Request for Proposals: Whole Genome Sequencing (WGS) of Mycobacterium tuberculosis complex (MTBC) Positive Primary MGIT Culture

Revised: July 29,19

Application Due date: August 8, 2019

Submit to: Anne Gaynor, Manager of HIV, Viral Hepatitis, STD and TB (Anne.Gaynor@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 identify up to 10 state or local public health laboratories to participate in an evaluation of performing whole genome sequencing (WGS) from primary (i.e., diagnostic) BD BACTEC MGIT cultures positive for *Mycobacterium tuberculosis* complex (MTBC). Laboratories will obtain the samples for WGS (minimum of 32) through one of the following approaches.

Option 1. Utilize samples from a defined jurisdiction (e.g., city, county, region, or state)
Option 2. Collaborate with another jurisdiction to obtain a sufficient number of samples.

Background

In 2012, the DTBE began using WGS data to investigate select clusters of tuberculosis (TB) cases initially identified by conventional genotyping methods. In comparison to conventional methods, WGS typically provides higher resolution data resulting in more focused targeting of limited public health resources. These resources lead to more effective epidemiologic field investigations and an improved ability to identify where public health intervention will have the greatest impact. Based on this initial success, the National Tuberculosis Molecular Surveillance Center was established in 2018 to provide universal WGS of all culture-confirmed TB cases in the United States. By 2021, WGS will replace conventional genotyping for the detection of TB clusters, outbreaks and possible transmission networks when combined with epidemiological data.

To date, WGS has primarily been used for surveillance purposes on a national level in the US. However, WGS can be employed for the identification of MTBC as well as for molecular detection of drug resistance. When carried out in a regulated environment the resulting data can be used for clinical management as is the current approach of at least one jurisdiction in the US. To be most effective, both WGS and the data analysis should occur quickly meaning that the starting material for DNA extraction needs to be as close to the initial diagnosis of TB as possible. At present, the typical starting material for WGS is a subculture. This is not ideal for clinical management due to the time required for isolation of MTBC from specimens. Ideally, WGS would be performed directly on patient specimens. However, the number of MTBC cells in patient samples can vary in proportion to the number of other cells present, and since current DNA extraction protocols are largely nonspecific, DNA from all cells in the specimen are extracted alongside MTBC DNA. In many cases, the non-MTBC DNA represents a majority of the total DNA which can limit the level of information obtainable about MTBC. With existing technology, a MTBC positive primary MGIT culture is potentially a better source material for WGS since it is closer to the patient than a subculture, but more enriched for MTBC than the primary specimen.

APHL in collaboration with CDC seeks to partner with state or local public health laboratories to evaluate WGS performed on MTBC positive primary MGIT cultures with residual volume (i.e. amount left after standard patient testing). Applicants may propose any jurisdiction—city, county, region, or state—from

which they will acquire residual material (at least 1 mL) from MTBC positive primary MGIT cultures. The jurisdiction(s) should have a combined total of at least 32 primary (i.e. diagnostic) MTBC positive cultures/year. For the purposes of this study, no more than three positive diagnostic cultures from the same patient should be used for sequencing. Laboratories awarded funding will extract and sequence DNA from MTBC positive primary MGIT cultures (minimum of 32 MTBC positive primary MGIT cultures, maximum number will be determined based on the number of selected sites and capacity of each site) and electronically deliver sequence files (FASTQ format) to DTBE. If the isolate used for WGS is also tested for first-line drug susceptibility, DNA should also be extracted from the no drug growth control/subculture and sequenced.

APHL and CDC are seeking, through this competitive announcement, to identify up to 10 state or local public health laboratories perform DNA extraction and WGS on MTBC positive primary MGIT cultures. This work will provide the data necessary to evaluate use of MTBC positive primary MGIT cultures as source material for generation of WGS data of sufficient quality and quantity for mycobacterial identification, molecular epidemiology and prediction of drug resistance. This project will aid in development of a potential strategy for a national system.

Eligibility

APHL is looking for up to 10 eligible laboratories including all member public health laboratories with the following capabilities, resources and facilities in place.

