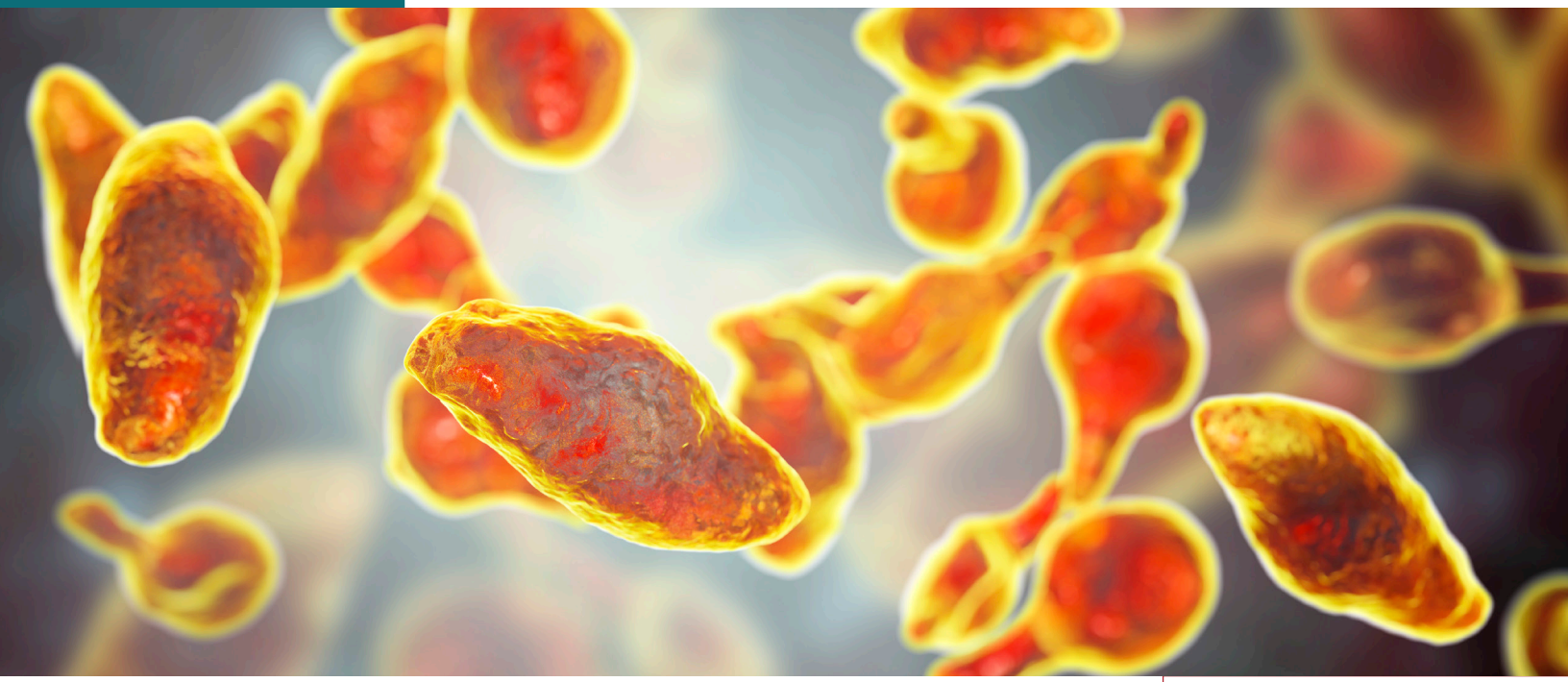
2020 *Mycoplasma genitalium* Laboratory Testing Survey Report



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APHL ASSOCIATION OF PUBLIC HEALTH LABORATORIES®

BACKGROUND

Mycoplasma genitalium is an emerging sexually transmitted disease (STD). Although frequently asymptomatic, infection has been strongly associated with non-gonococcal urethritis in men and tentatively associated with pelvic inflammatory disease, cervicitis and adverse pregnancy outcomes in women.[1–5] Prevalence estimates of *M. genitalium* in the US have varied depending on the study and population. Estimates range from 1% among young adults in a longitudinal study to 19% among patients at STD clinics.[6–9]

