Request for Proposals (RFP): National Public Health Laboratory (PHL) Drug Susceptibility Testing (DST) Reference Center for *Mycobacterium tuberculosis* (MTBC)

Application Due date: September 27, 2024

Submit to: Sarah Buss, Manager of HIV, Viral Hepatitis, STD and TB (sarah.buss@aphl.org)

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Summary

The Association of Public Health Laboratories (APHL), in cooperation with the US Centers for Disease Control and Prevention (CDC) Division of Tuberculosis Elimination (DTBE), is seeking to recompete the National Public Health Laboratory (PHL) Drug Susceptibility Testing (DST) Reference Center for *Mycobacterium tuberculosis* (MTBC) providing services for PHLs with low to moderate incidences of MTBC. APHL is seeking to identify one (1) state or local public health laboratory to serve as the Reference Center. This Reference Center will serve as an extension of the CDC DTBE Laboratory Branch and provide services that are complementary to those at CDC. Services provided for PHLs with lower volumes of DST (<50 isolates per year) will include:

1) molecular detection of drug resistance
2) growth-based first-line and second-line DST, as applicable;
3) submission of whole genome sequencing data to CDC for national molecular surveillance purposes

Background

Performing DST is technically demanding; maintaining proficiency in performing DST and interpreting results is critical to ensuring testing accuracy. In recent data from CDC's Model Performance Evaluation Program for DST of MTBC, 77% (46/60) of participants were PHLs.[1] Thirty-seven percent (22/60) of the particpating laboratories reported performing ≤50 DST per year.[1] CDC currently recommends referral testing for laboratories performing DST for fewer than 50 isolates per year.[2]

Second-line DST is critical when isolates are resistant to rifampin (RMP) or any two first-line drugs and in situations where additional information is needed to design an effective treatment regimen (e.g., drug intolerance). Second-line DST methods are not standardized and currently, there are no FDA-cleared assays for this purpose. Therefore, laboratories may choose to follow established consensus guidelines (e.g., CLSI or WHO) or evaluate their own in-house test concentrations and interpretive criteria. In the National TB Laboratory Aggregate Report, only 21% (12/58) of PHLs performed second-line DST while other PHLs referred second-line DST to another laboratory for testing.

Molecular detection of mutations associated with drug resistance provides rapid results within hours or days versus the weeks required for growth-based DST. Performing molecular testing such as sequencing requires technical expertise and extensive experience in interpreting test results. Laboratories performing this testing must have competent staff, be able to provide consultative services, and continually adapt to advancements in the field. These requisites may limit the number of laboratories providing molecular testing for drug resistance, however, advancements in the predictive value of genetic determinants are rapidly progressing[3] with some laboratories choosing to provide molecular testing as a primary methodology.

In addition to performing quality assured testing, it is imperative that testing and reporting of DST results is performed in a timely manner to ensure the greatest impact to aid clinical decision making. The goal of the National PHL DST Reference Center for MTBC is to offer molecular detection of drug resistance ideally within an average of 11 days (maximum 14), first-line DST within 17 days, and second-line DST results within 21 days of receipt of isolate at the Reference Center. To meet turnaround time (TAT) requirements for DST and result reporting, extensible laboratory information systems (LIMS) and infrastructure must be available or adopted to support DST and resulting workflows. In addition, Electronic Test Order and Results (ETOR) is an important technical capability for PHLs.[4] ETOR allows a PHL to offer a higher level of service to its submitters, reduces the impact of manual data entry and reporting methods, and increases communication efficiencies across a network of clinical and public health partners.

To address the gap in access to quality assured and cost-effective DST for PHLs that perform less than 50 DSTs per year, APHL and CDC established the National PHL DST Reference Center for MTBC in March 2015. As of June 2024, there are 22 enrolled PHL submitters. From 2021–2023, the National PHL DST Reference Center for MTBC received a total of 1,124 samples (988 isolates and 136 specimens) for DST. Between 2021 and 2023, molecular DST was performed on 491 samples, first-line DST was performed on 954 samples, and second-line DST was performed on 170 samples.

This request for funding proposal is for continuation of a National TB DST Reference Center for MTBC in a PHL with the ability to perform testing for up to 500 additional samples per year to assist lower volume PHLs.

Eligibility

Eligible laboratories include all PHLs with the following capabilities, resources, and facilities in place. Specific expectations regarding the methodologies to be used by the Reference Center are outlined in Appendix A: *Expectations for National PHL DST Reference Center for MTBC*. All applicants are required to agree to the following minimum requirements (as outlined in Appendix B: Minimum Requirements for National PHL DST Reference Center for MTBC):

1. Availability of necessary equipment (e.g., MGIT) or ability to purchase additional equipment if necessary, anticipating testing for up to 500 samples per year (molecular and first-line DST);
2. Availability of adequate laboratory space (including infrastructure for unidirectional workflow for molecular testing) or space to accommodate additional equipment if necessary, anticipating up to 500 additional samples per year (molecular and first-line DST);
3. Sufficient workforce capacity for expanded testing volume or ability to hire additional qualified staff;
4. Established capacity for MTBC culture and both first- and second-line phenotypic DST methods;
5. Established capacity to perform molecular susceptibility testing for MTBC
    a. Applications that include molecular testing as the primary method are preferred;

   b. Whole genome sequencing (WGS) must be available in the laboratory for MTBC
      - Applicants may have established WGS for surveillance purposes with an intent to fully implement for CLIA-compliant molecular susceptibility testing by the date of contract award
6. Participation in CDC's Model Performance Evaluation Program (MPEP);
7. Willingness to alter or amend existing testing protocols;
8. Willingness to increase frequency of performing certain methods (if required) to meet expected turnaround times;
9. Willingness to amend specimen submission form(s) to include additional variables;
10. Willingness to alter existing reporting language to a standardized reporting language with input from APHL/CDC;
11. Willingness to share copies of QA or biosafety documentation associated with relevant procedures to APHL and CDC upon request;
12. Informatics capabilities:
    a. **Laboratory Information Management System** in place and able to be enhanced or modified to meet susceptibility test algorithms, workflows, submission requirements, and reporting language and

       Electronic Test Order and Results (ETOR)
    b. Proven capability to support ETOR, either through an existing web portal or through standardized messaging

       OR

    c. Ability to adopt APHL's LabWeb Portal Solution, hosted on the APHL Informatics Services platform (AIMS) using LIMSConnect

13. Ability to perform and report results from laboratory developed tests according to applicable regulatory requirements including those from FDA.

