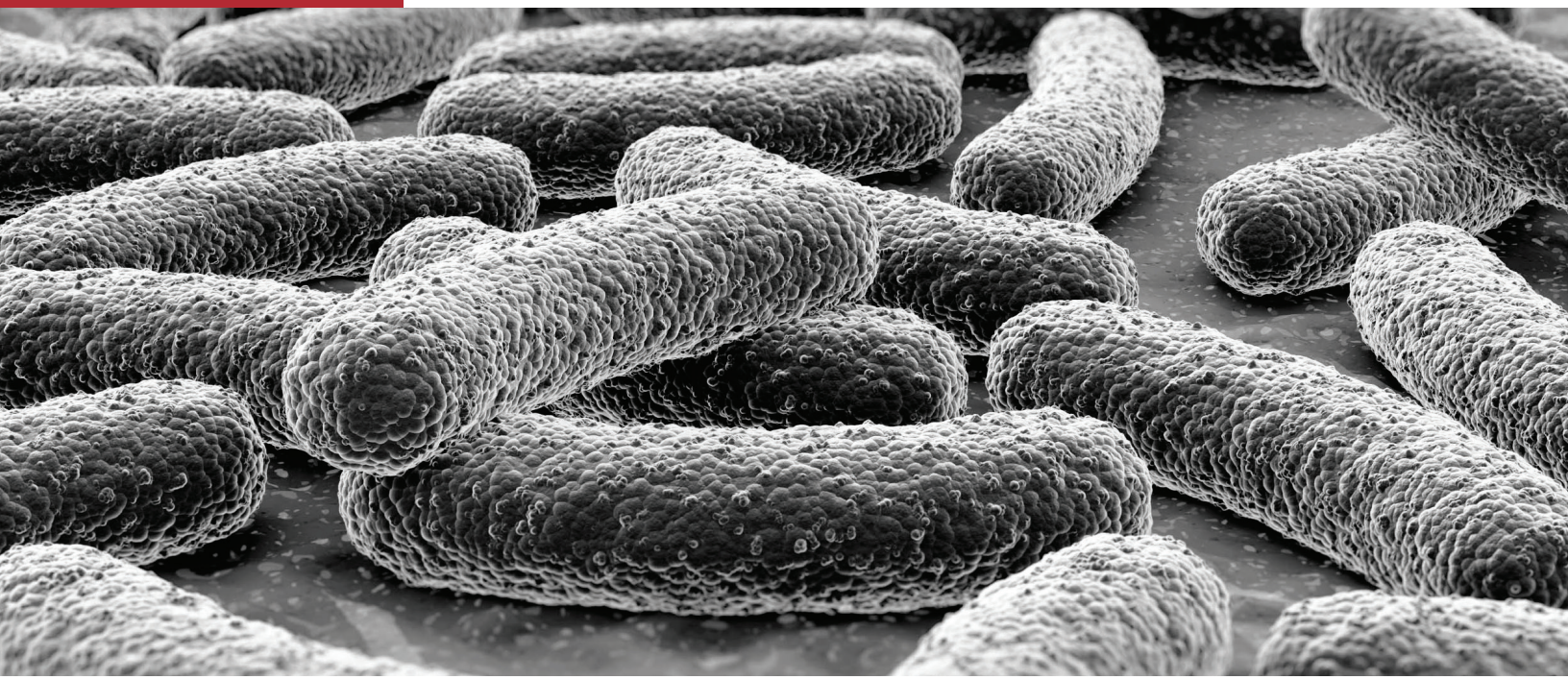
2020 TB NAAT Utilization Survey Report



APRIL 2022

APHL ASSOCIATION OF PUBLIC HEALTH LABORATORIES®

OVERVIEW

This report provides a summary of responses from the Association of Public Health Laboratories' (APHL) 2020 Tuberculosis (TB) Nucleic Acid Amplification Test (NAAT) Utilization Survey. The TB NAAT Utilization Survey was fielded to public health laboratories and examined their capacities and capabilities to perform NAATs for the direct detection of *Mycobacterium tuberculosis* complex (MTBC). The survey also explored the ability of public health laboratories to perform and bill for TB NAAT on specimens received from outside their jurisdictions. The survey was fielded January 2020 through March 2020, with responses received from 89% (n=93 out of 104) of all invited participants. The goal of this survey and report is to provide comprehensive information regarding NAAT capacity and capability within public health laboratories and, subsequently, improve public health response and clinical outcome for TB patients and their potential contacts through efficient testing practices.