M. genitalium has rapidly acquired resistance to macrolide and some quinolone antibiotics. Estimates of the prevalence of drug resistance in circulating strains range from approximately 18% to greater than 66%, depending on geography, sex and population.[7,10–12] The high prevalence of drug resistant strains and the lack of knowledge surrounding the natural history of the infection prompted the US Centers for Disease Control and Prevention (CDC) to name multidrug-resistant *M. genitalium* on its 2019 Antibiotic Threat Report's Watch List.[13] Despite the potentially high prevalence and growing resistance to first line antibiotics, there are few diagnostic tests available in the US and currently no screening recommendations. The Food and Drug Administration (FDA) granted clearance to the Hologic® Aptima *Mycoplasma genitalium* assay in January 2019 and to the Roche cobas® TV/MG assay in May 2019.[14,15]

This survey aimed to assess the status of testing availability in the US and gather relevant information regarding the future of *M. genitalium* testing in the US. Specifically, this survey focused on *M. genitalium* prevalence testing, clinical testing and drug susceptibility testing. The survey also assessed the barriers to bringing testing in-house, gaps in information that could influence testing decisions and future plans regarding testing.

METHODOLOGY

Sample

A total of 110 APHL member laboratories were invited to participate in this survey. However, two laboratories were excluded due to self-reporting that STD testing of this kind was irrelevant to their laboratories. Thus, 108 APHL member laboratory responses will be evaluated. The survey was sent to local (n=55) and state/territorial (n=55) public health laboratories (PHLs). For the purposes of this report, state and territorial public health laboratories will be referred to as "state" laboratories. State PHLs included all 50 states and the District of Columbia, as well as Guam, Northern Mariana Islands, Puerto Rico and the US Virgin Islands.

Survey Development and Administration

This survey was launched on March 31, 2020. Survey links were emailed to PHL directors and, when contact information was available, to a second relevant contact within the PHL, such as microbiology supervisors and STD contacts. Survey reminders were emailed to non-respondents on April 20 and 21, 2020. The survey was programmed using SurveyMonkey and data was collected from March 31, 2020 through May 1, 2020.

RESULTS

Sixty-five state and local PHLs responded to the survey, producing a 60.2% (out of 108) response rate. Thirty-nine of 55 state PHLs (70.9%) and 26 of 53 local PHLs (49.1%) completed the questionnaire. Nine PHLs submitted incomplete surveys without their contact information or laboratory name and were not included in the analyses. This survey was launched during the COVID-19 pandemic response, which likely contributed to the low response rate from APHL members compared to similar APHL surveys.

M. genitalium Prevalence Studies

Overall, as of May 2020, 36.9% of the PHLs surveyed will have assessed or will have begun assessing prevalence within the next year. Twenty-two state PHLs (56.4%) and 19 local PHLs (73.1%) have no plans to assess *M. genitalium* prevalence in the near future (Table 1).

Table 1. Status of *M. genitalium* Prevalence Studies.

Prevalence Study Status	Total (n=65) n (%)	State (n=39) n (%)	Local (n=26) n (%)
Completed	8 (12.3%)	4 (10.3%)	4 (15.4%)
In progress	3 (4.6%)	3 (7.7%)	0 (0.0%)
Future plans	13 (20.0%)	10 (25.6%)	3 (11.5%)
No plans	41 (63.1%)	22 (56.4%)	19 (73.1%)

M. genitalium Clinical Testing

Four local PHLs (6.1%) out of the 65 respondents are currently offering clinical testing for *M. genitalium* and had no plans to change their testing practices in the next 12 months (Table 3). Three of these laboratories had previously evaluated the prevalence in their jurisdiction and are utilizing the Hologic® Aptima *Mycoplasma genitalium* assay. Two laboratories indicated that a clinical criterion (patients must be symptomatic) must be met in order to submit specimens for testing. All four PHLs accepted urine (male and female) and clinician-collected vaginal swabs for testing. Additionally, endocervical specimens, rectal swabs, urethral swabs and self-collected vaginal swabs were each accepted at two laboratories. One PHL accepted penile meatal swabs. The four PHLs were asked to indicate the most common specimen type for male and female patients (Table 2).

Table 2. Most Commonly Submitted Specimen Types.

	Female Specimens	Male Specimens
Laboratory 1	Urine	Urine
Laboratory 2	Urine	Urine
Laboratory 3	Urine	Rectal Swab
Laboratory 4	Vaginal Swab	Urine

Two additional laboratories indicated they refer clinical specimens to other laboratories for *M. genitalium* testing. No PHLs performed or referred specimens for drug susceptibility testing.