Anticipated RFP Schedule

August 5, 2024	–	RFP Issued
August 26, 2024	**–**	**Letter of Intent Due to APHL (see below)**
August 29, 2024	–	Informational Teleconference, if necessary (Q&A)
September 27, 2024	–	**RFP Responses Due**
October 11, 2024	–	Proposal Reviews Completed
October 14-16, 2024	–	Follow-up Interviews and Updated Proposals Due (as needed)
October 18, 2024	–	Final Review Completed and Awardee Selected
Spring 2025	–	Site visit, Harmonization, Validations, and Other Pre-Planning (as needed)

Submit the Letter of Intent (Due 08/26/24) and completed application (Due 09/27/24) to Sarah Buss, sarah.buss@aphl.org with copy to infectious.diseases@aphl.org.

July 1, 2025 – First Year Contract Awarded

APHL will communicate any modification to this anticipated schedule on APHL's procurement website (www.aphl.org/rfp) and via email blast to PHLs.

Response Submittal

Confirmation of Intent to Respond

APHL requires that prospective applicants submit a brief email statement indicating an intent to submit a proposal. APHL must receive this email by no later than **11:59pm EST on August 26, 2024.** To allow for appropriate review process planning, **a letter of intent is required** for consideration.

Final Response

APHL must receive complete responses by **11:59 pm EST on September 27, 2024.** Please see Proposal-Required Submissions section for items that must be included in the completed proposal. Applicants may send proposals via email to sarah.buss@aphl.org with copy to infectious.diseases@aphl.org.

APHL will send an email acknowledging receipt of your application; if you do not receive an acknowledgement within 48 hours, please email the RFP point of contact above to confirm receipt.

Award

One laboratory will be selected. The amount of award will be based on submitted budgets and may vary year to year based on testing performed and volume of specimens submitted. Anticipated volume is approximately 350-500 samples per year, although not all test methods will be performed on all samples received. The maximum annual compensation is estimated at $440,000, to be distributed based on per sample rates. Funding is distributed through an annual contract with APHL. By accepting this award, the laboratory agrees to the negotiated rate for up to a five (5) year time span barring substantive changes in scope or material expenses at APHL's discretion.

Use of Funds: The awarded laboratory should use the funding for testing of referred samples (including retesting due to laboratory/personnel error), reagents, and consumables and personnel time required to conduct these activities. Funding may also be used for necessary equipment upgrades or expansions, equipment maintenance and service agreements or validation of new testing services.

Term of Project

The project term will be from July 1, 2025 through June 30, 2030. Additional activities may precede this start term if needed to establish testing capacity, data transmissions and proficiency demonstrations to ensure operational expectations are in place for the contracted period.

The potential for annual renewals (with each additional funding year running from July 1 to June 30) may be considered by APHL based on availability of funds and performance of the awardee for a

maximum of four additional years (to end June 30, 2030). Each of the potential renewals may involve some adjustment to the scope of work, including the potential for expanded test volume, in order to address any change in the funding received by APHL and to accommodate CDC programmatic needs in that funding year. The awardee will be notified in advance of any modification to the anticipated scope of work for a future funding year.

Evaluation Team

APHL staff, led by the HIV, Viral Hepatitis, STD and TB (HHST) Program Manager, will conduct an initial review of all proposals for completeness. Any application that is incomplete as of the proposal due date specified in the Anticipated RFP Schedule section above will not be considered and will not receive a formal evaluation.

Complete proposals will be reviewed by a team of three subject matter experts (SMEs) from CDC's Division of Tuberculosis Elimination and a panel of three APHL members selected from non-applicant PHLs. SMEs from CDC will be identified and selected by the DTBE Laboratory Branch Chief based on their familiarity with laboratory techniques and project requirements. APHL member experts will be identified from among the non-applicant laboratories by the APHL HHST Program Manager and will have expertise in laboratory testing methods described in this RFP and familiarity with APHL's Reference Center structure. Once potential reviewers have been identified, APHL's Director of Infectious Disease Programs will have final approval over the review team's composition.

Conflict of Interest

APHL will ask potential reviewers to complete and sign APHL's **Conflict of Interest Disclosure Statement** in order to disclose any real or perceived conflict of interest prior to the start of the evaluation process. Reviewers will have to affirm that they have no conflict of interest that would preclude an unbiased and objective review of the proposals received. A copy of the disclosure statement and the related Fiduciary Responsibility and Conflict of Interest Policy is attached as **Appendix D**: Conflict of Interest Disclosure Statement and Policy. APHL will not select reviewers with a perceived or potential conflict of interest. This Conflict of Interest Disclosure Statement is provided in the RFP for Applicant review only. **Applicants should not complete the Conflict of Interest Disclosure Statement unless instructed by APHL.**

Evaluation Criteria

The evaluation team will evaluate proposals based on responses to the questions in the Proposal – Required Submissions section and will give a numeric score of up to 100 maximum points based on the scorecard template in Appendix C.

Laboratories meeting the following criteria have preference in the evaluation:

1. Extensive experience with the test methods;
2. Ability to handle increased volume;

3. Existing in-house subject matter expertise;
4. Experience and past performance serving as a Reference Center;
5. Current usage of APHL's LabWeb Portal Solution;
5. Ability to comply with expectations laid out in Appendix A; and
6. Ability to meet minimum expectations outlined in Appendix B.

Evaluation Process

The evaluation team will conduct the review via a combination of email communication between APHL's HHST Program Manager and members of the evaluation team, or among evaluation team members and teleconference and/or webinar evaluation sessions. APHL's HHST Program Manager will coordinate the review process and the evaluation sessions.

The reviewers may request follow-up interviews with all or some of the applicant laboratories and, following these interviews, may request supplemental information on an applicant's proposal. The evaluation team will use these interviews and any supplemental information to clarify a laboratory's capacity or experience in one or more of the evaluation criteria, or to explain other information contained in an applicant's proposal.

There will be no formal evaluation performed by a member of APHL staff. In cases where all other evaluation criteria are substantially similar, APHL will have the ability to advise the evaluation team on selections that would provide geographical spread or otherwise diversify APHL's funding allocations. In addition, the evaluation team may receive documentation from APHL staff on an applicant's past performance in other capacities as part of the evaluation criteria.