- Minimum of 32 MTBC positive primary MGIT cultures/year (can partner with other jurisdictions to meet this requirement) from at least 10 unique patients
- Capacity for isolating chromosomal DNA from MTBC suitable for WGS
- Established and demonstrated performance of WGS for bacterial pathogen(s)
- Sufficient equipment, laboratory space and workforce for the project

Anticipated RFP Schedule

June 27, 2019	–	RFP Issued
July 11, 2019	–	Informational Teleconference (Q&A)
July 15, 2019	**–**	**Letter of Intent Due to APHL (see below)**
August 8, 2019	–	**RFP Responses Due**
August 12-23, 2019	–	Proposal review completed
August 26-27, 2019	–	If needed, follow-up interviews and updated proposals due
August 30, 2019	–	Final review completed and awardees selected
September 16, 2019	–	Draft contracts submitted to APHL Legal Dept. for final internal review

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

Response Submittal

Confirmation of Intent to Respond

APHL requests that prospective applicants submit a brief email statement indicating an intent to submit a proposal. APHL must receive this email by no later than **5:00pm EST on July 15, 2019**

Final Response

APHL must receive complete responses by **5:00 pm EST on August 8, 2019**. Please see Proposal-Required Submissions section for items that must be included in the completed proposal. Applicants may send proposals via email to Anne.Gaynor@aphl.org

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

Award

APHL will select up to 10 laboratories to participate. Award amounts will depend on the total number of specimens tested with a minimum award of $4,000 and additional funding will be allocated based on invoicing at $250 per specimen tested with a minimum of 500,000 reads and WGS data successfully transferred to CDC. APHL will distribute awards in accordance with the terms of a contract administered by APHL. The final award amount will be based on total funding received by APHL, the number of specimens to be tested, and the number of PHLs selected for the project.

Term of Project

The project term will be from the date of notification through June 30, 2020. The expected contract term will cover the period from October 1, 2019 through June 30, 2020. APHL anticipates that from the date of notification to the start date of the contract, the selected site will work with APHL and the CDC work group to define the specimen set, review the proposal, and ensure mechanisms are in place for specimen and data transfer between the participated laboratory and the CDC.

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.

Due to the expected volume of applicants, a team of four subject matter experts (SMEs) from CDC DTBE and a panel for four APHL members from non-applicant public health laboratories will review complete proposals. Each application will be reviewed by two CDC DTBE reviewers and two APHL members. APHL will identify and select SMEs from CDC based on their familiarity with laboratory techniques and project requirements. APHL member experts will be identified from among the non-applicant PHLs by the APHL HHST Program Manager. They will have expertise in the laboratory testing methods described in this RFP. 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 E: 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/Appendix C section and will give a numeric score of up to 100 maximum points based on the scorecard template in Appendix D.

The evaluation team will give preference based on extensive experience with the test methods, ability to handle test volume, ability to comply with expectations laid out in Appendix A, and the ability to meet the 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 the members of the evaluation team, or among the 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 laboratories within 10 business days of the completion of the evaluation and will post the names of the recipient(s) to APHL's procurement website, www.aphl.org/rfp on the same day. Unsuccessful applicants will receive notification of these results by e-mail or by U.S. mail within 30 days of the date the name of the selected applicant is posted.

All applicant laboratories are 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. Laboratories must agree to comply with expectations outlined in Appendix A.

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

Proposal – Required Submissions

In order to be considered for selection, submit the completed response table (Appendix C) (font size ≥ 11pt, 1 inch margins, response table must not exceed 6 pages) and attach a letter of support from any collaborating laboratories. Additional Information and Deadlines for Applications Submission below.

Include a completed response table/Appendix C.

Include a completed and signed copy of Appendix B as an attachment.

If Applicable: Include a letter of support from any collaborating laboratories.

Additional Information and Deadlines for Application Submission

Applicants must direct all questions to Anne Gaynor at anne.gaynor@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 (www.aphl.org/rfp).

Applicants must submit applications to Anne Gaynor at APHL (anne.gaynor@aphl.org; 8515 Georgia Ave Suite 700, Silver Spring, MD, 20910; telephone: 240-485-2739; fax: 240-485-2700).

