provide evidence to substantiate change within your laboratory, such as methodologies, protocols, or staffing.

Please contact your LCT consultant with any questions regarding data requirements for the CDC TB Cooperative Agreement or your laboratory's specific data. In addition, any recommendations concerning the Aggregate Report and its content are welcome.

Glossary

AFB: Acid-fast bacilli

AP: Agar proportion

CDC: United States Centers for Disease Control and Prevention

DST: Drug susceptibility testing

DTBE: Division of Tuberculosis Elimination

Hain LPA: Hain Lifescience. Commercial line probe assays that identify MTBC and can detect mutations associated with both rifampicin and isoniazid resistance.

HP 2020: Healthy People 2020

HPLC: High Performance Liquid Chromatography

ID: Identification

IGRA: Interferon-Gamma Release Assay

INNO-LiPA®: Fujirebio. Commercial line probe assays that identify MTBC and can detect mutations associated with rifampin resistance.

LB: Laboratory Branch

LCT: Laboratory Capacity Team

MALDI-TOF: Matrix-assisted Laser Desorption Ionization Time of Flight. A mass-spectrometry-based assay for bacterial identification.

BacTec MGIT™: Mycobacterium Growth Indicator Tube, Becton Dickinson and Co. A commercial non-radiometric broth-based mycobacterial culture system.

MTBC: *Mycobacterium tuberculosis* complex

MTD™: Mycobacterium Direct Test, Gen Probe, Inc. A commercial molecular assay for direct detection of MTBC in clinical specimens.

NAAT: Nucleic acid amplification test. Generic terminology for molecular method used for direct detection of MTBC in clinical specimens.

PCR: Polymerase chain reaction

PHL: Public health laboratory

PRA: PCR restriction analysis

Quantiferon®: Qiagen. A commercial blood test used to aid in diagnosis of TB infection. (IGRA)

Trek Sensititre: ThermoScientific. A commercial microtiter plate for minimum inhibitory concentration (MIC) testing of 12 antituberculosis drugs simultaneously.

TAT: Turnaround time

TB: Tuberculosis

T-SPOT®: Oxford ImmunoTec. A commercial blood test used to aid in diagnosis of TB infection. (IGRA)

Xpert™ MTB/RIF: Cepheid, Inc. A commercial molecular assay for direct detection of MTBC and mutations associated with rifampin resistance in clinical specimens.

Technical Notes

1. Unless otherwise specified, the source of all data and information for the tables and figures in this report originates from Annual Performance Reports of the TB Elimination and Laboratory Cooperative Agreement submitted to CDC by US Public Health Laboratories that receive Cooperative Agreement funding.
2. For Figure 3, public health laboratories were required to report data for each category for inclusion in the analysis.
3. For Figure 5, data for courier service were interpreted as accurately as possible from project narratives of Cooperative Agreement Annual Performance Reports.
4. For Figures 6–9, data for test methods were interpreted as accurately as possible from project narratives of Cooperative Agreement Annual Performance Reports.

Laboratory Workload

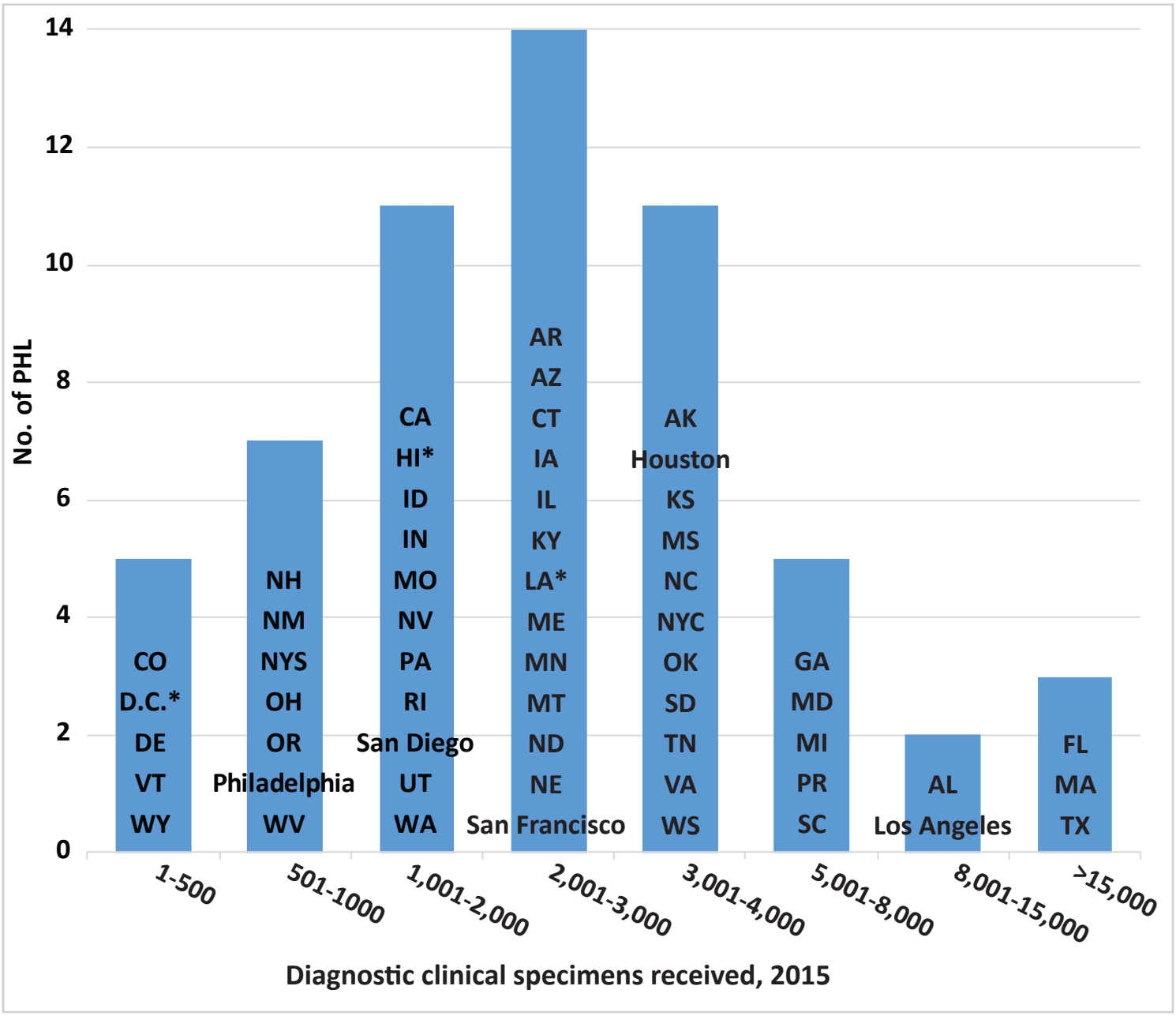
Table 1. National Workload Data, 2012–2015.