INTRODUCTION

Mycobacterium tuberculosis is a pathogenic bacterium that causes TB disease and latent TB infection (LTBI). *M. tuberculosis* can cause serious, sometimes fatal, infections that are spread through the air (person-to-person) from an individual with active TB disease. The most well-known form of TB disease infects the lungs (pulmonary TB) and can result in chest pain and prolonged coughing that produces blood and/or sputum. Despite drastic declines in TB over the past several decades, more than 8,900 cases of TB were reported in the US in 2019, and up to 13 million people in the US are estimated to be living with LTBI.[1] Of note, while persons with LTBI are asymptomatic and not infectious, if untreated, 5-10% of persons with LTBI progress to active TB disease, putting the infected individual and their contacts at risk.[2]

Public health laboratories play a critical role in the diagnosis of TB in the US. By utilizing NAAT, public health laboratories can directly detect MTBC and drug resistance to rifampin, a marker for multidrug-resistant TB (MDR TB), in clinical specimens. Thus, NAAT can offer rapid and significant clinical benefits to patients and has the potential for a significant impact on public health. This efficient and accurate technology allows for earlier and more precise clinical diagnosis and treatment and supports earlier public health interventions to reduce transmission. While many public health laboratories offer NAAT for detection of MTBC from common respiratory specimens, it may be challenging to obtain NAAT for specimens not commonly validated or not included as part of a commercially available FDA-approved method. Specifically, the most difficult specimens to test are extrapulmonary specimens and non-sputum respiratory specimens, such as bronchoalveolar lavage (BAL) or bronchial wash (BW).

METHODS

In order to assess the capacities and capabilities of US public health laboratories to perform TB NAAT for diagnostic and referral specimens, APHL fielded the TB NAAT Utilization Survey to 104 member public health laboratories between January and March 2020. The 16-question, web-based survey was developed by APHL's TB Subcommittee and Infectious Disease Committee and administered through Qualtrics®. Fifty local public health laboratories and 54 state and territorial public health laboratories, including Washington, DC, received the survey. For the purposes of this report, state and territorial public health laboratories will be referred to as "state" laboratories. Recipients received survey links and instructions via email and completed the survey online. The survey requested information regarding:

- Methods performed for the detection of MTBC
- Validated specimen types, including pulmonary and extrapulmonary specimens, for each of the various methods
- Ability to receive specimens from outside jurisdictions (i.e., outside their county or state) and relevant experiences accepting these specimens
- Billing requirements and capabilities related to performing NAAT on specimens from outside jurisdictions

RESULTS

Laboratories and NAAT Methods

Ninety-three public health laboratories, including 54 state and 39 local laboratories, submitted responses (**Figure 1**). The overall response rate was 89%; state laboratories had a 100% response rate and local laboratories had a 78% response rate. Of the 93 entries, one submission was partially completed and one submission was received after the survey closed.

Of all respondents, 73 public health laboratories (78.5%) performed NAAT for the direct detection of MTBC in clinical specimens. The majority of state laboratories (n=51, 94%) performed NAAT, while just over half (n=22, 56%) of local laboratories performed NAAT (**Figure 2**). However, of note, one local laboratory performing NAAT submitted an incomplete survey and did not provide additional information regarding methods used, specimens accepted, etc. For the remainder of this report, 72 public health laboratories performing NAAT have provided data.

Figure 1. Distribution of Respondents by Laboratory Type (n=93)

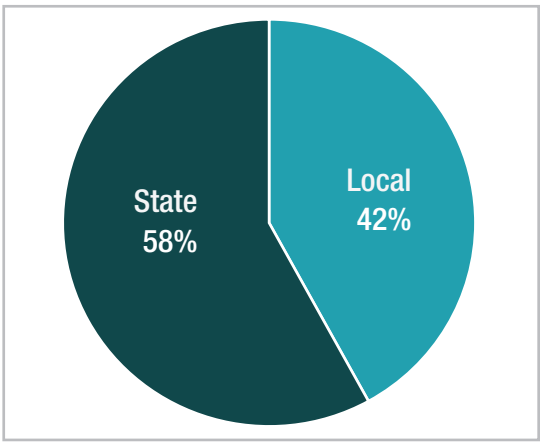
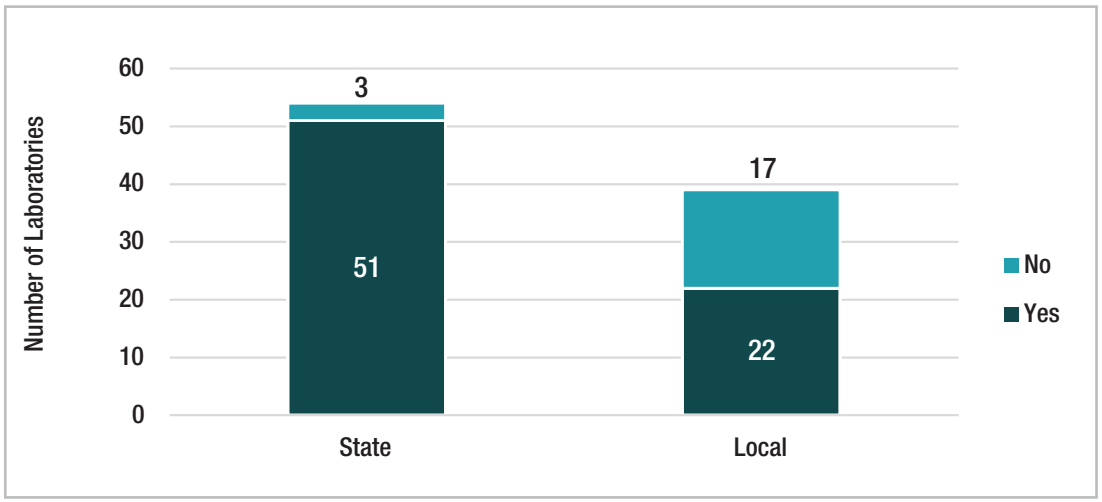