Post-Evaluation Procedures

APHL staff will notify the selected laboratory within ten business days of the completion of the evaluation and will post the name of the recipient to APHL's procurement website, www.aphl.org/rfp, within three (3) business days of the laboratory's acceptance of the award. Unsuccessful applicants will receive notification of these results by e-mail within 30 days after the name of the selected awardee is posted.

All applicant laboratories will be entitled to utilize APHL's RFP Appeals Process to formulate a protest regarding alleged irregularities or improprieties during the procurement process. Specific details of this policy are located on the procurement website.

Conditions of Award Acceptance

The eligible laboratory must be able to contract directly with APHL or have an existing relationship with a third-party organization that can contract directly with APHL on behalf of the laboratory. The laboratory must agree to comply with expectations outlined in Appendix A. Acceptance of the award means agreement to the compensation structure and amounts agreed upon with the awardee and APHL.

Submit the Letter of Intent (Due 08/26/24) and completed application (Due 09/27/24) to Sarah Buss, sarah.buss@aphl.org with copy to infectious.diseases@aphl.org.

Prior to making the official award, a group of individuals from CDC and APHL will be entitled to elect to tour the facilities to assess compliance with requirements for testing and/or have a teleconference with the applicant laboratory. Post award, monitoring site visits may be conducted to include an assessment of continued compliance.

Following selection and prior to making the official award, APHL will require the finalist to submit a letter of support from the LIMS vendor confirming the following items as applicable: Confirming the respondents capability to modify and maintain the DST specific test algorithms, and reporting language within the LIMS, confirming the ability of the respondent to connect the LIMS to APHL's instance of the LabWeb Portal using the LIMSConnect Solution on the AIMS cloud-based platform and confirming the applicants ability and willingness to extend any current ETOR capability to support the requirements of this project.

Proposal – Required Submissions

An interested laboratory must submit both a letter of intent to apply (due August 26, 2024) and a proposal (due September 27, 2024). Applications must comply with submission requirements set out in the Additional Information and Deadlines for Application Submission below. A complete proposal will include the following items:

- **A completed and signed copy of Appendix B,**

  Note: If your laboratory cannot respond "yes" to each of the minimum requirements, your laboratory does not meet the minimum qualifications required to apply for this award.

- **A letter of support from your institution's IT department:**
  a. **Current Reference Center Only:** Confirming your commitment to maintain connectivity to the AIMS LabWeb Portal environment using the LIMSConnect solution (see reference documents: ETOR-LWP-LIMSConnect Slides, LWP.v8 Architecture General Information and LIMS Connect Overview) with the support of a designated IT staff member **OR**

  b. Confirming your ability to establish connectivity to the AIMS LabWeb Portal environment using the LIMSConnect solution (see reference documents: ETOR-LWP-LIMSConnect Slides, LWP.v8 Architecture General Information and LIMS Connect Overview) **OR**

  d. Confirming your current ETOR capability using an existing web portal or through standardized messaging and that there is the capacity to onboard all submitting laboratories (current submitter list available upon request) to the system including any costs associated with such onboarding **AND**

  Confirming that the applicant will have the support of a designated IT staff member to support this work.

- **Responses to Questions (below)**

Submit the Letter of Intent (Due 08/26/24) and completed application (Due 09/27/24) to Sarah Buss, sarah.buss@aphl.org with copy to infectious.diseases@aphl.org.

- Responses should be limited to no more than ten (10) single spaced pages (font size ≥ 11pt, 1 inch margins)
- Proposal should include responses to the questions below, including each aspect of the question. Proposal should indicate what question is being answered.

Response to Questions

Physical Environment

1. Describe your laboratory's ability to accommodate or absorb an increased workload in performing phenotypic and molecular testing for drug resistance at current staffing levels by defining the additional monthly volume your laboratory would be able to undertake for phenotypic DST (first- and second-line) as well as molecular-based testing (of isolates and primary specimens).
    a. Does the facility have laboratory space available for additional instrumentation or staff, if needed, to accommodate increased workload? Please describe the existing space, equipment and staff to handle testing volume(s) for all three aspects of testing as well as ability to expand, as applicable?
    b. Does the laboratory have sufficient staffing or the ability to hire additional staff to accommodate workload if necessary? If yes, please describe approximate timelines associated with posting and hiring new positions.

Workforce

2. Does your laboratory have staff with the subject matter expertise to provide guidance to submitting laboratories and interpretation of phenotypic and molecular test results including discordant results?
    a. Please describe the qualifications and experience staff have in providing consultative services.

Molecular DST Methods

3. Please describe the current methodology and algorithms used in your laboratory for molecular susceptibility testing for MTBC. Include information on:
    a. method/platform(s) used
    b. how often testing performed
    c. how long the methodology has been used
    d. sample types tested
    e. information on algorithm(s) and reflex testing associated with molecular DST

f. which genetic loci are evaluated
g. how interpretations are determined and bioinformatic pipeline used
h. annual volume (2022 and 2023 Calendar Year, if available)
i. average turnaround time (primary specimen and isolate, as applicable)
j. number of laboratory staff and their experience with the test method(s) including years of experience of each trained staff member
k. any training staff has received
l. any planned changes to current testing procedures

Phenotypic DST Methods

4. Please describe the current methodology used in your laboratory for phenotypic first-line DST for MTBC. Include information on:
    a. how long the methodology has been in use
    b. how often testing is performed
    c. information on testing algorithm(s) and reflexes associated with first-line DST
    d. annual volume (2022 and 2023 Calendar Year)
    e. average turnaround time (from diagnostic specimens and reference isolates)
    f. number of laboratory staff and their experience with the test method(s) including years of experience of each trained staff member
    g. any training staff has received
    h. any planned changes to current testing procedures

5. Please describe the current methodology used in your laboratory for phenotypic second-line DST for MTBC. Include information on:
    a. how long the methodology has been in use
    b. how often testing performed
    c. information on testing algorithm(s) and reflexes associated with second-line DST
    d. annual volume (2022 and 2023 Calendar Year)
    e. average turnaround time (from diagnostic specimens and reference isolates)
    f. number of laboratory staff and their experience with the test method(s) including years of experience of each trained staff member
    g. any training staff has received
    h. any planned changes to current testing procedures

Reporting Results/Information Technology

6. Please describe all LIMS, tools, and infrastructure available to support the work outlined in Appendix A including ordering, testing and resulting workflows (e.g., LIMS, ETOR HL7, ETOR web portal, or

secure fax, etc.). Respondents must identify any ETOR capability available to support the reporting requirements of the National PHL DST Reference Center for MTBC including ability to modify LIMS to agreed upon reporting language (current reporting language available at www.aphl.org/tbdst) and capacity to onboard submitting sites to the ETOR solution and any/all back-up reporting mechanisms. Please also include the process and estimated timeline to onboard current submitting PHLs (roster of submitting sites is available upon request).