	Total No. (Range among individual laboratories)				Four Year Change
	2012	2013	2014	2015	No. (% change)
Clinical specimens[a] received	237,761 (273—21,082)	223,363 (239—19,275)	222,660 (200—21,592)	207,018 (251—21,071)	**-30,743 (-12.9)**
Patients for whom a specimen was submitted[b]	103,475 (152—10,695)	97,632 (107—11,487)	100,197 (104—11,311)	92,169 (130—10,017)	**-11,306 (-10.9)**
Patients culture positive for MTBC	4,270 (1—560)	4,210 (1—584)	3,748 (0—639)	3,868 (2—663)	**-402 (-9.4)**
Patients for whom a reference isolate was submitted[c]	17,945 (0—2,242)	17,433 (0–2,175)	15,696 (0—1,958)	15,766 (0—2,313)	**-2,179 (-12.1)**
Patients with a reference isolate identified as MTBC	2,984 (0—304)	3,084 (0—308)	3,073 (0—448)	3,307 (0—592)	**323 (10.8)**
Patients for whom DST was performed	6,854 (1—685)	6,429 (0—752)	5,929 (0—762)	6,006 (2—834)	**-848 (-12.4)**
Patients tested by NAAT or other rapid test	14,720 (2—5,599)	16,610 (1—5,197)	19,011 (0—5,466)	20,053 (0—5,101)	**5,813 (39.5)**
Patients NAAT positive for MTBC	3,045 (0—706)	2,918 (1—382)	2,631 (0—345)	3,244 (1—485)	**199 (6.5)**
IGRA	Not available	85,968 (0—16,718)	112,384 (0—26,702)	91,519 (0—23,709)	**5,551 (6.5)[d]**

[a]Processed and cultured, not including isolates referred from other laboratories, [b]Processed and culture inoculated, [c]Received to either rule out or confirm the identification MTBC, [d]2015 compared to 2013

Changes in laboratory workload reported by PHL from 2012 through 2015 are listed by key variables in Table 1. While some variations in volume were noticed annually for this four year period, PHL reported a decrease in the number of clinical specimens received, patients for whom a specimen was submitted, patients culture positive for MTBC, patients for whom a reference isolate was submitted, and patients for whom a DST was performed. However, the number of patients tested by NAAT or other rapid test increased 39.5% while patients NAAT-positive for MTBC increased 6.5%, providing evidence that PHL have increased use of molecular methods for detection of MTBC. In 2013, PHL began reporting use of IGRA for detection of TB infection as part of the Cooperative Agreement. A comparison of data collected in 2013 and 2015 showed a 6.5% increase in the number of IGRA tests performed in PHL.

Figure 1. Distribution of PHL Testing Volumes Measured by Total Number of Clinical Specimens Received, 2015.



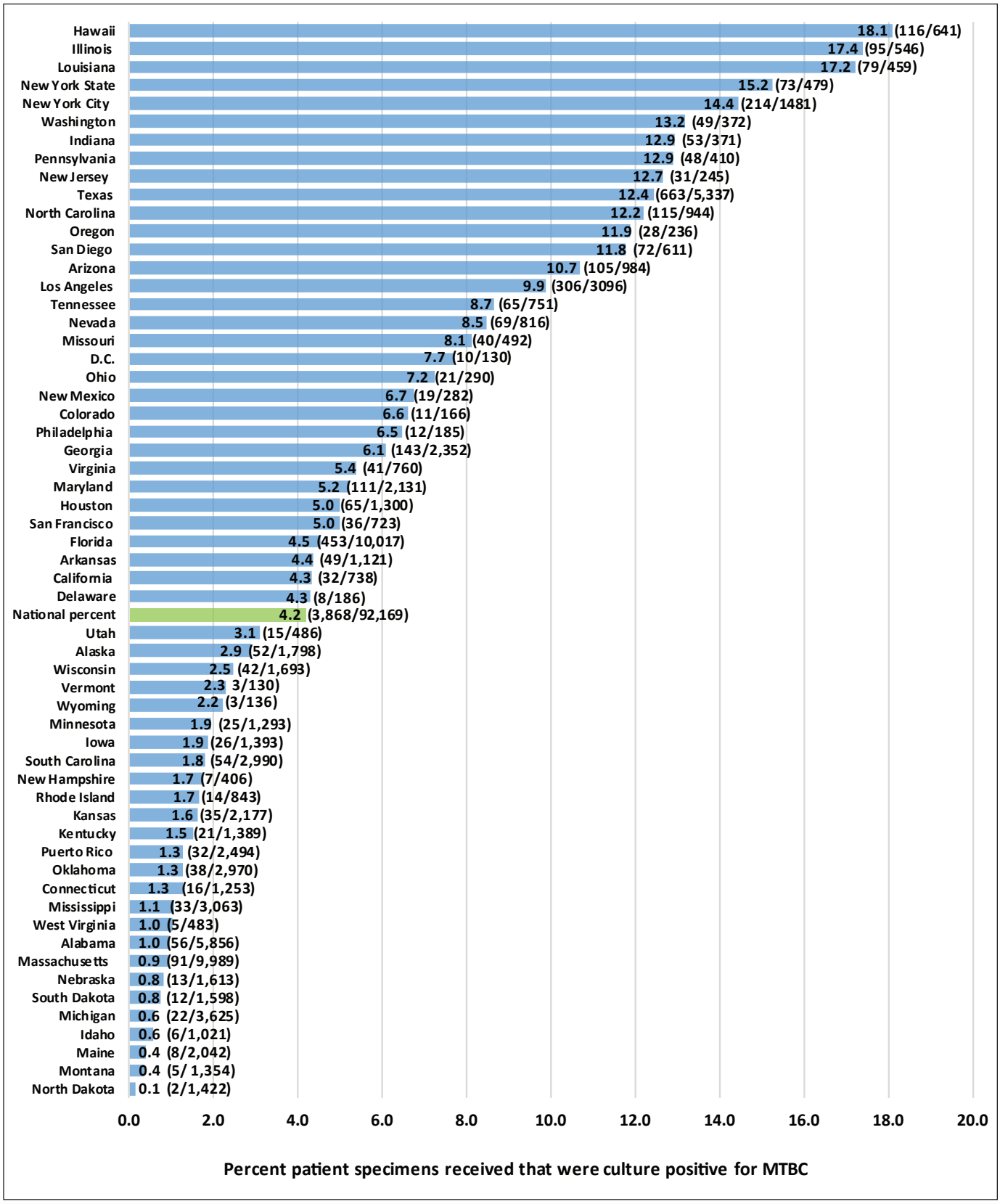
*These jurisdictions referred all TB testing to another laboratory.
Note: D.C. = Washington, D.C., NYS = New York State, NYC = New York City, PR = Puerto Rico. All others are US Postal Service state abbreviations or cities.

The volume of public health diagnostic testing for TB is variable, as evidenced by widely distributed measurements of clinical specimens received. In 2015, 11 PHL received 1,000 or fewer specimens for AFB smear and culture, while 3 PHL processed more than 15,000 specimens. Most PHL (n = 36) processed between 1,001 and 5,000 specimens.