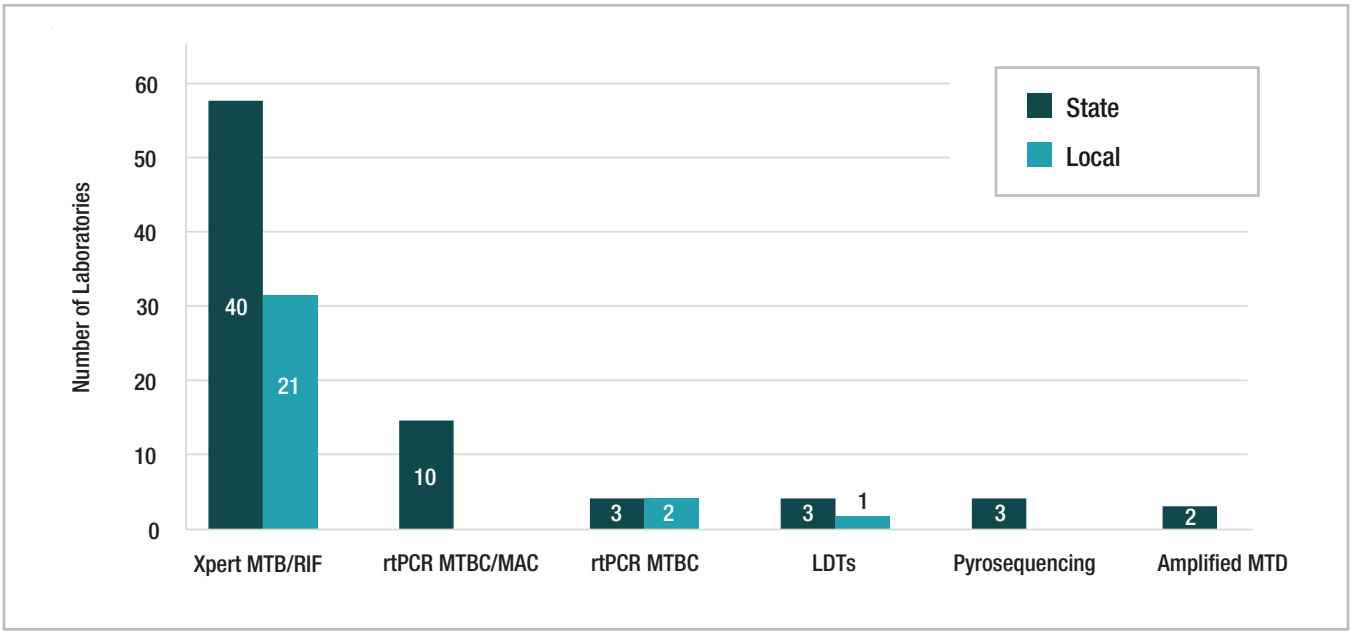
Figure 2. Public Health Laboratories Performing TB NAAT by LaboratoryType (n=93)



Respondents (n=72) were asked to identify which NAAT methods their laboratories had validated (**Figure 3**). A majority of laboratories (n=61, 85%) validated the Cepheid GeneXpert MTB/RIF® (Xpert MTB/RIF). Real-time PCR MTBC/*Mycobacterium avium* complex (rtPCR MTBC/MAC) was the second most commonly validated method and was performed by 10 laboratories (14%). Six laboratories (8%) utilized real-time PCR MTBC (rtPCR MTBC). Other PCR-based laboratory developed tests (LDTs), pyrosequencing and Hologic's Amplified Mycobacterium Tuberculosis Direct Test® (Amplified MTD) were validated by 3-4% of public health laboratories.

Of note, 12 public health laboratories (17%) offered two or more NAAT methods. All but one of these laboratories offered Xpert MTB/RIF as one of the two methods. All NAAT methods were validated by at least two state public health laboratories. Local public health laboratories validated two methods: Xpert MTB/RIF and rtPCR MTBC.

Figure 3. NAAT Methods Validated by Public Health Laboratories (n=72)