Eight state and three local PHLs have plans to implement clinical testing within the next 12 months. If all 11 laboratories start performing clinical testing, the total number of PHLs offering *M. genitalium* testing will nearly quadruple from 6.1% to 23.1%. However, due to the COVID-19 pandemic response these implementations may have been delayed and will need to be re-assessed

Approximately 33% of PHLs (n=61) not currently testing expressed an interest in implementing clinical *M. genitalium* testing, but had no plans to do so in the next 12 months. Forty-nine percent (n=61) not currently testing indicated they had no plans to implement testing in the near future (Table 3).

Table 3. Status of *M. genitalium* Clinical Testing.

Clinical testing	Total (n=65) n (%)	State (n=39) n (%)	Local (n=26) n (%)
Currently performing	4 (6.1%)	0 (0.0%)	4 (15.4%)
Plan to implement	11 (16.9%)	8 (20.5%)	3 (11.5%)
Interested, but no plans to implement	20 (30.8%)	14 (35.9%)	6 (23.1%)
No plans to implement	30 (46.2%)	17 (43.6)	13 (50.0%)

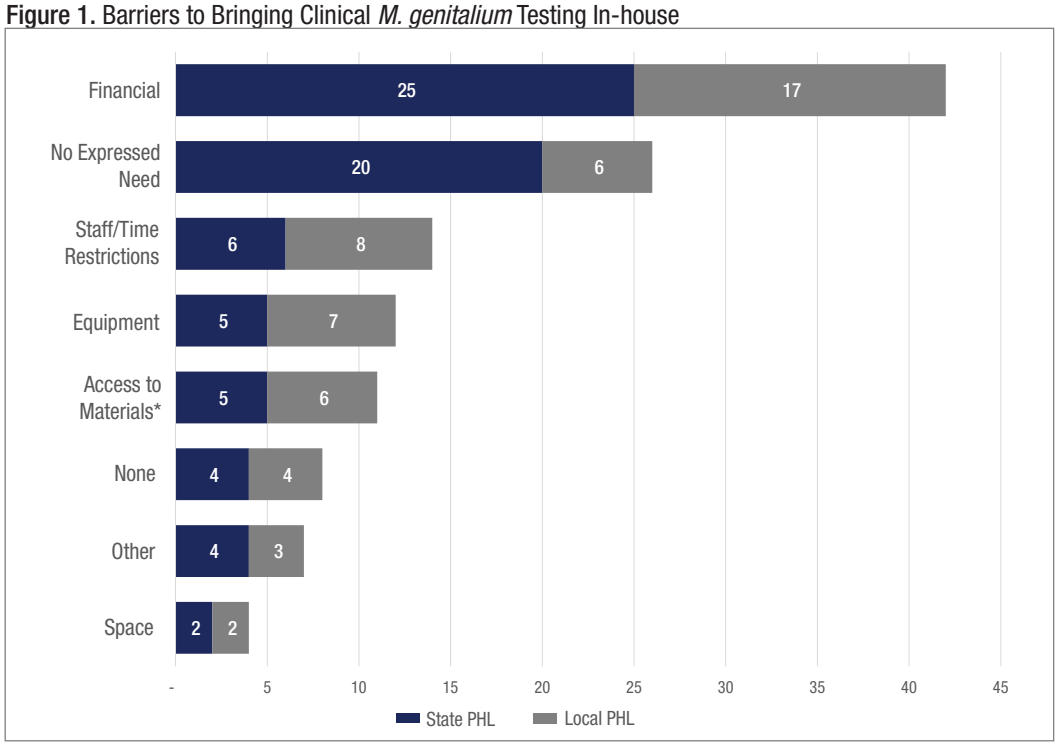
Barriers to Testing

All PHLs were asked to report the barriers to bringing clinical testing in-house and could select multiple barriers (Figure 1). See Question 14 in Appendix A for offered options.

Sixty-four PHLs responded, selecting as many barriers as were appropriate, and 124 responses were recorded. Overall, laboratories most frequently indicated finances (n=42, 65.6%), no expressed need for testing (n=26, 40.6%) and staff and/or time restrictions (n=14, 21.9%) as barriers to bringing testing in-house. State PHL (n=39) responses mirrored these results. Local PHLs (n=25), however, reported finances, staff and/or time restrictions and lack of equipment most frequently as barriers.