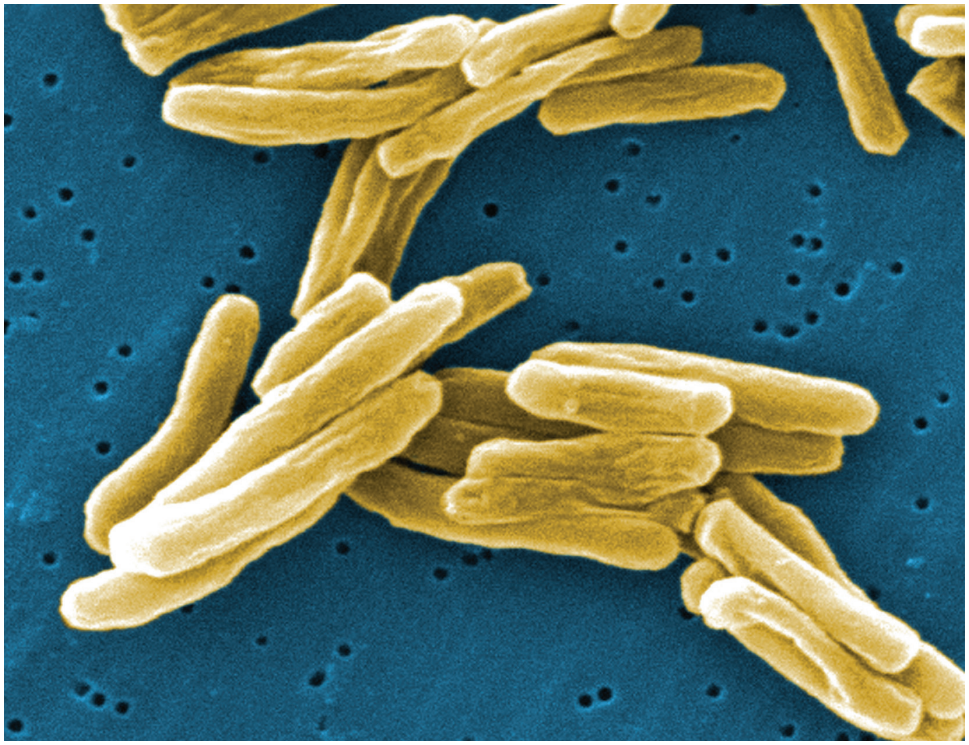
Some PHL process few clinical specimens, but may serve primarily as reference laboratories. These PHL may receive isolates and inoculated media from other laboratories within their jurisdictions. CDC and APHL recommend processing a minimum of 20 specimens per week[1] (approximately 1,000 specimens per year) to maintain proficiency and recommend that laboratories with insufficient specimen volumes or those unable to provide accurate results in a timely manner consider sending specimens or cultures to qualified full service laboratories. Testing volume is only one potential indicator of proficiency. Many other factors contribute to the decision for a laboratory to continue mycobacteriology services, including staff expertise, dedicated quality assurance programs, and regional assessments of the need for essential services[2].

MTBC Culture Positivity

Figure 2. Positivity of Cultures by Cooperative Agreement Site, 2015.

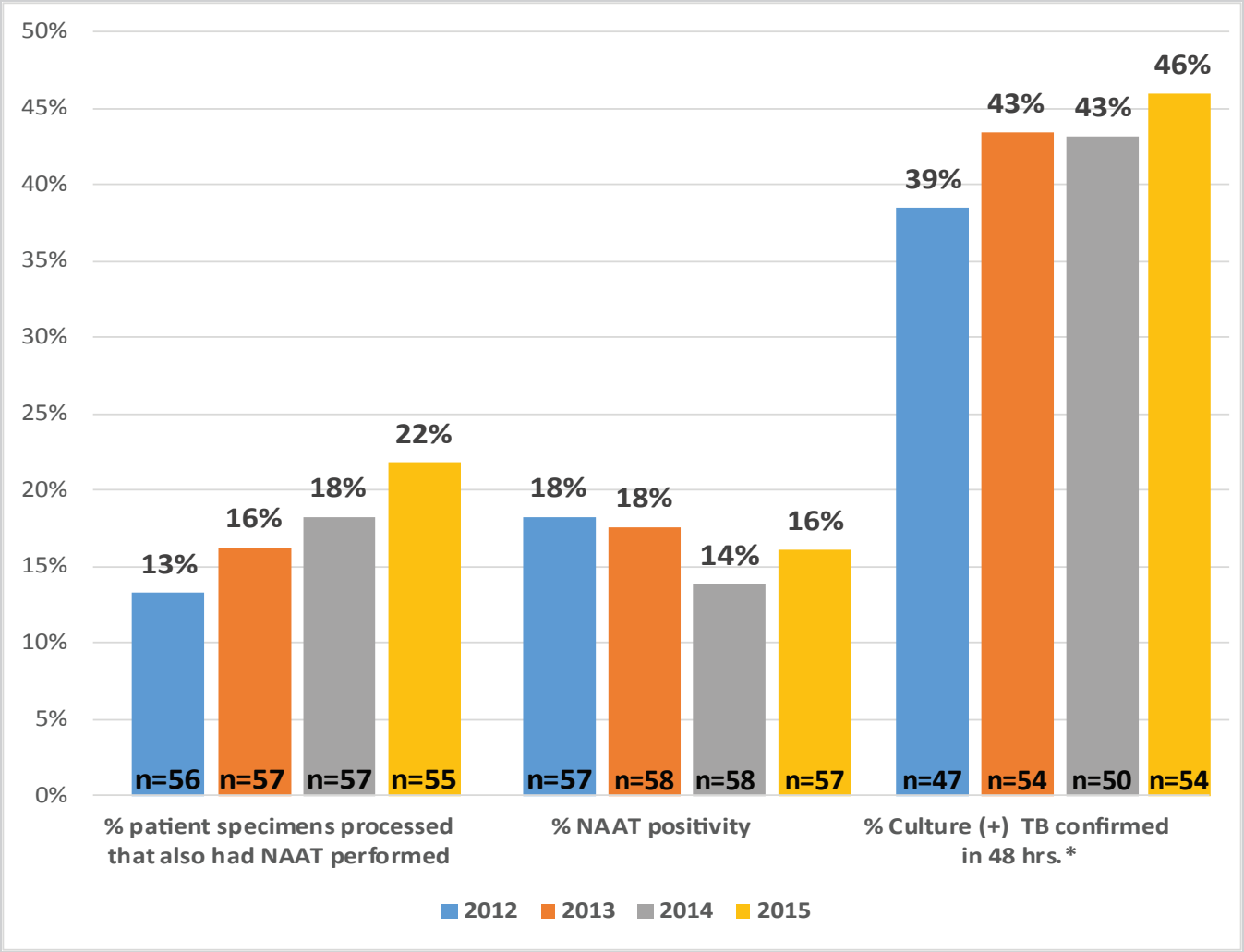


The wide range of MTBC culture positivity (percent of individual patients' specimens that were positive for MTBC in culture) observed among PHL is shown in Figure 2. This range may be indicative of differences in incidence of TB disease among patient populations served by PHL or may reflect the widely variable roles that PHL serve within their jurisdictions. For instance, in some areas, the state PHL may be the sole facility processing AFB specimens and therefore, may see a lower percent of cultures positive for MTBC; but in other areas, the PHL may function primarily in a reference laboratory capacity by receiving follow-up specimens after diagnosis and therefore, might encounter a relatively higher MTBC culture positivity. A number of other factors may influence MTBC culture positivity, including the nature of the patient population served by PHL, differences in clinicians' practices in evaluating patients, or local incidence of nontuberculous mycobacteria (NTM) disease. The national culture positivity displayed is not indicative of a nationwide goal, but rather reflects the percent of all specimens received in PHL in 2015 that were positive for MTBC in culture, measured on a per-patient basis. It is important for individual laboratories to determine baseline MTBC culture positivity and monitor this percentage over time to detect fluctuations. While some variation might indicate change in disease incidence or patient population changes, significant incremental deviations in this indicator could also indicate potential laboratory issues such as false-positive cultures. Laboratories may wish to use the information in this graph to compare culture positivity among their peers in terms of similar testing volumes or geographic location.