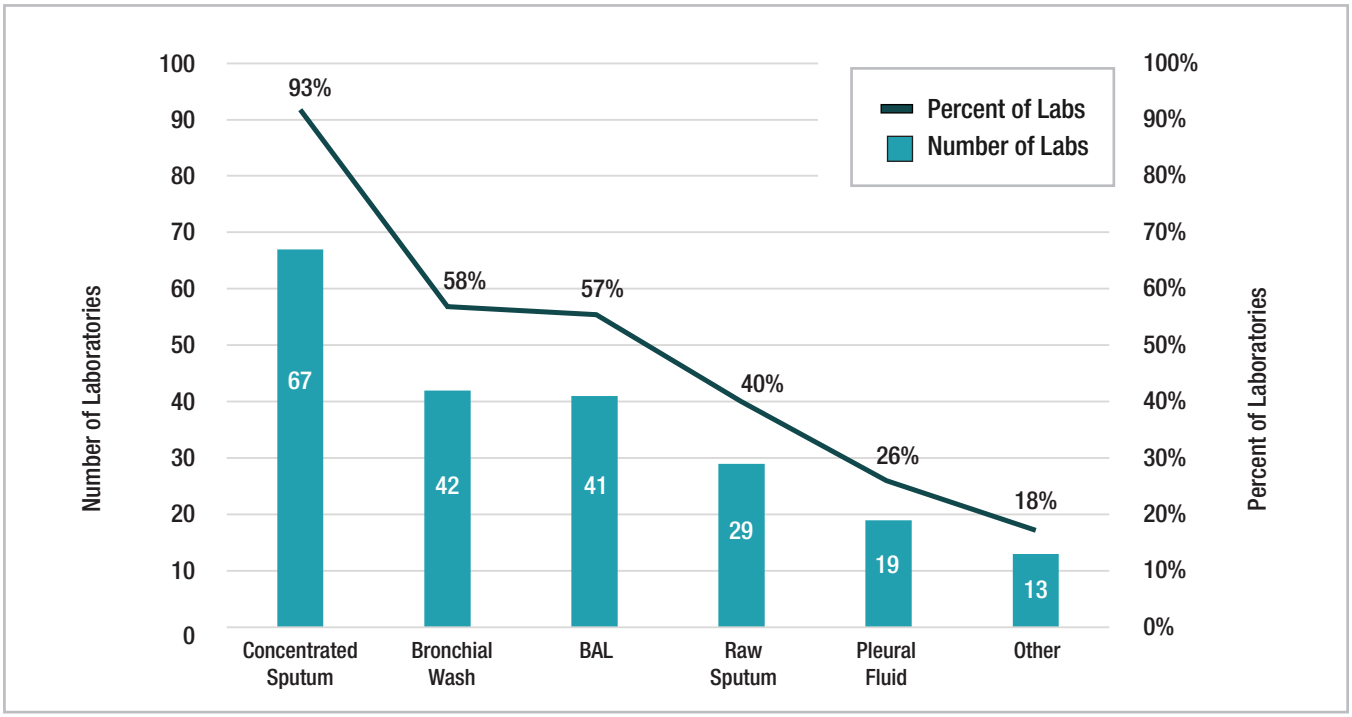


NAAT Specimen Types

For each NAAT method, laboratories were asked which pulmonary and extrapulmonary specimen types had been validated for clinical care (**Figures 4** and **5**).

Concentrated sputum was the most frequently validated pulmonary specimen among all public health laboratories (**Figure 4**). It was the most or one of the most validated specimen types for five NAAT methods: Xpert MTB/RIF, rtPCR MTBC/MAC, rtPCR MTBC, pyrosequencing and LDTs. Of note, raw sputum or concentrated sputum are the only approved specimen types for Xpert MTB/RIF. BAL and BW specimens were also commonly validated specimen types. Both specimen types were frequently validated for Amplified MTD, rtPCR MTBC and LDTs.

Figure 4. Pulmonary Specimen Types Validated by Public Health Laboratories* (n=72)