In this study, "no expressed need" refers to the PHL not having received any requests to implement testing, or any demand from submitters or the PHL itself to implement testing. Laboratories that selected "None" on the survey indicated that there are no barriers restricting their ability to bring testing in-house. Three of the eight PHLs that reported no barriers to bringing testing in-house have already implemented clinical testing.

Figure 1. Barriers to Bringing Clinical *M. genitalium* Testing In-house



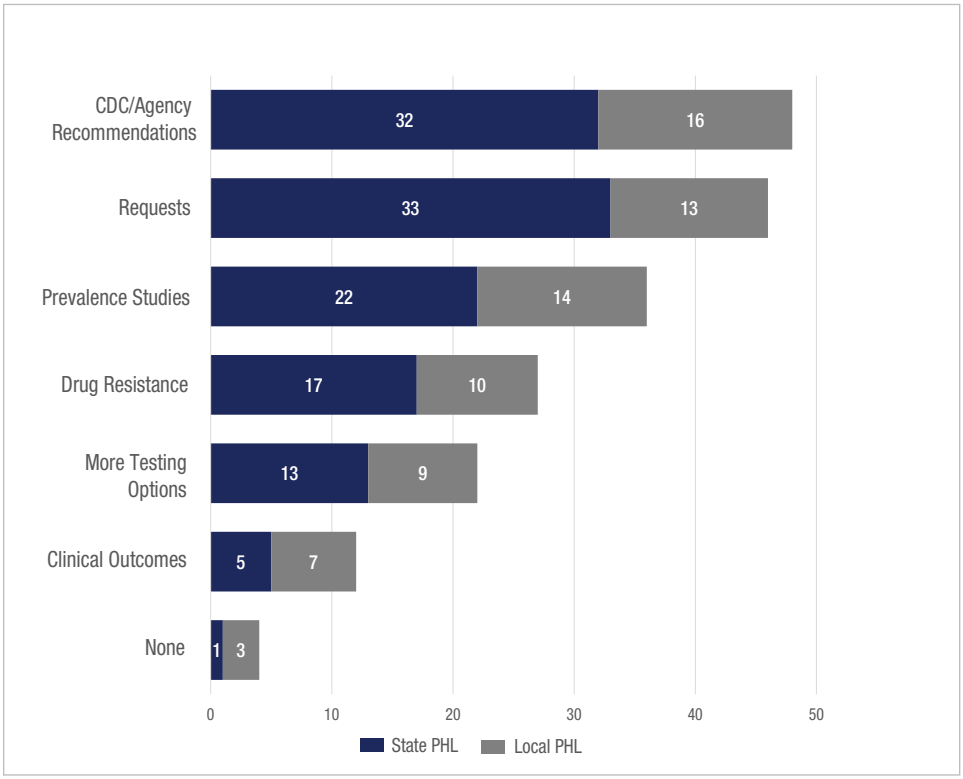
*Access to materials for validating/verifying *M. genitalium* assays

Additional Information/Resources

All PHLs were asked to indicate if any additional information/resources/recommendations would inform or change their decision with regard to providing *M. genitalium* testing services. See Question 15 in Appendix A for the offered options.

Sixty-four PHLs responded and 195 responses were collected. Recommendations from CDC or other agencies was the most common response (n=48, 75.0%), followed closely by requests from jurisdictional epidemiologists or program directors (n=46, 71.9%) and prevalence studies indicating the need for testing services in the jurisdiction (n=36, 56.3%) (Figure 2).

Figure 2. Additional Information That Would Inform Bringing Clinical Testing In-house



Future Technology

Each PHL was asked to select the technology/method their laboratory would be most interested in evaluating or bringing in house, if it became available. See Question 19 in Appendix A for a list of options.

Sixty PHLs responded, and over half (55.0%) indicated that they are most interested in a *M. genitalium* NAAT with the ability to detect molecular markers for antibiotic susceptibility. One-quarter (25.0%) indicated that their preferred future technology or method would be an STD panel that included *M. genitalium*. The remaining PHLs were most interested in:

- A molecular assay for detection of antibiotic resistance/susceptibility markers (13.0%)
- FDA-cleared *M. genitalium* NAAT from a different manufacturer (5.0%)
- A technology not listed (1.7%).

Five PHLs specified the STD panel on which they would want *M. genitalium* included. All laboratories indicated *Neisseria gonorrhoeae* and *Chlamydia trachomatis* on the panel; three indicated *Trichomonas vaginalis* should also be included; and one included herpes simplex virus as well.