Trends in Nucleic Acid Amplification Testing (NAAT)

Figure 3. Trends in NAAT, 2012–2015.



Note: n = number of laboratories reporting data. % NAAT positivity = percent of nucleic acid amplification tests performed that were positive for MTBC.

*Beginning in 2013, clarification was provided to indicate only those patients with culture-positive TB should be counted. In 2014, 2 laboratories had 0 patients with culture-positive TB; these were excluded from analysis.

The use of NAAT as part of a laboratory's testing algorithm is essential for rapid detection of patients with TB. From 2012 to 2015, while the percent of NAAT positivity decreased, expanded use of NAAT in PHL increased, as did improvement towards achievement of the HP 2020 goal of 77% of culture-confirmed TB detected by NAAT within 48 hours. Since 2012, NAAT algorithms have evolved and consequently, the percent of patient specimens tested by NAAT has increased. PHL should consider examining local data to determine characteristics of MTBC culture positive patients, adjust their NAAT algorithm accordingly to detect more cases, and work with their TB Control Program to ensure testing of appropriate patients. Please see Technical Note #2 for explanation of how the number of laboratories was derived.

Turnaround Times

Table 2. Turnaround Time Indicators, 2015.

	Benchmark			
	Specimen receipt within 1 day of collection	AFB smear result within 1 day of receipt	ID of MTBC within 21 days of receipt	DST within 17 days of ID of MTBC
National Target (% of specimens that should meet benchmark)	**67%**	**92%**	**74%**	**69%**
No. laboratories meeting or exceeding National Target*	**12**	**31**	**25**	**20†**
National average* (% of specimens meeting benchmark)	**48%**	**90%**	**69%**	**61%**
No. laboratories meeting or exceeding national average*	**31**	**33**	**29**	**26†**

*Number of laboratories reporting = 57. †10 PHL referring isolates to the DST Reference Center for first-line DST are excluded from analysis of the DST TAT for 2015.

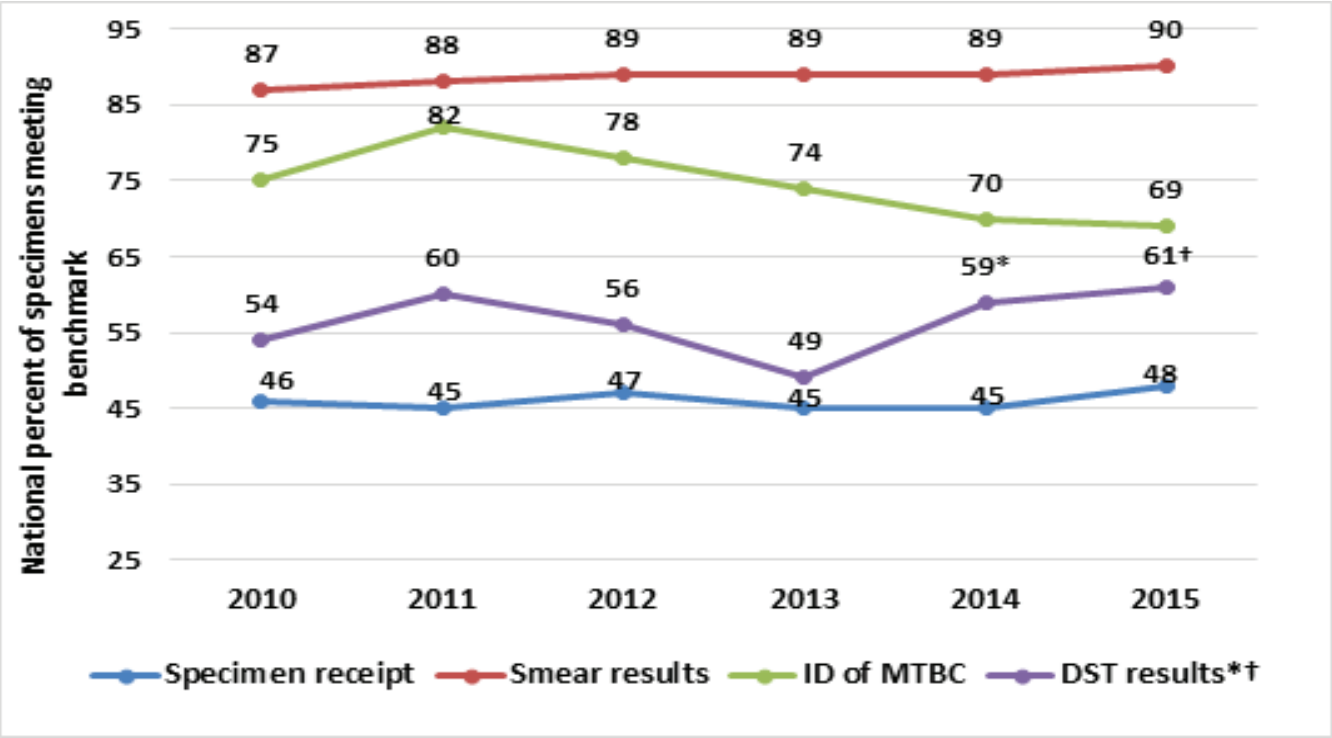
New DST TAT Benchmark

DST TAT is dependent on growth of MTBC in culture, as evidenced by the strong correlation between ID of MTBC and DST TATs ($p < .05$ for 2010 – 2013) reported in the Third Edition of the Aggregate Report[3]. To more accurately assess DST TAT measurement independent of growth of MTBC in culture prior to ID of MTBC, the benchmark was changed in 2014 to percent of DST results within 17 days of ID of MTBC, rather than the previous measurement of 28 days from specimen receipt. Specific national targets for each benchmark were set[4]. Analysis of 2014 TAT data supports this change, as no correlation between ID of MTBC and DST TAT was observed (correlation analysis, SPSS version 21).