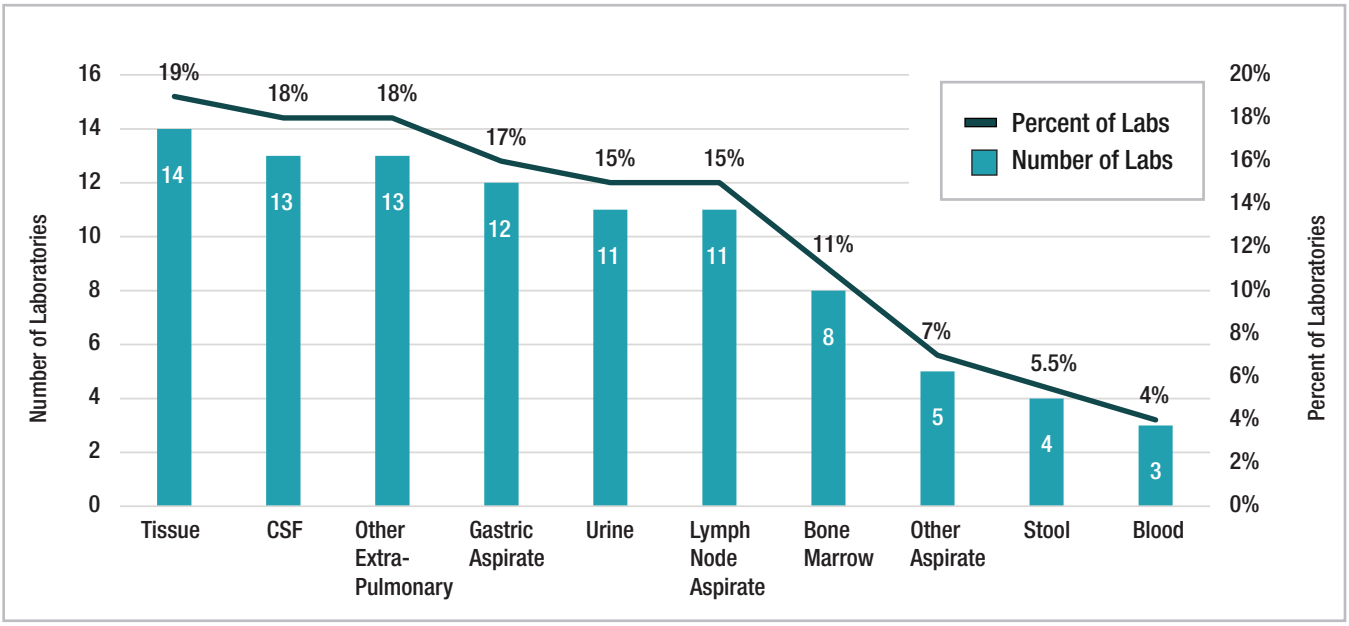


*Each laboratory is counted only once, even if they validated a specimen type for more than one method.

Among 16 public health laboratories that reported validating extrapulmonary specimens, the most validated extrapulmonary specimen types were tissue, lymph node aspirate, cerebrospinal fluid (CSF) and gastric aspirate. Bone marrow was also commonly validated for rtPCR MTBC. However, public health laboratories frequently reported not validating extrapulmonary specimens. Among the most validated methods, Xpert MTB/RIF (n=61) and rtPCR MTBC/MAC (n=10), 84% and 50% of public health laboratories did not validate extrapulmonary specimens, respectively.

Although tissue, lymph node aspirate, CSF and gastric aspirate were the most validated specimens among NAAT methods, the greatest number of public health laboratories validated tissue, "other" extrapulmonary specimens and CSF specimens (**Figure 5**). Fifty-six public health laboratories (78%) reported not validating extrapulmonary specimens for at least one method.

Figure 5. Extrapulmonary Specimen Types Validated by Public Health Laboratories (n=72)*



*Each laboratory is counted only once, even if they validated a specimen type for more than one method.

Table 1 provides an overview of each NAAT method, specifying the number of public health laboratories that have validated the methods and the specimen types that are most frequently validated. **Table 2** displays the count of laboratories that have validated specimen types by NAAT method.

Table 1. NAAT Methods and Validated Specimen Types*

NAAT Method	Validated Pulmonary Specimens	Validated Extrapulmonary Specimens
Xpert MTB/RIF (n=61)	• Any Specimen Type: 100% • Most Common: Concentrated Sputum, n=56	• Any Specimen Type: 20% • Most Common: Tissue, n=10
Amplified MTD (n=2)	• Any Specimen Type: 100% • Most Common: Bronchial Wash, BAL, n=2	• Any Specimen Type: 50% • Most Common: Pure Culture from Suspect Colonies, n=1
rtPCR MTBC/MAC (n=10)	• Any Specimen Type: 100% • Most Common: Concentrated Sputum, BAL, n=9	• Any Specimen Type: 70% • Most Common: Tissue, CSF, Gastric Aspirate, Lymph Node Aspirate, n=4
rtPCR MTBC (n=6)	• Any Specimen Type: 100% • Most Common: Concentrated Sputum, Bronchial Wash, BAL, n=6	• Any Specimen Type: 50% • Most Common: Tissue, Bone Marrow, Lymph Node Aspirate, n=3
Pyrosequencing (n=3)	• Any Specimen Type: 100% • Most Common: Concentrated Sputum, n=3	• Any Specimen Type: 66% • Most Common: Tissue, CSF, Lymph Node Aspirate, Gastric Aspirate, n=2
Other LDTs (n=3)	• Any Specimen Type: 100% • Most Common: Concentrated Sputum, Bronchial Wash, BAL, Pleural Fluid, n=3	• Any Specimen Type: 75% • Most Common: Tissue, CSF, Lymph Node Aspirate, n=3

*Any Specimen Type: the percent of labs that have validated and are performing this method on any specimen type

Most Common: the most common specimen type(s) validated for this method, n=the number of laboratories that have validated the most common specimen type(s)

Table 2. Count of Public Health Laboratories that have Validated Specimen Types by NAAT Methods