*If no current ETOR system is in place or the system is unable to be used for this work, the laboratory will be expected to adopt APHL's ETOR Lab Web Portal solution. Respondents should review the referenced Lab Web Portal reference documents (*ETOR-LWP-LIMSConnect Slides, LWP.v8 Architecture General Information and LIMS Connect Overview*) and evaluate their capability to connect to the Lab Web Portal Solution hosted on APHLs Informatics Messaging Service platform.*

Reference Center Testing

7. Briefly describe your laboratory's experience, if any, in providing reference testing for other PHLs in a shared service model including, but not limited to, coverage for a limited period of time to assure continuity of operations.

New Technology and/or Laboratory Developed Tests

8. If selected, would your laboratory be willing to evaluate and incorporate additional new technologies and/or testing algorithms, including but not limited to adding new drugs to susceptibility panels and/or new molecular targets?
    a. Please briefly describe your experience in participating in method or platform evaluation(s).
    b. Briefly describe your procedures for validating laboratory developed tests (LDTs) to include regulatory compliance.

Budget

9. Provide a 1 year budget outlining at least the following line items: equipment purchase or upgrade based on the methods requirements outlined in Appendix A (if needed); staff time; charge per specimen/isolate tested by each method; and anticipated overhead charges if any.

Additional Information and Deadlines for Application Submission

Applicants must direct all questions to Sarah Buss (sarah.buss@aphl.org). APHL will post questions received from interested PHLs, together with the answers provided by APHL or CDC staff to APHL's procurement website associated with the specific RFP (www.aphl.org/rfp).

Submit the Letter of Intent (Due 08/26/24) and completed application (Due 09/27/24) to Sarah Buss, sarah.buss@aphl.org with copy to infectious.diseases@aphl.org.

To allow for appropriate review process planning, a **letter of intent is required for consideration**. Applicants should submit letters by email to Sarah Buss at APHL (sarah.buss@aphl.org) with copy to infectious.diseases@aphl.org no later than **11:59 pm EST on Monday, August 26, 2024.**

Applications are due to Sarah Buss at APHL (sarah.buss@aphl.org) with copy to infectious.diseases@aphl.org **by close of business (11:59pm ET) September 27, 2024.** APHL will send an email acknowledging receipt of your application. If you do not receive an acknowledgement within two (2) business days, call 240.485.3901 to confirm receipt.

If necessary, APHL will hold an optional teleconference on Thursday August 29, 2024 at 2:00pm ET. The purpose of this call will be to provide a brief overview of the project and to allow potential applicants to ask CDC and APHL questions. Please come with questions prepared.

Teleconference Registration Information is below, or please contact sarah.buss@aphl.org or infectious.diseases@aphl.org no later than 8:00 am ET on August 29, 2024 to receive registration instructions.

Register in Advance for this Zoom Meeting
https://aphl.zoom.us/meeting/register/tZ0ucOCqqzMqHdZdp0oqH-8tHWt6fCwfBIny

References:

1. Centers for Disease Control and Prevention. (2023). *Mycobacterium tuberculosis* Complex Drug Susceptibility Testing Program-Model Performance Evaluation Program, Report of Results. Atlanta, GA. Available at: https://www.cdc.gov/tb/topic/laboratory/mpep/pdf/March-2023-MPEP-Final-Report.pdf
2. Association of Public Health Laboratories. (2007). TB Drug Susceptibility Testing Expert Panel Meeting Summary Report. Silver Spring, MD. Available at: http://www.aphl.org/aphlprograms/infectious/tuberculosis/Documents/ID_2007Dec_TB-DST- Report.pdf
3. World Health Organization (2023). Catalogue of mutations in *Mycobacterium tuberculosis* complex and their association with drug resistance, 2nd ed. Geneva, Switzerland. Available at: https://www.who.int/publications/i/item/9789240082410
4. Dudik I, Dennis M, Higginbotham K, Johnson S, Sankrithi N, Shepard R, Weding M. The public health need for ETOR, presented at APHL 2019, St. Louis, MO, June 2019. Available at: https://www.aphl.org/rfp/Documents/ID_TB-DST-RC-ETOR%20Poster_2019%20AM.pdf

Appendix A: Expectations for National PHL DST Reference Center for MTBC

Methods and Test Algorithms

Molecular Testing

- Molecular detection of drug resistance testing needs to be performed to provide an expeditious turnaround time from sample receipt. This turnaround time may vary depending on methodology (e.g., whole genome sequencing (WGS) vs. targeted next generation sequencing (tNGS)) employed.
- When WGS is employed, the proposed workflow should include universal molecular testing on all isolates (referred or cultured from primary specimens), provided that generated WGS data will be shared with CDC for purposes of national molecular surveillance.
- The minimum panel for testing will include the following targets:
    - Rifampin
        - *rpoB* RRDR (codons 426-452)
        - codon 170 in *rpoB*
        - codon 491 in *rpoB*
    - Isoniazid (INH)
        - *fabG1-inhA* promoter region (-4 to -20)
        - *katG* (entire ORF)
        - *fabG1* (codon 203)
    - Fluoroquinolones
        - *gyrA* QRDR
        - *gyrB* QRDR
    - Pyrazinamide
        - *pncA*
    - Second-line injectables (amikacin, capreomycin, and kanamycin)
        - *rrs*
        - *eis*
    - Ethambutol
        - *embB*
    - Bedaquiline
        - *rv0678*
        - *atpE*
        - *pepQ*
        - *mmpL5*
        - *mmpS5*

  - Clofazimine
    - *rv0678*
    - *pepQ*
    - *mmpL5*
    - *mmpS5*
  - Linezolid
    - *rrl*
    - *rplC*
  - Results for *rpoB* should be reported using MTBC codon numbering rather than the historic (*E. coli*) numbering schemes
- Laboratory must have a validated heat inactivation protocol and provide documentation of verification upon request.
- The Reference Center will accept NAAT positive **sediments** for testing. Sediments submitted for confirmation of an Xpert MTB/RIF result "rifampin resistance detected", may be tested and referred to CDC's MDDR from the Reference Center following confirmation.
  - Cultures will be set up from sediments for phenotypic first-line DST and whole genome sequencing, if applicable.
  - When rifampin resistance is detected, an aliquot of the residual sediment (if available), heat-kill, or isolate may be referred to CDC's MDDR for additional testing.
  - A system will be established (e.g., trigger in LIMS) for identifying problematic samples requiring extensive time for growth (>2 weeks) whereby an isolate can be requested from the submitting laboratory for first-line DST.