DST Reference Center

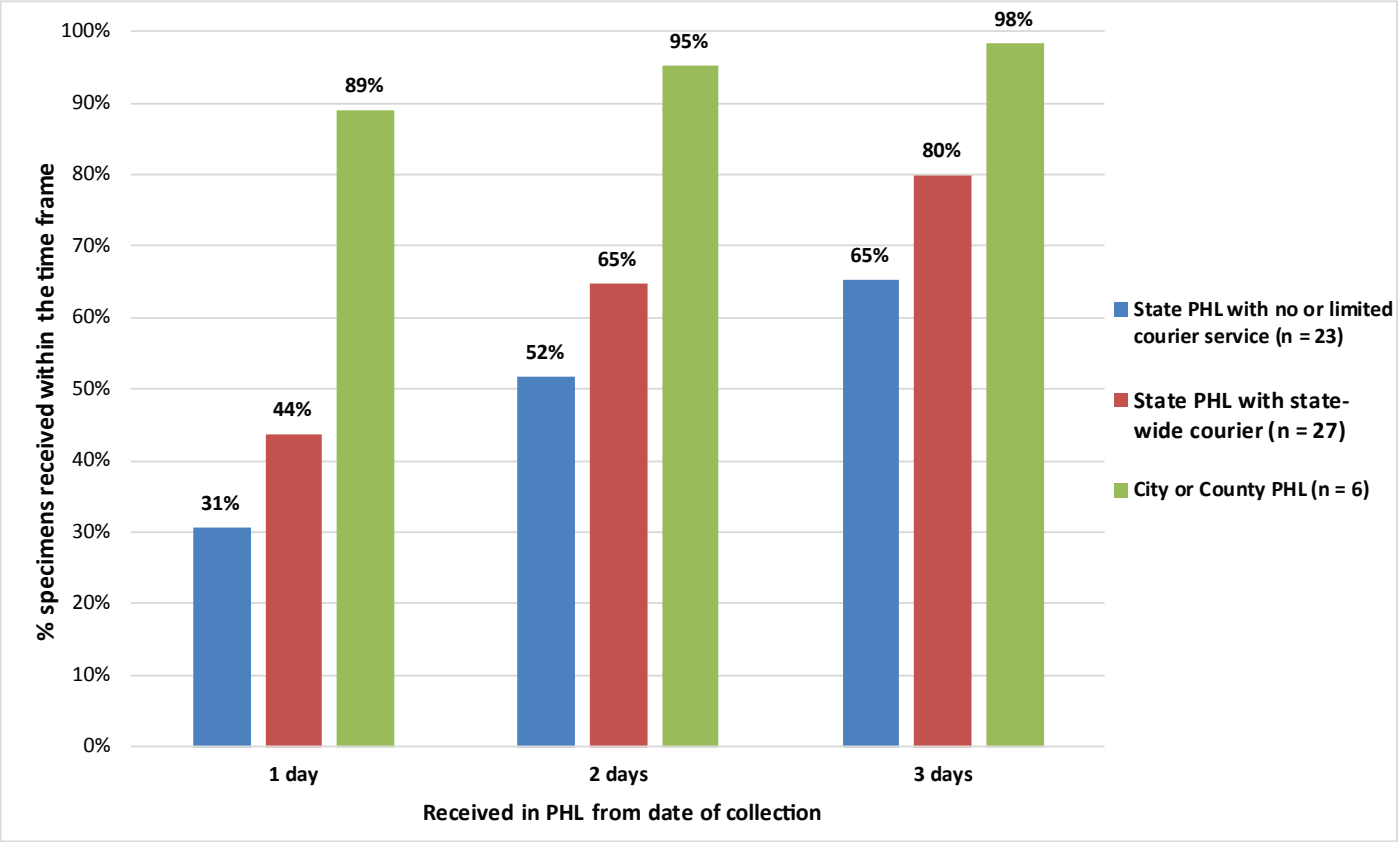
Beginning in 2015, DTBE in collaboration with APHL, established the National TB DST Reference Center at the California Microbial Diseases Laboratory. Among other services, the reference center performs first-line DST for those laboratories performing fewer than 50 DSTs per year. Currently, 10 PHL use the Reference Center for first-line DST. Those laboratories are excluded from analysis of the DST TAT for 2015.

Figure 4. Trends in Turnaround Times, 2010–2015.

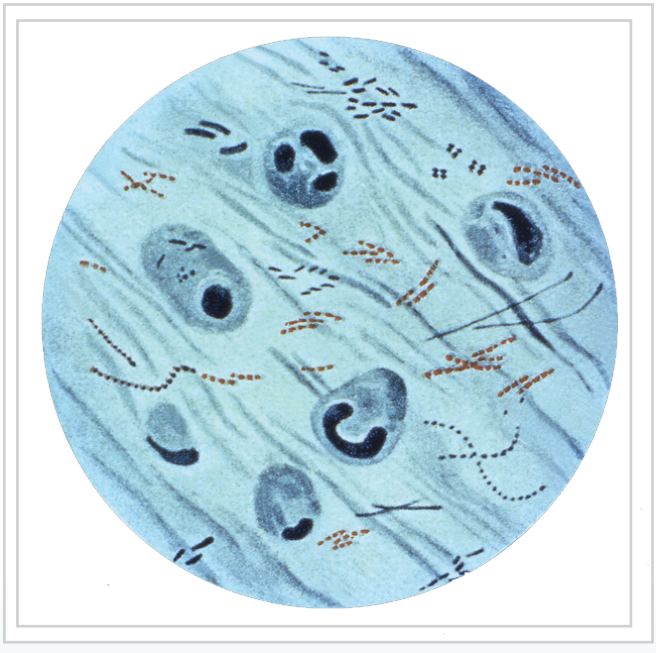


*In 2014, the DST benchmark was changed to reflect the new recommendation of DST results within 17 days of ID of MTBC.
†10 PHL referring isolates to the DST Reference Center for first-line DST are excluded from analysis of the DST TAT for 2015.

Figure 5. Specimen Receipt TAT Comparisons by Courier Availability, 2015.



State PHL that had availability of a statewide courier service achieved TAT for specimen delivery at higher levels than did those with no or limited courier service. While city and county PHL achieved this benchmark at higher levels, rapid specimen delivery remains challenging for state laboratories: many of which are located in large geographical areas and depend on a patchwork of delivery services, including U.S. Postal Service, commercial couriers, and other transportation methods. Please see Technical Note #3 for explanation of how courier availability was determined.

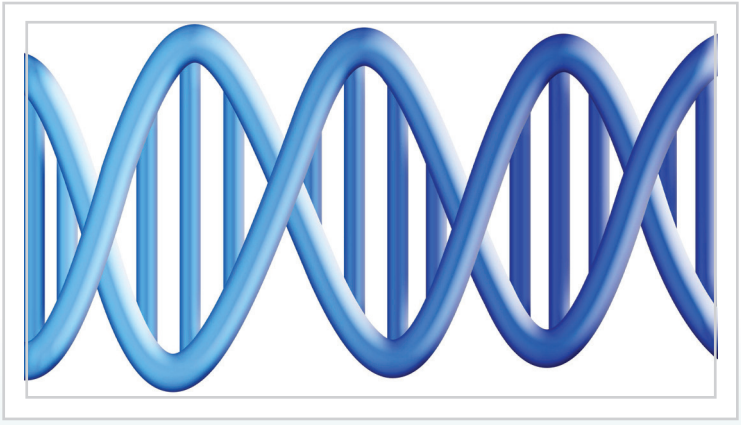


Comparison of PHL Testing to Surveillance Reports

Table 3. Comparison of National TB Surveillance Data and PHL Self-Reported Data, 2012–2015.