		NAAT Methods					
		Xpert MTB/RIF n=61	Amplified MTD, n=2	rtPCR MTBC/ MAC, n=10	rtPCR MTBC, n=6	Pyro-sequencing, n=3	LDT, n=3
Pulmonary	Raw Sputum	24 (39%)	1 (50%)	3 (30%)	3 (50%)	0 (0%)	1 (33%)
	Concentrated Sputum	56 (92%)	1 (50%)	9 (90%)	6 (100%)	3 (100%)	3 (100%)
	Bronchial Wash	28 (46%)	2(100%)	8 (80%)	6 (100%)	2 (67%)	3 (100%)
	BAL	27 (44%)	2 (100%)	9 (90%)	6 (100%)	2 (67%)	3 (100%)
	Pleural Fluid	10 (16%)	1 (50%)	4 (40%)	5 (83%)	2 (67%)	3 (100%)
	Other	7 (11%)	1 (50%)	2 (20%)	1 (17%)	1 (33%)	0 (0%)
	None	1 (2%)	0 (0%)	1 (10%)	0 (0%)	0 (0%)	0 (0%)
Extrapulmonary	Urine	6 (10%)	0 (0%)	3 (30%)	2 (33%)	1 (33%)	2 (66%)
	Tissue	10 (16%)	0 (0%)	4 (40%)	3 (50%)	2 (67%)	3 (100%)
	Stool	3 (5%)	0 (0%)	1 (10%)	2 (33%)	0 (0%)	0 (0%)
	Blood	1 (2%)	0 (0%)	1 (10%)	1 (17%)	1 (33%)	0 (0%)
	CSF	7 (11%)	0 (0%)	4 (40%)	2 (33%)	2 (67%)	3 (100%)
	Bone Marrow	5 (8%)	0 (0%)	3 (30%)	3 (50%)	1 (33%)	1 (33%)
	Gastric Aspirate	7 (11%)	0 (0%)	4 (40%)	2 (33%)	2 (67%)	2 (66%)
	Lymph Node Aspirate	7 (11%)	0 (0%)	4 (40%)	3 (50%)	2 (67%)	3 (100%)
	Other Aspirate	3 (5%)	0 (0%)	1 (10%)	1 (17%)	1 (33%)	0 (0%)
	Other Extrapulm.	5 (8%)	1 (50%)	3 (30%)	2 (33%)	1 (33%)	2 (66%)
	None	50 (82%)	1 (50%)	3 (30%)	3 (50%)	1 (33%)	0 (0%)

Specimens Submitted from Outside Jurisdictions

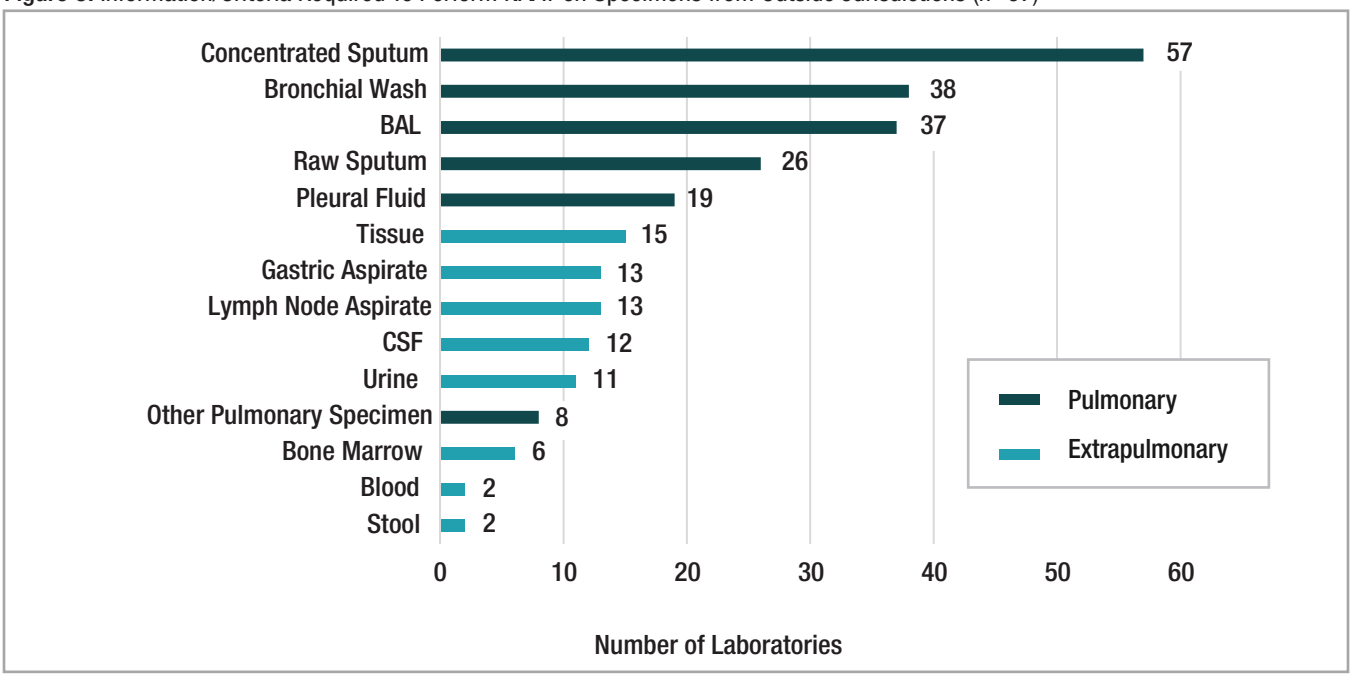
Public health laboratories were asked to indicate if they accepted specimens from outside their jurisdictions and, if so, which specimen types they accepted and whether they were able to charge submitters for NAAT services (**Figure 6**).