Genotyping

- When the National PHL DST Reference Center for MTBC utilizes WGS for either molecular detection of drug resistance or surveillance only, data (i.e., fastq files) will be shared with CDC for the purpose of national molecular surveillance.
  - Isolate information will be entered into the Tuberculosis Genotyping Information Management System (TB GIMS) by the Reference Center.
  - WGS should be completed in a timely manner but ideally with an average turnaround time of 11 days (maximum 14).

Phenotypic first-line DST (FL-DST)

- Testing will be performed as needed to meet the TAT goal of 17 days from date of receipt at the Reference Center.
- FL-DST will be performed with a panel of rifampin (RIF), isoniazid (INH) (0.1 µg/mL), pyrazinamide (PZA), ethambutol (EMB) and moxifloxacin (MOX) as requested.
  - Applications that include molecular testing as the primary method will be accepted; applicants may propose alternative FL-DST workflows that include phenotypic testing

only as a follow-up to certain molecular results. However, all applicants must have the ability to conduct phenotypic FL-DST with the defined panels.
    - Reflex to higher concentration of INH as needed.
    - Submitting laboratories will be asked to refer an aliquot of positive growth (optimally from broth) as soon as the culture becomes positive and identification of MTBC is confirmed
    - Purity plate will be set up
- If phenotypic or molecular resistance to any first-line drug is detected, reflex testing to confirm resistance and for second-line drugs will be performed.
- If phenotypic testing reveals resistance to rifampin, isolate may be referred to CDC's MDDR as soon as possible for additional testing. Second-line DST will also be performed at the Reference Center.

Phenotypic second-line DST (SL-DST)

- Testing will be performed as often as needed when ordered by the submitter and with a TAT goal of 21 days from date of receipt at the Reference Center to result reported
- At a minimum, the testing panel must include the following:
    - Second-line injectables (amikacin, capreomycin, and / or kanamycin)
    - Ethionamide
    - Rifabutin
    - Moxifloxacin
- SL-DST methods may include agar proportion, automated liquid broth systems (i.e., MGIT), or minimum inhibitory concentration (MIC) by broth microdilution.
- SL- DST will be performed on reflex when resistance is detected by molecular or phenotypic methods to first-line drugs.
- SL-DST will be performed when requested due to clinical need (e.g., drug intolerance).
- It is expected that SL-DST will be performed as soon as possible when needed.
- DTBE/LB Reference Laboratory may provide access to isolates needed for validation.
- DTBE/LB can assist with training if needed/as applicable.

Electronic Test Order and Resulting

- Laboratory Information Management System in place and able to be enhanced or modified to meet DST test algorithms, workflows, submission requirements and reporting language.
    - Current reporting language for molecular detection of drug resistance is available at: www.aphl.org/tbdst
- Proven Electronic Test Order and Results (ETOR) capability:
    - Ideally: Established connectivity to the AIMS LabWeb Portal environment
    - Alternatively: Through an existing web portal or through standardized messaging
- Capacity and capability to adopt APHL's ETOR LabWeb Portal Solution, hosted on the APHL Informatics Services platform (AIMS) using LIMSConnect. (See supplemental Lab Web Portal

documentation for more details: LIMS Connect Overview, ETOR-LWP-LIMSConnect Slides and LWPv8 architecture general).

- Capacity to engage and onboard all submitting sites to the ETOR solution within the first two-three months of contracted work.
- Back-up reporting mechanisms in place to meet reporting requirements outside of ETOR/LIMS (such as secure fax).

Performance Management and Evaluation

APHL in collaboration with CDC/ DTBE Laboratory Branch will monitor workload, reasons for submission to Reference Center, data quality, transport times, TATs, data anomalies and outliers, discordant results, level of drug resistance, types of mutations detected, appropriate use of reporting language, appropriate use of reflex testing algorithms, effective consultative services, customer satisfaction, referrals to CDC, and service costs on a monthly basis through the following mechanisms:

Data Review

- On a monthly basis, as defined in the contract, a complete report including elements similar to those outlined below, will be provided to APHL and CDC.
    - Monthly Report
        - Aggregate data including: TATs, number of RIF-resistant and INH-resistant samples detected by sequencing
        - Line Listed Specimens and Isolates including fields agreed upon by APHL, CDC and the Reference Center. Fields may include but are not limited to: accession number, submitting state, test(s) requested, test(s) performed, comments on condition and reflex testing, date of specimen collection, date of receipt at the Reference Center, specimen type, date testing performed (molecular) or setup (DST), submission criteria (if applicable), date results reported, date and reason for referral to CDC (if applicable), final result for sample (susceptible, or noting which resistance was detected) and date of referral of fastq files to CDC for national molecular surveillance.
        - Test results will include genotypic data (e.g., locus, nucleotide sequence, amino acid substitution [when applicable] and interpretive comments) and associated phenotypic data (to include contaminated and no growth when applicable) for each sample tested, as applicable.
        - Listing of nonconforming events, complaints, and QC failures related to the project.
            - If a non-conforming event, complaint, or QC failure has the potential to have significant repercussions, the Reference Center should perform an investigation and determine appropriate remediation and prevention strategies. The Reference Center will also complete and submit an incident tracking form (provided by APHL) to APHL and CDC within one week of the request by CDC or APHL unless otherwise specified. If additional time is needed for appropriate investigation, APHL and CDC should be notified. If

complaints are related to compliance with FDA regulatory requirements for LDTs, this information should be documented as well for sharing with APHL/CDC.

  - The Reference Center may develop additional QA monitors, in conjunction with CDC, for their own performance and that of submitting laboratories.
- Pending phenotypic data will be matched with genotypic data during the subsequent collection period, as applicable. Data will be provided with any personal identifying information (PII) removed prior to submitting to APHL and CDC.
  - If matching of patient results between CDC and the National PHL DST Reference Center for MTBC is needed, a representative from the DTBE Reference Laboratory Team will coordinate communication to protect PII.
- Data will be analyzed by a team at APHL and CDC with feedback provided to the Reference Center within 1 month of receipt either by email or during a teleconference, if appropriate timing.
- Genotypic and correlated phenotypic data will be added to the DTBE Reference Laboratory database.