		Year			
		2012	2013	2014	2015
National TB Surveillance data	Total no. TB cases	9,945	9,565	9,421	9,557
	No. culture-confirmed TB cases	7,598	7,358	7,226	7,410
	No. culture-confirmed TB cases with DST reported	7,250	7,108	6,949	7,209
Self-reported PHL data (n=58 PHL reporting)	No. NAAT positive MTBC patients (% of culture-confirmed TB cases as reported for national surveillance)	3,045 (40%)	2,918 (40%)	2,631 (36%)	3,244 (44%)
	No. MTBC culture-positive patients (% of culture-confirmed TB cases as reported for national surveillance)	4,270 (56%)	4,201 (57%)	3,748 (52%)	3,868 (52%)
	No. patient DST performed (% of culture-confirmed TB cases as reported for national surveillance)	6,854 (95%)	6,434 (91%)	5,929 (85%)	6,006 (83%)

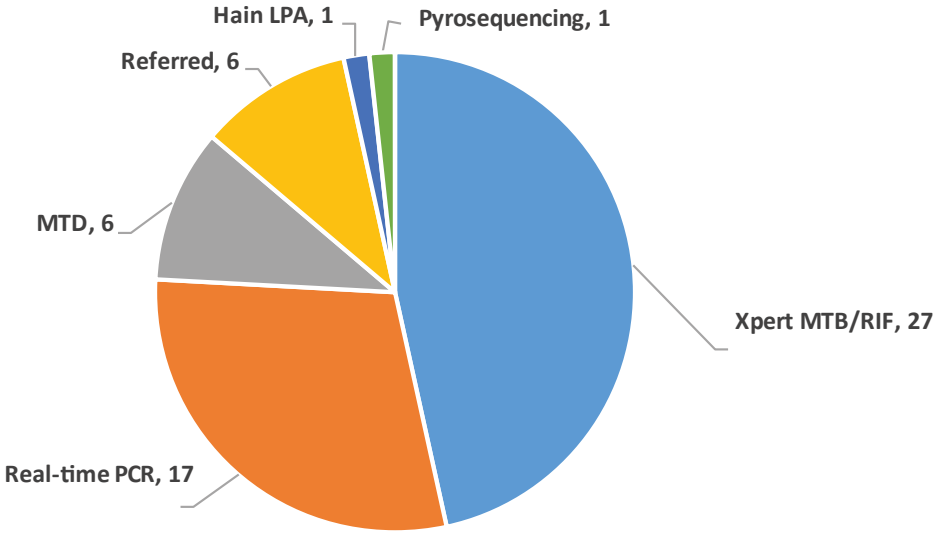
In Table 3, self-reported Cooperative Agreement data are compared to National TB surveillance data[5] for 2012–2015. In this analysis, PHL appeared to have identified approximately half of the reported culture confirmed TB cases and detected 36–44% of MTBC by direct detection (NAAT). PHL also appeared to have performed a greater percentage of more complex testing such as DST for culture confirmed cases. Because these data are drawn from different sources and may not reflect redundant testing, this comparison represents an estimation of the contribution of PHL services to overall TB testing in the United States



Methods in Public Health Laboratories

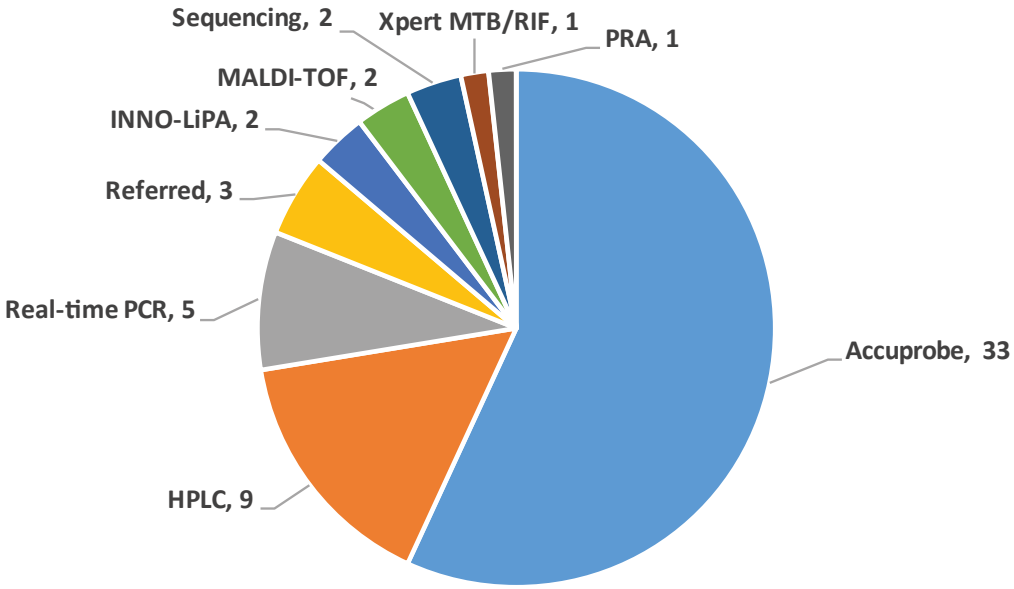
Methods used by PHL supported, in part, by the TB Cooperative Agreement for NAAT, ID, DST, and IGRA, are displayed in Figures 6–9. For each figure, total number of PHL equals 58. As new technology emerges and laboratories adjust testing algorithms, methods used will continue to evolve. Please see Technical Note #4 for explanation of how methods were determined.

Figure 6. NAAT Methods, 2016.



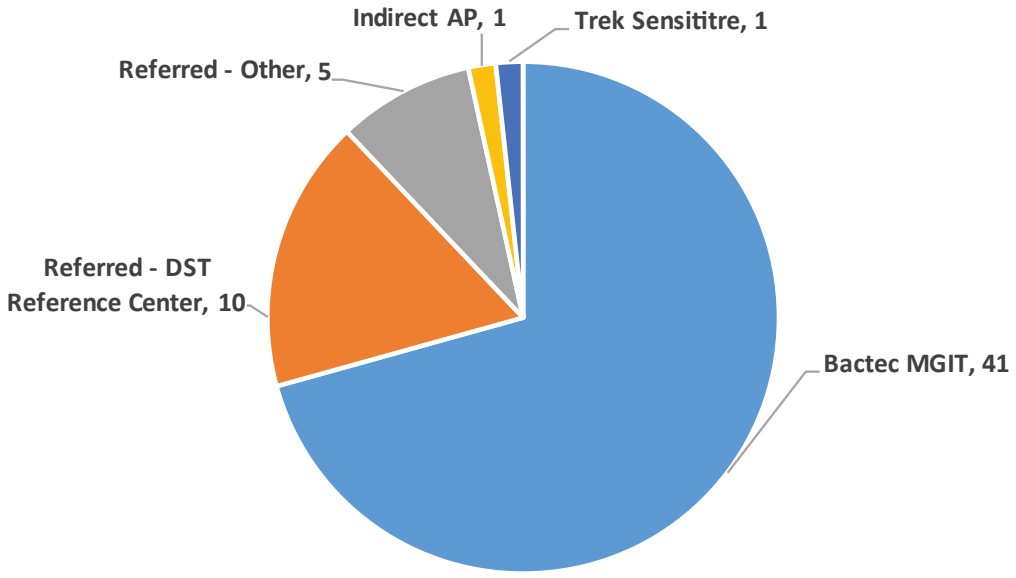
Xpert™ MTB/RIF, real-time PCR, and MTD™ assays make up 86% of NAAT methods used.

Figure 7. Primary ID Methods, 2016.