Out of 72 responding laboratories, over 90% of public health laboratories (n=67) indicated that they would be able to perform NAAT on specimens from outside their jurisdictions. Of these laboratories that would accept non-jurisdictional specimens:

- 37 would accept specimens without other requirements or special circumstances
- 14 would require an agreement in place with the submitters
- 12 would accept specimens under special circumstances
- 4 indicated that “other” conditions would need to be met, but that accepting specimens from outside jurisdictions would be feasible

Approximately 7% of public health laboratories (n=5) were unable to receive and perform NAAT on specimens from outside their jurisdictions.

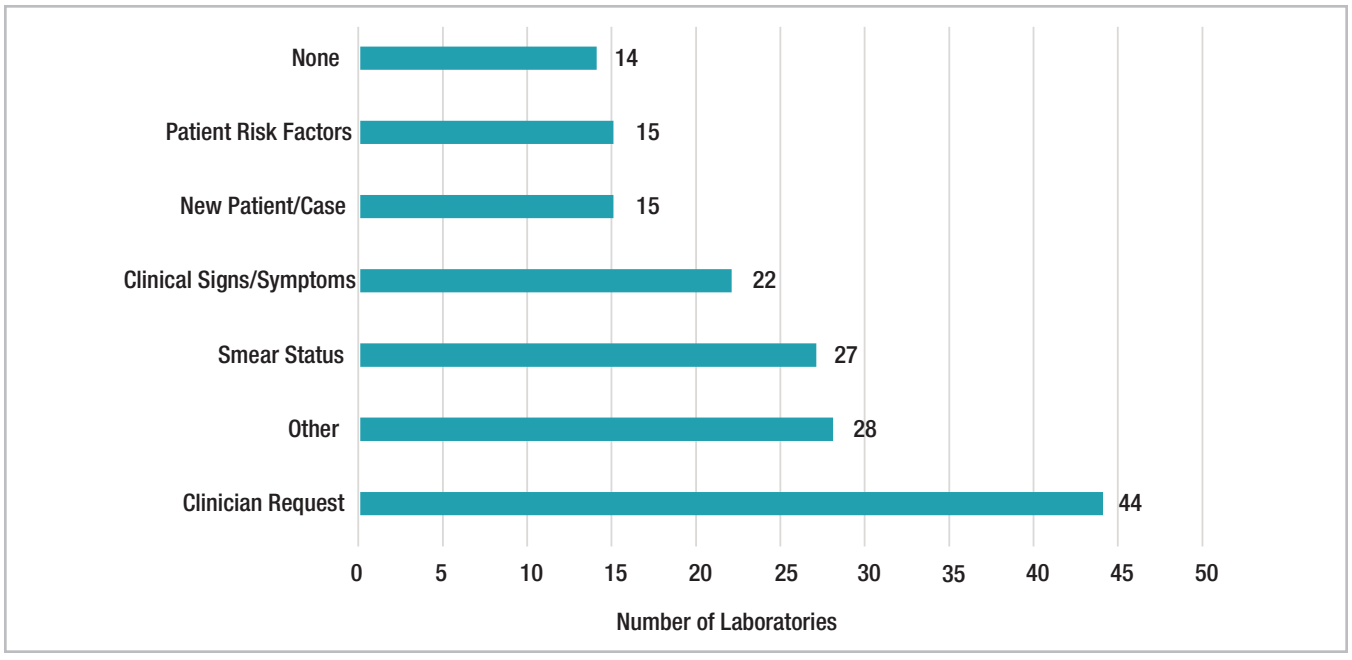
Figure 6. Information/Criteria Required To Perform NAAT on Specimens from Outside Jurisdictions (n=67)



Concentrated sputum, bronchial wash and BAL were the most frequently accepted specimen types. Laboratories were more likely to accept pulmonary specimen types than extrapulmonary specimen types. "Other" accepted specimen types included lung biopsy (tissue), isolates, peritoneal fluid, other aspirates and culture growth.

In order to accept pulmonary specimens from outside jurisdictions, laboratories frequently required additional information before processing (**Figure 7**). Nearly two-thirds of all laboratories (n=44) required a clinician request; approximately 40% of all laboratories (n=27) required a smear status and/or "other" information (n=29). These requirements were also the most frequently required criteria for extrapulmonary specimens. "Other" requirements frequently cited were involvement or approval from the local TB Control program.

Figure 7. Information/Criteria Required to Perform NAAT on Specimens from Outside Jurisdictions (n=67)