Site visits and Teleconferences

- APHL in collaboration with CDC will perform site visits as needed. Additional monitoring visits may be needed based on data review and any ongoing challenges mutually identified. Site visits could include data review, review of laboratory workflow, procedural observation, QC information, worksheets for DST, and review of sequencing data.
- APHL, CDC, and the Reference Center will participate in teleconferences every other month to review reports, assess successes and challenges, and discuss potential resolutions.

Customer Satisfaction

APHL may perform customer satisfaction surveys that may include key informant interviews with select submitters to assess satisfaction with service, turnaround time, reporting format, expert consultation, and continued use of Reference Center.

Performance Assessment

- Reference Center is required to participate in the CDC sponsored Model Performance Evaluation Program (MPEP) twice a year and to test the panel(s) against all funded methods. In addition to MPEP, APHL may collaborate with CDC to provide no more than two isolate challenges each year to specifically assess genotypic and phenotypic testing, if needed. Blinded testing will be performed by CDC staff concurrently if a panel separate from MPEP is provided.
- Quality of consultations will be assessed through outreach to participating PHLs and TB Programs.

Reporting Language

- Reporting language and disclaimers harmonized with the DTBE Reference Laboratory must be used by the Reference Center. Genotypic results must be provided in an interim or preliminary

report with phenotypic results to follow as applicable.

- Annual review of reporting language (including a catalog of interpretative comments for wild-type, novel mutations, and common mutations) and sensitivity/specificity documents to ensure they are up to date. The document will be updated as necessary per discussions by all partners on teleconferences.
- Final reports should include a categorical result of 'R' or 'S' for each drug, as applicable. Perceived discordance between genotypic and phenotypic testing should be clearly indicated and additional interpretative comments provided. CDC can assist with language around discordant results.

Consultation

- Subject matter expertise within the National PHL DST Reference Center for MTBC should be available for consultation by phone or dedicated email address.
- CDC DTBE Reference Laboratory may be consulted when discordant results are observed.
- Reference Center will maintain dedicated lines of communication for submitters (i.e., telephone number, email, website).
- APHL will host a dedicated website available to submitting laboratories to include appropriate contact information and National PHL DST Reference Center for MTBC documents.

Archiving Isolates

- Isolates will be stored frozen by the Reference Center for a period of 2 years.
- Isolates may be requested to be shipped to CDC for longterm storage prior to destruction at the end of the 2 year period.

Continuity of Operations Assurance

- In the event that CDC is unable to provide TB testing due to extenuating circumstances (e.g., laboratory shutdown), the Reference Center may be requested to perform testing for additional specimens on an as needed basis on behalf of CDC after consultation. Invoicing for this testing would be in accordance with the fee schedule established in the annual contract.

Appendix B: Minimum Requirements for National PHL DST Reference Center for MTBC

Please review and respond to each of the minimum requirements below. By signing this agreement, you are affirming that your laboratory can meet each of the minimum requirements described.

YES	NO	MINIMUM REQUIREMENT
		Does your laboratory have the necessary equipment or ability to purchase additional equipment if necessary?
		Does your laboratory have adequate laboratory space (including infrastructure for unidirectional workflow for molecular testing) and to accommodate additional equipment if necessary?
		Does your laboratory have sufficient workforce capacity for expanded testing volume or ability to hire additional qualified staff?
		Does your laboratory have established capacity for MTBC culture and to perform phenotypic first-line DST and second-line DST methods to detect drug resistance in MTBC?
		Does your laboratory have established capacity for molecular detection of drug resistance for MTBC?
		Does your laboratory have established capacity for whole genome sequencing?
		Does your laboratory participate in the Model Performance Evaluation Program (MPEP)?
		Is your laboratory willing to alter or amend existing testing protocols at the request of APHL and CDC?
		Is your laboratory willing to increase the frequency of performing certain methods (if required) to meet expected turnaround times?
		Is your laboratory willing to amend specimen submission form(s) to include additional variables?
		Is your laboratory willing to alter existing reporting language to a standardized reporting language with input from APHL and CDC?
		Is your laboratory willing to provide copies of QA or biosafety documentation to APHL and CDC upon request?
		Does your laboratory have the necessary informatics capabilities including a LIMS and either proven capability to support ETOR or ability to adopt APHL's LabWeb Portal Solution?
		Is your laboratory able to perform and report diagnostic test results from LDT assays?

On behalf of the applicant laboratory, I agree that the applicant laboratory is able to meet the minimum requirements necessary to apply for this award as outlined above.

Signature: _____ Date: _____

Printed Name: _____

Submit the Letter of Intent (Due 08/26/24) and completed application (Due 09/27/24) to Sarah Buss, sarah.buss@aphl.org with copy to infectious.diseases@aphl.org.

Appendix C: Score Card

The following table is a copy of the score card that will be used to evaluate RFP responses.

Category/Question	Maximum Value	Score	Comments (REQUIRED)
Physical Environment 1. Does the applicant demonstrate the ability to handle the testing volume for all required methods? Consider the availability of existing staff, equipment and space and ability of the laboratory to purchase additional equipment or hire additional staff. **Ideal** (11-15 points): Describes ability to handle testing volume for all activities; describes appropriate staffing, equipment and space or ability to obtain additional equipment or staffing in a timely manner. **Adequate** (6-10 points): Describes ability to meet most testing volume requirements but may have to adjust workflow and/or staffing to accommodate work; has some deficiencies in their staffing, equipment or ability to obtain additional resources. **Limited** (1-5 points): Applicant describes limited ability to meet testing volume requirements; has many deficiencies in their staffing, equipment or ability to obtain additional resources. **Inadequate** (0 points): Applicant does not demonstrate the ability to handle the testing volume for all methods and neither has the current staffing or equipment or ability to obtain the unmet needs and/or does not demonstrate a clear understanding of the requirements.	15		Type comments here. (REQUIRED)
2. Does the applicant describe in-house subject matter expertise that is sufficient to provide consultation to submitting laboratories on discordant results or other issues? **High** (8-10 points): Applicant has a strong history of relevant experience, subject matter expertise: at least 1.0 FTE with > 5 years or 2.0 FTEs with > 3 years of experience providing consultation to submitters on interpretation of results including discordant results. **Moderate** (4-7 points): Applicant has some relevant experience, but will require additional training, guidance or technical assistance from others, subject matter expertise: >1.0 FTE with ≥ 3 years of experience providing consultation to submitters on interpretation of results including discordant results. **Low** (1-3 points): Deficiencies in staffing in this area, subject matter expertise: ≤ 1 FTE with <3 years of experience	10		Type comments here. (REQUIRED)