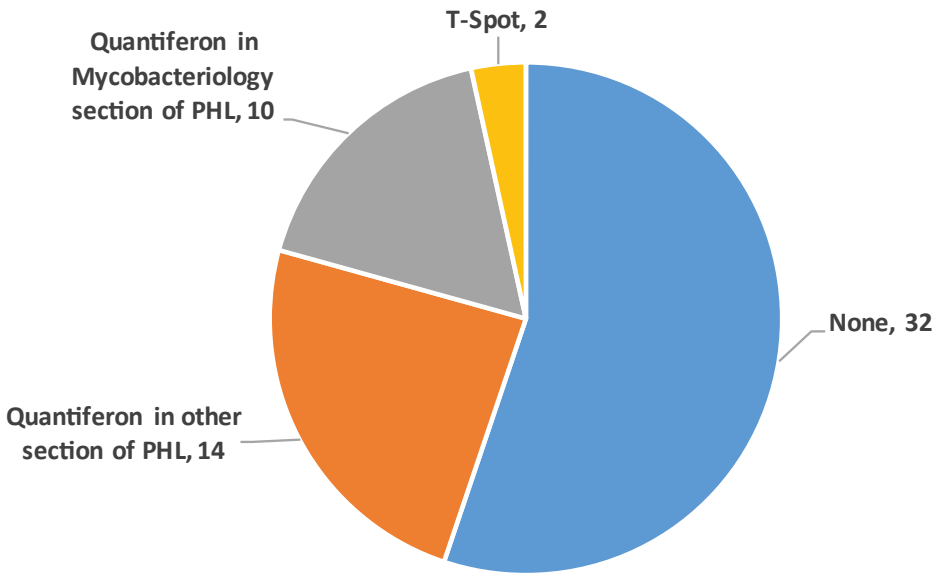
Although many PHL utilize more than one method within their ID algorithm, the primary method described from report narratives is included for each laboratory.

Figure 8. First-line DST Methods, 2016.



The majority of PHL continue to perform first-line DST via the Bactec MGIT™ system. Over the past year, 10 laboratories performing less than 50 DST per year have utilized the APHL/CDC National TB DST Reference Center for susceptibility testing.

Figure 9. IGRA Methods, 2016.



As use of IGRA expands throughout public health laboratories, 24 laboratories performed Quantiferon®, with 10 of these performing testing within the Mycobacteriology section and 14 testing within another section of the PHL. Two laboratories utilized T-Spot® by referring specimens to a national testing center. The majority of PHL, however, are not currently performing IGRA testing.

References

1. Beavis K, Bernardo J, Blank E, Desmond E, Harris R, Humes R, et al. The Future of TB laboratory services; a framework for integration, collaboration, leadership: a report from an APHL task force. Silver Spring, MD: 2004.
2. Livingston KA, Lobato MN, Sosa LE, Budnick GE, Bernardo J. Mycobacterium tuberculosis testing practices in hospital, commercial and state laboratories in the New England states. IJTLD, the official journal of the International Union against Tuberculosis and Lung Disease. 2011;15(9):1218-22,
3. CDC. Tuberculosis Laboratory Aggregate Report. Atlanta, GA: U.S. Department of Health Services, CDC; 2014. http://www.cdc.gov/tb/publications/reportsarticles/labreports.htm
4. APHL. TB Cooperative Agreement Toolkit. Silver Spring, MD; 2016. https://www.aphl.org/programs/infectious_disease/tuberculosis/Pages/TB-Cooperative-Agreement.aspx
5. CDC. Reported tuberculosis in the United States, 2014. Atlanta, GA: US Department of Health and Human Services, CDC; 2015. http://www.cdc.gov/tb/statistics/reports/2014/default.htm

Resources

APHL Resources

APHL TB Web page https://www.aphl.org/programs/infectious_disease/tuberculosis/Pages/default.aspx

APHL White Paper on PZA (2016) http://www.aphl.org/AboutAPHL/publications/Documents/ID-PZA_WhitePaper_0216.pdf#search=PZA

APHL White Paper on Ethambutol (2016) https://www.aphl.org/aboutAPHL/publications/Documents/ID-MTBC_DrugSusceptibility_0216.pdf#search=ethambutol

CDC Resources

CDC TB Website http://www.cdc.gov/tb/

CDC Molecular Detection of Drug Resistance (MDDR) Service http://www.cdc.gov/tb/topic/laboratory/default.htm

MMWR on use of Xpert http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6241a1.htm?s_cid=mm6241a1_e

MMWR on use of Xpert for removal of patients from respiratory isolation http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6407a8.htm?s_cid=mm6407a8_w

Regional Training and Medical Consultation Centers http://www.cdc.gov/tb/education/rtmc/default.htm

Report of Expert Consultations on Rapid Molecular Testing to Detect Drug-Resistant Tuberculosis in the United States http://www.cdc.gov/tb/topic/laboratory/rapidmoleculartesting/default.htm

Updated Guidelines for Using Interferon Gamma Release Assays to Detect Mycobacterium tuberculosis Infection—United States, 2010: http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5905a1.htm?s_cid=rr5905a1_w

Guide to the Application of Genotyping to Tuberculosis Prevention and Control http://www.cdc.gov/tb/programs/genotyping/manual.htm

TB Notes Newsletter http://www.cdc.gov/tb/publications/newsletters/default.htm

CDC Model Performance Evaluation Program http://www.cdc.gov/tb/topic/laboratory/mpep/

Other Resources

TB Education and Training Resources http://www.findtbresources.org/

Journal Articles of Interest

Biosafety

Delaney J, Pentella M, Rodriguez J, et al. 2011. Guidelines for Biosafety Laboratory Competency. CDC and the Association of Public Health Laboratories. MMWR Supplements / 60(02);1-6. https://www.cdc.gov/mmwr/preview/mmwrhtml/su6002a1.htm

Miller JM, Astles R, Baszler T, et al. 2012. Guidelines for Safe Work Practices in Human and Animal Medical Diagnostic Laboratories. MMWR Supplements / 61(01);1-101. https://www.cdc.gov/Mmwr/preview/mmwrhtml/su6101a1.htm

Xpert™ MTB/RIF

Luetkemeyer AF, Firnhaber C, Kendall MA, et al. 2016. Evaluation of Xpert MTB/RIF versus AFB Smear and Culture to Identify Pulmonary Tuberculosis in Patients with Suspected Tuberculosis from Low and Higher Prevalence Settings. Clin Infect Dis. 62 (9): 1081-1088. https://www.ncbi.nlm.nih.gov/pubmed/26839383

McAlister AJ, Driscoll J, Metchock B. 2015. DNA sequencing for confirmation of rifampin resistance detected by Cepheid Xpert MTB/RIF assay. J Clin Microbiol 53(5):1752-3. www.ncbi.nlm.nih.gov/pubmed/25740782

Williamson DA, Basu I, Bower J, et al. 2012. An evaluation of the Xpert MTB/RIF assay and detection of false-positive rifampicin resistance in Mycobacterium tuberculosis. Diagnostic Microbiology and Infectious Disease 74(2):207-209. https://www.ncbi.nlm.nih.gov/pubmed/22819240

Laboratory Practices

Han LL, Elvin P, Bernardo J. 2012. Nonclinical selection criteria for maximizing yield of nucleic acid amplification tests in tuberculosis diagnosis. J Clin Microbiol 50(8): 2592-2595. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3421530/

Mitchell K, Halse T, Kohlerschmidt D, et al. 2015. A Model of Shared Mycobacteriology Testing Services: Lessons Learned. Public Health Rep 130(6):623-31. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4612171/