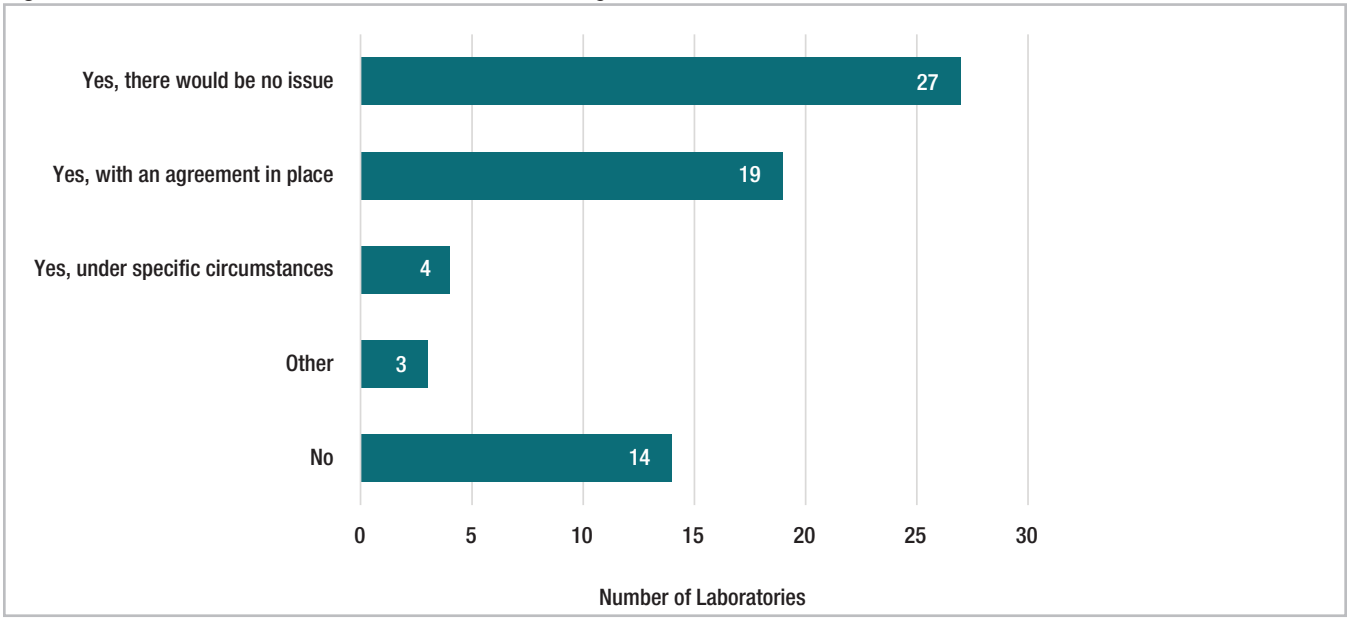
Public health laboratories may also implement a fee to recuperate costs associated with performing NAAT. Nearly 80% of laboratories (n=53 out of 67) that accepted TB specimens from outside their jurisdictions could charge a fee for their services (**Figure 8**). Of these laboratories:

- 51% could charge for NAAT services with no additional documentation
- 36% indicated that they must have an agreement already in place
- 13% could only charge under specific circumstances or when "other" conditions were met

Approximately one-fifth of laboratories (n=14) that could accept TB specimens from outside their jurisdictions could not or did not charge for NAAT services.

Forty-eight out of 53 public health laboratories that could charge this fee for testing provided a brief description of their relevant experience; 17 laboratories had limited or no experience billing outside their jurisdiction while 31 laboratories had routine experience billing for these specimens.

Figure 8. Number of Public Health Laboratories Able to Charge Outside Jurisdictions for TB NAAT



CONCLUSION

Direct detection of MTBC by NAAT offers earlier and more precise diagnosis than growth-based methods. In this survey of US public health laboratories, 93 responses were received, and 78.5% of laboratories utilized TB NAAT. Broken down by jurisdiction type, 94% of state laboratories performed NAAT for direct detection, but only 56% of local laboratories offered this testing service. A majority of public health laboratories performed TB NAAT on concentrated sputum, which was expected as this is a common specimen type and one of the only approved specimen types for the Xpert MTBC/RIF. Less than 60% performed the same testing on other respiratory specimens and less than 25% validated these methods to provide clinical results for extrapulmonary specimens.

The majority of public health laboratories, 85%, validated the Xpert MTBC/RIF. rtPCR MTBC/MAC and rtPCR MTBC were validated in 22% of laboratories. Other LDTs, pyrosequencing and Amplified MTD were validated by a smaller group of 3–4% of laboratories. Of note, 16% of public health laboratories offered two or more NAAT methods. Additional conversations to better understand the decisions to offer two or more methods may be of interest. It is likely that cost, turnaround time and specimen types played a role in decision making.

Jurisdictional level data was shared with the TB Centers of Excellence (where approval was given by the laboratory in the survey) in order to increase awareness of public health laboratory capacity for NAAT. Moving forward, the data examined in this report will benchmark NAAT utilization and help improve partnerships and collaboration related to TB NAAT.

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ASSOCIATION OF PUBLIC HEALTH LABORATORIES

The Association of Public Health Laboratories (APHL) works to strengthen laboratory systems serving the public's health in the US and globally. APHL's member laboratories protect the public's health by monitoring and detecting infectious and foodborne diseases, environmental contaminants, terrorist agents, genetic disorders in newborns and other diverse health threats.

This project was 100% funded with federal funds from a federal program of $1,629,896. This publication was supported by Cooperative Agreement #NU60OE000104-02 from the US Centers for Disease Control and Prevention (CDC). Its contents are solely the responsibility of the authors and do not necessarily represent the official views of CDC.

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