providing consultation to submitters on interpretation of results including discordant results. **No Experience** (0 points): Applicant does not demonstrate internal subject matter expertise is this area.			
First-Line DST Methods 3. Does the applicant have sufficient capacity and experience performing first-line DST for MTBC? Consider experience with described method(s), experience of existing staff? **High** (11-15 points): Describes extensive experience performing method, sufficient capacity and staff experience to handle additional volume, describes appropriate staffing and equipment, and regularly meets target TATs as recommended in the CDC Tuberculosis Elimination and Laboratory Cooperative Agreement. **Moderate** (6-10 points): Describes sufficient experience performing method, some concerns about appropriate capacity to handle additional volume and/or does not regularly meet target TATs as recommended in the CDC Tuberculosis Elimination and Laboratory Cooperative. **Low** (1-6 points): Describes experience performing method, deficiencies in workforce experience and/or ability to meet target TATs and/or handle additional volume. **No Experience** (0 points): Applicant does not demonstrate internal subject matter expertise is this area.	15		Type comments here. (REQUIRED)
Second-Line DST Methods 4. Does the applicant have sufficient capacity and experience performing second-line DST? Consider experience with described method(s), experience of existing staff? **High** (11-15 points): Describes extensive experience performing method, sufficient capacity and staff experience to handle additional volume, describes appropriate staffing and equipment, and regularly meets target TATs as recommended in the CDC Tuberculosis Elimination and Laboratory Cooperative. **Moderate** (6-10 points): Describes sufficient experience performing method, some concerns about appropriate capacity to handle additional volume and/or does not regularly meet target TATs as recommended in the CDC Tuberculosis Elimination and Laboratory Cooperative. **Low** (1-6 points): Describes experience performing method, deficiencies in workforce experience and/or ability to meet target TATs and/or handle additional volume. **No /Unclear** (0 points): Applicant does not demonstrate internal subject matter expertise is this area.	15		Type comments here. (REQUIRED

Molecular DST Methods 5. Does the applicant have sufficient capacity and experience performing molecular detection of drug resistance for TB? Consider experience with described method(s), experience of existing staff? **High** (11-15 points): Laboratory utilizes whole genome sequencing for molecular DST (additional molecular methods may also be in place). Describes extensive experience performing method, sufficient capacity and staff experience to handle additional volume, describes appropriate staffing and Equipment, and regularly meets target TATs as recommended in the CDC Tuberculosis Elimination and Laboratory Cooperative. **Moderate** (6-10 points): Laboratory utilizes whole genome sequencing for surveillance purposes and is working towards completing CLIA validation of the method prior to July 1, 2025. Describes sufficient experience performing method, some concerns about appropriate capacity to handle additional volume and/or does not regularly meet target TATs as recommended in the CDC Tuberculosis Elimination and Laboratory Cooperative. **Low** (1-6 points): Describes experience performing method, deficiencies in workforce experience and/or ability to meet target TATs and/or handle additional volume. **No /Unclear** (0 points): Applicant does not demonstrate internal subject matter expertise is this area.	15		Type comments here. (REQUIRED)
Reporting 6. What is the applicants' ability to offer electronic test ordering and reporting? **Ideal** (10 points): Applicant already has a connection to AIMS/LWP for electronic ordering and reporting **Adequate** (5 points): Applicant has an ETOR system in place and/or the ability to connect to AIMS/LWP for electronic ordering and reporting **Inadequate** (0 points): Applicant does not have an ETOR system or ability to connect to AIMS/LWP	10		Type comments here. (REQUIRED)
Reference Center Testing 7. Rate the applicant's level of experience in providing reference testing services for other public health laboratories in a shared service model. **Rate on a scale of 0-5 points** (5= Applicant has served as a reference center for other PHLs on an ongoing basis with submissions from and reporting to	5		Type comments here. (REQUIRED)

multiple out-of-jurisdiction submitters; 0=applicant has no experience serving as a reference center for other PHLs)			
New Technology and/or Laboratory Developed Tests 8. How well does the laboratory demonstrate a willingness and ability to evaluate and incorporate additional new technologies and or alter algorithms to address changing needs? **High** (6-10 points); Applicant has experience with bringing on new test technology, adding new drugs to phenotypic susceptibility panels or adding targets to panels for molecular detection of drug resistance. Procedures for validation are appropriate including general approach and sample size. **Moderate** (1-5 points); Applicant has limited experience with bringing on new test technology, adding new drugs to phenotypic susceptibility panels or adding targets to panels for molecular detection of drug resistance. **No experience** (0 points); Applicant does not demonstrate expertise is this area.	10		Type comments here. (REQUIRED)
Budget 10. Rate the appropriateness of the applicants budget **Rate on a scale of 0-5 points** (5=most cost-effective budget; 0=budget is inappropriate)	5		Type comments here. (REQUIRED)
TOTAL SCORE	**100**	____	

Appendix D: Conflict of Interest Disclosure Statement and Policy

Association of Public Health Laboratories
Conflict of Interest Disclosure Statement

Applicability: Disclosure of the following information is required of all Officers, Directors, committee members, staff members and other volunteers who have been designated and who have accepted responsibility to act on behalf of APHL ("APHL Personnel"). Please answer the following questions and, where indicated, include the same information for your immediate family members (your parents, your spouse or partner, your children and your spouse/partner's parents).

APHL will keep your completed disclosure statement in the corporate records of the association.

1. Please list the name, address, phone number, email address and type of business of your current employer. If you are self-employed, please note that below and provide us with the address, phone number, email address and type of business you operate.

_____

_____

_____

2. Do you, or does any family member, currently serve as an officer, director, committee member, or other volunteer (or work as an employee of or a paid consultant to) any organization serving the interest of laboratory science or public health laboratories other than APHL or your state or local laboratory?

☐ **Yes** ☐ **No**

If yes, please list the organization(s) and provide detail on your or your family member's interest or position in the organization(s).

_____

_____

_____

3. Do you, or any family member, have an existing or potential interest in, or compensation arrangement with, any third party providing goods or services to APHL, or with which APHL is currently negotiating?