CONCLUSIONS

This survey launched during the COVID-19 pandemic, when PHLs were overwhelmed by response efforts. Thus, there was a lower response rate compared to typical APHL surveys, with 60.2% of PHLs completing the survey.

As of May 2020, eight (12.3%) PHLs have completed prevalence testing in their jurisdiction, three (4.6%) are in the process of assessing prevalence and 13 (20.0%) have plans to assess prevalence in the next 12 months. Four (6.1%) PHLs currently perform clinical testing, 11 (16.9%) plan to implement testing within the next 12 months and 20 (30.8%) expressed interest in clinical testing, but had no plans to implement in the near future. While approximately half of the PHLs not currently performing clinical testing have no plans to begin an *M. genitalium* testing program, almost 37% of the laboratories surveyed will have assessed or will be assessing *M. genitalium* prevalence in their jurisdictions during the next calendar year. Additionally, if PHLs with plans to bring testing in-house are able to implement testing as planned, then PHLs performing clinical testing will nearly quadruple from approximately 6.1% to 23.1%.

Both state and local PHLs reported the biggest barrier to bringing *M. genitalium* testing in-house to be financial barriers, which is common and expected for a newly-cleared test and lack of national screening recommendations. Lack of expressed need and staff/time restrictions were the second most important barriers respectively. Additional information that would inform decisions regarding in-house testing services were similar between state and local PHLs. The most indicated as factors impacting decision making were CDC or other agency recommendations, jurisdictional prevalence studies indicating a need for testing services and requests from jurisdictional epidemiologists or program directors. When asked about future technology, PHLs expressed the most interest in evaluating and/or bringing in-house *M. genitalium* NAAT with the ability to detect molecular markers for antibiotic susceptibility and an STD panel that included *M. genitalium*.

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APPENDIX A: *MYCOPLASMA GENITALIUM* LABORATORY TESTING SURVEY

APHL invites you to participate in a short survey on *Mycoplasma genitalium* testing practices in order to capture information on current *M. genitalium* testing capacity and capabilities in US public health laboratories.

Mycoplasma genitalium is associated with various clinical symptoms and complications. In men, infection is strongly associated with non-gonococcal urethritis and in women, although commonly asymptomatic, infection is linked to cervicitis, pelvic inflammatory disease and infertility among other conditions. Large gaps in knowledge still exist though, including the long term implications of *M. genitalium* infection and substantial epidemiologic data. Additionally, with up to 50% of infections resistant to macrolide antibiotics, the CDC's 2019 Antibiotic Resistance Threats in the US named drug-resistant *Mycoplasma genitalium* on its "Watch List." While there are a few FDA-cleared diagnostic assays available, there is limited and variable data on prevalence, no screening guidelines and no commercially available method for detecting resistance in the US.

The survey should take less than 20 minutes to complete and may be completed by the laboratory director, microbiology supervisor or relevant staff member.

1. Has your laboratory performed any testing to evaluate the prevalence of M. genitalium in your jurisdiction?
   - Yes, a limited study was conducted (go to Q2)
   - Yes, a study is ongoing (go to Q2)
   - No (go to Q4)
2. Briefly describe your study design (male vs female, symptomatic vs asymptomatic, specimen types, etc.), any findings and any plans for what the data will be used for (i.e. to determine if you will offer testing in the future, publication, etc.) (go to Q3)
3. Would you be willing to share more details with APHL if we contacted you directly? (go to Q5)
   - Yes
   - No
4. Does your laboratory have any plans to evaluate the prevalence of M. genitalium in your jurisdiction in the next 12 months? (go to Q5)
   - Yes, please describe
   - No

   Please describe your plans to evaluate the prevalence of M. genitalium in your jurisdiction in the next 12 months: (Comment box)
5. Does your laboratory currently provide clinical diagnostic testing for M. genitalium?
   - Yes (go to Q6)
   - No (go to Q12)
6. Which test(s) does your laboratory provide for the clinical diagnosis of M. genitalium? Select all that apply (go to Q7)
   - Aptima Mycoplasma genitalium Assay (Hologic, Inc)
   - cobas® TV/MG (Roche)
   - Other, please specify
7. Are there any clinical criteria requirements for submitting specimens for diagnostic testing?
   - Yes (go to Q8)
   - No (go to Q9)