Peralta G, Barry P, Pascopella L. 2016. Use of Nucleic Acid Amplification Tests in Tuberculosis Patients in California, 2010-2013. Open Forum Infect Dis. 2016 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5146759/

Pfyffer GE, Wittwer F. 2012. Incubation time of mycobacterial cultures: how long is long enough to issue a final negative report to the clinician? J Clin Microbiol 50(12):4188-9. http://jcm.asm.org/content/50/12/4188

Tans-Kersten J, Grace Lin SY, Desmond E, et al. 2016. Evaluating Shared Laboratory Services: Detecting Mycobacterium Tuberculosis Complex and Drug Resistance Using Molecular and Culture-Based Methods. Public Health Rep 131(1):117-25. https://www.ncbi.nlm.nih.gov/pubmed/26843677

Tyrrell FC, Budnick GE, Elliott T, et al. 2012. Probability of negative Mycobacterium tuberculosis complex cultures based on time to detection of positive cultures: a multicenter evaluation of commercial-broth-based culture systems. J Clin Microbiol 50(10): 3275-3282. http://www.ncbi.nlm.nih.gov/pubmed/22837326

Tyrrell F, Stafford C, Yakrus M, et al. 2016. Trends in Testing for Mycobacterium tuberculosis Complex From US Public Health Laboratories, 2009–2013. Public Health Reports: 132(1): 56-64. https://www.ncbi.nlm.nih.gov/pubmed/28005481

Pyrazinamide

Piersimoni C, Mustazzolu A, et al. 2013. Prevention of False Resistance Results Obtained in Testing the Susceptibility of Mycobacterium tuberculosis to Pyrazinamide with the Bactec MGIT 960 System Using a Reduced Inoculum. J Clin Microbiol 51(1): 291-294. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3536208/

MALDI-TOF

Buckwalter SP, Olson SL, Connelly BJ, et al. 2016. Evaluation of Matrix-Assisted Laser Desorption Ionization-Time of Flight Mass Spectrometry for Identification of Mycobacterium species, Nocardia species, and Other Aerobic Actinomycetes. J Clin Microbiol; 54(2):376-84. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4733196

Molecular Drug Resistance

Dominguez J, Boettger EC, Cirillo D, et al. 2016. Clinical implications of molecular drug resistance testing for Mycobacterium tuberculosis: a TBNET/RESIST-TB consensus statement. Int J Tuberc Lung Dis 20(1):24-42. https://www.ncbi.nlm.nih.gov/pubmed/26688526

Lin S-YG, Desmond EP. 2014. Molecular Diagnosis of Tuberculosis and Drug Resistance. Clinics in Laboratory Medicine 34(2):297-314 www.labmed.theclinics.com/article/S0272-2712(14)00019-5/references

Rigouts L, Gumusboga M, et al. 2013. Rifampin resistance missed in automated liquid culture system for Mycobacterium tuberculosis isolates with specific rpoB mutations. J Clin Microbiol; 51(8): 2641-2645. https://www.ncbi.nlm.nih.gov/pubmed/23761146

Van Deun A, Aung KJ, Bola V, et al. 2013. Rifampin drug resistance tests for tuberculosis: challenging the gold standard. J Clin Microbiol 51(8):2633-40. https://www.ncbi.nlm.nih.gov/pubmed/23761144

Yakrus MA, Metchock B, Starks AM. 2015. Evaluation of a U.S. Public Health Laboratory Service for the Molecular Detection of Drug Resistant Tuberculosis. Tuberculosis Research and Treatment 2015:7. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4352467/

Zhang Y, Yew WW. 2015.Mechanisms of drug resistance in Mycobacterium tuberculosis: Int J Tuberc Lung Dis. 19 (11):1276-89. https://www.ncbi.nlm.nih.gov/pubmed/19861002

Next Generation Sequencing

Denkinger CM, Kik SV, Cirillo DM, et al. 2015. Defining the needs for next generation assays for tuberculosis. J Infect Dis 211 Suppl 2:S29-38. https://www.ncbi.nlm.nih.gov/pubmed/25765104

Köser CU, Bryant JM, Becq J, et al. 2013. Whole-Genome Sequencing for Rapid Susceptibility Testing of M. tuberculosis. New England Journal of Medicine 369 (3):290-292. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3836233/

General

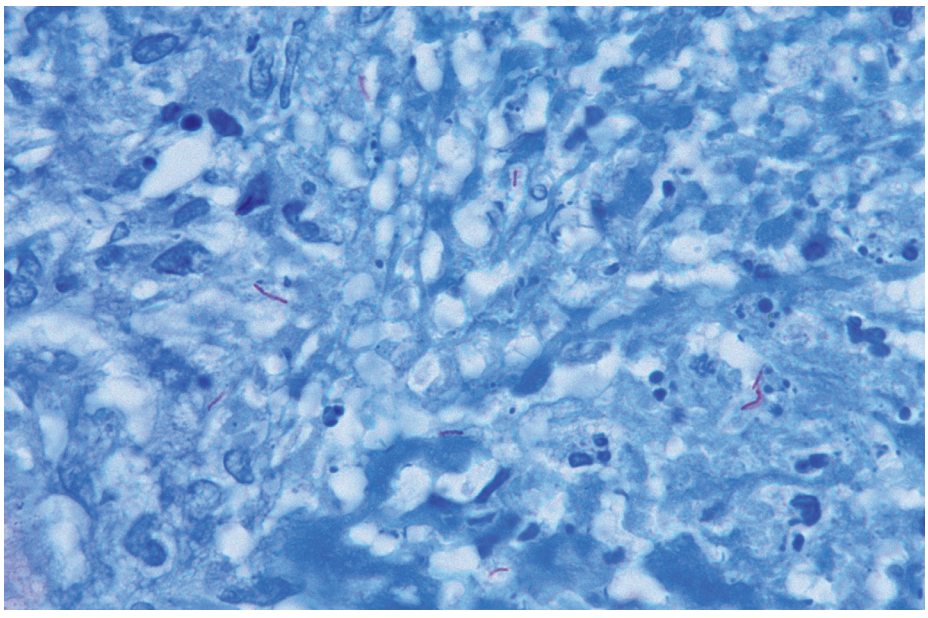
Salinas JL, Mindra G, Haddad MB, et al. 2016. Leveling of Tuberculosis Incidence — United States, 2013–2015. MMWR Morb Mortal Wkly Rep 65:273–278. http://dx.doi.org/10.15585/mmwr.mm6511a2

Updates

Official American Thoracic Society/Centers for Disease Control and Prevention/Infectious Diseases Society of America Clinical Practice Guidelines: Treatment of Drug-Susceptible Tuberculosis. 2016. Clin Infect Dis. 63(7):e147-95 https://www.ncbi.nlm.nih.gov/pubmed/27516382

Official American Thoracic Society/Infectious Diseases Society of America/Centers for Disease Control and Prevention Clinical Practice Guidelines: Diagnosis of Tuberculosis in Adults and Children. 2017. Clin Infect Dis. 64(2):111-115 https://www.ncbi.nlm.nih.gov/pubmed/28052967

Screening for Latent Tuberculosis Infection in Adults: US Preventive Services Task Force Recommendation Statement. JAMA. 2016. 316(9):962-969. http://jamanetwork.com/journals/jama/fullarticle/2547762



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