☐ **Yes** ☐ **No**

If the answer is yes, please provide the name of the organization below and describe in detail the nature of the position held.

4. Please note any other financial or business interest you may have with any organization serving the interests of public health laboratories.

If you have none, please check this box: ☐

5. Do you, or does any family member, have any other interest or affiliation that is likely to compromise your ability to provide unbiased and undivided loyalty to APHL, or that could come in conflict with your official duties as an Officer, Director, committee member, staff member or other volunteer who has been designated and who has accepted responsibility to act on behalf of APHL?

☐ **Yes** ☐ **No**

If you answered yes, please describe in detail below the nature of each such interest or affiliation.

6. If you are currently aware of any actual or possible conflict of interest that might otherwise hamper your ability to serve APHL to your best ability and with the highest degree of care, loyalty and obedience – ***including any potential conflict you or a family member may have with one or more of the RFP applicants*** – please describe them in detail below.

_____

_____

_____

_____

_____

7. Do you agree that so long as you are an Officer, Director, committee member, staff member or other volunteer who has been designated and who has accepted responsibility to act on behalf of APHL you will immediately disclose to the other Directors and/or Officers or, for staff members, the Executive Director and/or General Counsel the nature of any interest or affiliation which you may hereafter acquire, which is in or is likely to become in conflict with your official duties with APHL?

☐ **Yes** ☐ **No**

YOU MUST READ THIS SECTION AND THEN SIGN BELOW

I acknowledge that I have received and read APHL's Fiduciary Responsibility and Conflict of Interest Policy (the Policy). I have listed all my relevant fiduciary responsibilities and affiliations, and I have identified any actual or potential conflict of interest on this Disclosure Statement and I agree to abide by the Policy. I understand that it is my responsibility to inform APHL in writing of any change in circumstances relating to the Policy and this Disclosure Statement.

Signature: _____ Date: _____

Printed Name: _____

APHL Fiduciary Responsibility and
Conflict of Interest Policy

1. Policy Statement and Purpose

The members of the APHL Board of Directors understand the importance of serving APHL to the best of their ability and with the highest degree of obedience, loyalty and care. Accordingly, the Board adopts the following policy for APHL Officers and Directors, all staff, committee members, and other volunteers who have been designated and who have accepted responsibility to act on behalf of APHL ("APHL Personnel").

2. Individual Duty and Annual Disclosure

APHL Personnel will avoid any conflict of interest with APHL. APHL Personnel will not profit personally from their affiliation with APHL, or favor the interests of themselves, relatives, friends or other affiliated organizations over the interests of APHL. As used in this Policy, "Conflict of interest" includes any actual, apparent, and potential conflict of interest.

Upon commencing service with APHL, each APHL Personnel will file with the Board an annual statement disclosing all material business, financial, and organizational interests and affiliations they or persons close to them have which could be construed as related to the interests of APHL or the profession of public health laboratory science. Each APHL Personnel has an obligation to make an additional disclosure if a conflict of interest arises in the course of the individual's service to APHL, whether arising out of his/her employment, consulting, investments, or any other activity. These disclosures will be documented promptly in writing and recorded in the Board minutes and corporate records.

3. Procedure

Whenever APHL considers a matter, which presents an actual, apparent, or potential conflict of interest for APHL Personnel, the interested individual will fully disclose his/her interest in the matter, including the nature, type, and extent of the transaction or situation and the interest of the individual or that individual's relatives, friends or other affiliated organizations. The Board, after consultation with counsel as appropriate, will determine whether an actual and material conflict exists and, if so, what is the appropriate course of action under this policy and the Board vote will be recorded in the minutes.

Any Board member having a conflict of interest must either (i) voluntarily abstain from and be disqualified from participation in all deliberation and voting on all Board actions relating to the situation or matter that gives rise to the conflict of interest, or (ii) ask the Board to determine whether an apparent or potential conflict of interest is considered by the Board to be an actual and material conflict. In the event that the Board member in question requests that the Board evaluate the apparent or potential conflict, that Board member will abstain and be disqualified from participating in (and voting on) the determination of whether the issue presents an actual and material conflict. If the Board determines that an actual and material conflict exists, the Board member in question will abstain from all voting on, and will be disqualified from participation in all deliberation concerning all Board actions relating to the conflict of interest. The vote will be recorded in the minutes.

These procedures will neither prevent the interested individual from briefly stating his/her position on the matter, nor preclude him/her from answering pertinent questions of Board members, since his/her knowledge may be of assistance to the Board's deliberations.

APHL Personnel must be cautious and protective of the assets of APHL and insure that they are used in the pursuit of the mission of APHL. The association's policy requires APHL Personnel to avoid transactions in which APHL personnel may have a significant financial interest in any property which

APHL purchases, or a direct or indirect interest in a supplier, contractor, consultant, or other entity with which APHL does business. The Board, after consultation with counsel as appropriate, will determine whether an actual and material conflict exists and, if so, determine whether the transaction is nonetheless favorable to APHL before considering whether to approve it.

4. Other Duties and Obligations

Whenever any APHL Personnel discovers an opportunity for business advantage which is relevant to the activities of APHL, the opportunity belongs to APHL and the individual must present this opportunity to the Board. Only once the Board determines not to pursue the matter and relinquishes the opportunity may the individual consider it a matter of possible personal benefit.

APHL Personnel may not accept favors or gifts exceeding $75.00 from anyone who does business with APHL.

All APHL Personnel will keep confidential those APHL matters designated confidential. APHL Personnel are prohibited from disclosing information about APHL to those who do not have a need to know or whose interest may be adverse to APHL, either inside or outside APHL, and are prohibited from using in any way such information for personal advantage to the detriment of APHL.

All APHL Personnel who participate in APHL activities, including committee activities and international consultation activities, must be adequately prepared to fully participate as their position descriptions require and will do so in accordance with the applicable laws and regulations of their respective state or territory and APHL's Articles of Incorporation, Bylaws, and corporate policies. The APHL Board will read and understand the association's Articles of Incorporation, Bylaws, corporate policies and financial statements, and routinely verify that all state, federal, and local tax payments, registrations and reports have been filed in a timely and accurate manner.

Board members will never exercise authority on behalf of APHL except when acting in meetings with the full Board or the Executive Committee or as authorized by the Board. If any member of the Board has significant doubts about a course of action of the Board, he or she must clearly raise the concern with the Executive Director and the Board and, when appropriate, seek independent expert advice.