8. Which clinical criteria are required for submitting specimens for M. genitalium diagnostic testing? Select all that apply (go to Q9)

- Patient must be symptomatic
- Patient not responsive to prior treatment
- Patient must have had contact with an individual with a known M. genitalium infection
- Other, please specify

9. Which specimen types are accepted for diagnostic M. genitalium testing in your laboratory? Select all that apply (go to Q10)

- Endocervical specimen
- Endometrial biopsy
- Oropharyngeal/throat swab
- Penile meatal swab
- Rectal swab
- Urethral swab (Male)
- Urine (Female)
- Urine (Male)
- Vaginal swab (Clinician-Collected)
- Vaginal swab (Self-Collected)
- Other, please specify

10. Of the specimen types your laboratory accepts, which is the most common type received for M. genitalium testing on FEMALE specimens? Select one (go to Q11)

- Endocervical specimen
- Endometrial biopsy
- Oropharyngeal/throat swab
- Rectal swab
- Urine
- Vaginal swab (Clinician-Collected)
- Vaginal swab (Self-Collected)
- Other, please specify

11. Of the specimen types your laboratory accepts, which is the most common type received for M. genitalium testing on MALE specimens? Select one (go to Q13)

- Penile meatal swab
- Oropharyngeal/throat swab
- Rectal swab
- Urethral swab
- Urine
- Other, please specify

12. Does your laboratory have plans to begin offering diagnostic testing services for M. genitalium in the next 12 months? (go to Q14)

- Yes, please specify which test
- No plans to begin testing at this time, but interested in offering diagnostic M. genitalium testing in the future
- No plans to begin testing at this time

Please specify which test you plan to begin offering: (Comment box)

13. Is your laboratory considering or planning to change M. genitalium testing practices in the next 12 months? Select all that apply (go to Q14)

- Add test to be performed on site, please specify
- Eliminate M. genitalium testing services, please specify
- Modify an existing test, please specify
- Modify patient criteria for M. genitalium diagnostic testing
- Refer samples to another laboratory, please specify
- Refer positive samples for susceptibility testing, please specify
- Replace existing test, please specify
- Other, please specify
- No changes

Please expand on your answer if specified: (Comment box)

14. What barriers, if any, are there to bringing diagnostic M. genitalium testing services in-house? Select all that apply (go to Q15)

- Access to materials for validation/verification
- Equipment
- Financial
- No expressed need at this time
- Space
- Staff and/or time restrictions
- Other, please specify
- None

15. What additional information or resources would inform your laboratory's decision regarding providing M. genitalium testing services? Select all that apply (go to Q16)

- More evidence on clinical outcomes of M. genitalium
- More information on drug resistance in M. genitalium
- More testing options (i.e. available on different platform, more affordable options, etc.)
- Prevalence studies indicating need for testing services in your jurisdiction
- Recommendations from CDC or other agency
- Requests from jurisdictional epidemiologists or program directors
- Other, please specify

16. Does your laboratory currently refer M. genitalium specimens to another laboratory for testing? (go to Q17)

- Yes, for clinical specimens only
- Yes, for clinical specimens and for surveillance and/or prevalence testing
- Yes, for surveillance and/or prevalence testing only
- No

17. Does your laboratory currently perform or refer positive M. genitalium samples for detection of resistance markers?

- Yes, our laboratory performs testing for the detection of resistance markers (go to Q18)
- Yes, our laboratory refers samples to another laboratory for detection of resistance markers (go to Q19)
- No (go to Q19)

18. Which method(s) does your laboratory utilize for detection of drug resistance in M. genitalium samples? Select all that apply (go to Q19)
    - Detection of molecular markers of antibiotic susceptibility/resistance (i.e. NAAT or sequencing-based method)
    - Other, please specify
19. If a new testing technology were to become available in the future, which technology would your laboratory be most interested in evaluating or bringing in-house?
    - M. genitalium NAAT with detection of molecular markers for antibiotic susceptibility/resistance (i.e. both results available from single test or performed in parallel)
    - Molecular assay for detection of antibiotic resistance/susceptibility markers (i.e. method performed on M. genitalium positive samples only)
    - FDA-cleared M. genitalium NAAT from a different manufacturer, please specify manufacturer
    - Inclusion of M. genitalium on panel with other STDs, please specify ideal combination of pathogens

    Please expand on your answer if specified: (Comment box)

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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.

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