APHL will hold an optional teleconference on Thursday July 11, 2019 at 3:00pm 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 Call-in Information is below, or please contact anne.gaynor@aphl.org or infectious.diseases@aphl.org no later than 12:00pm ET on Thursday July 11, 2019 to be sent the calendar invitation.

Join Zoom Meeting
https://aphl.zoom.us/j/187003737

Call-in Information
+1-646-876-9923US OR
+1-669-900-6833US

Meeting ID 187 003 737

APHL must receive applications, attention Anne Gaynor by close of business (5:00pm ET) August 8, 2019. Either electronic or physical submission is acceptable. APHL will send an email acknowledging the receipt of each application; if you do not receive an acknowledgement within 48 hours, call 240-485-2739 to confirm receipt.

Appendix A: Using Growth from MTBC Positive Primary MGIT Culture as Source Material for Whole Genome Sequencing

Methods

1. It is necessary to extract chromosomal DNA from MTBC for WGS. Several methodologies can be found in the literature. As an example, the protocol used by the DTBE Laboratory Branch can be provided upon request via an email to APHL (anne.gaynor@aphl.org).
2. The Illumina MiniSeq/MiSeq/NextSeq are the preferred sequencing platforms for this study. Paired-end sequencing with read lengths of at least 150 bp and a minimum of 500,000 reads per specimen is required. If using the MiSeq, v3 chemistry with 250 bp paired-end reads is highly encouraged. The table below gives the maximum number of multiplexed specimens per run:

Instrument	Chemistry	Maximum number of specimens per run
MiniSeq	High-Output Kit	24
	Mid-Output Kit	8
MiSeq	MiSeq Reagent Kit v2	24
	MiSeq Reagent Kit v3 (250bp reads)	32

Procurement

The cost of reagents have been incorporated into the cost per specimen ($250). There will be no financial support for the procurement of equipment. Funding allocation is at the discretion of the awarded sites.

Data Management

Minimum acceptable quality scores are those defined in the specifications for the sequencing kit. Reports and sequencing files (FASTQ format) will be transferred to CDC electronically.

Performance Management and Evaluation

Sequence files (FASTQ format) should be delivered to CDC within two weeks of sequencing runs. Instructions for data transfer will be provided to selected laboratories and will likely utilize an SFTP site. Performance will be monitored by timeliness of responses to CDC and APHL requests and successful completion of the testing and reporting.

Reports

The laboratory will notify APHL and CDC prior to sequence file transfer by submitting a sequence run report via email. APHL will provide the sequence run report template for data collection which will include the following (or similar) elements for each specimen tested by WGS: specimen ID (standardized naming system will be implemented), date primary specimen received in laboratory, smear status of specimen (positive or negative), method used for identification of MTBC, date of MTBC identification, date of MGIT inoculation, date of MGIT positivity, time to positivity, growth indicator units when

removed from instrument, storage conditions of positive MGIT prior to identification, storage conditions prior to DNA extraction, date of DNA extraction, method of DNA library preparation, sequencing kit, sequence run identifier, date sequencing complete, cluster density, percentage of clusters passing filter , percentage of bases >Q30, estimated sequence yield, total number of reads passing filter, % indexing and date of sequence file (FASTQ) transfer to CDC.

A similar worksheet will be provided to capture information for any corresponding isolates from the DST no drug control for each MTBC positive primary MGIT culture tested.

Teleconferences

APHL, CDC and the awardee laboratories will participate in a kick-off teleconference, check-in calls as needed and a final call to conclude the study

Appendix B: Minimum Requirements

YES	NO	MINIMUM REQUIREMENT
		Does your laboratory receive at least 32 MTBC positive primary MGIT cultures/year (or will partner with other jurisdictions to meet this requirement and have included a letter of support in your application)?
		Does your laboratory have the capacity to isolate DNA from MTBC that is suitable for WGS?
		Does your laboratory have sufficient ancillary equipment, supplies, reagents, laboratory space, and workforce capability and capacity for the proposed work?

Signature: _____ Date: _____

Printed Name:

Appendix C: Response Table

To submit a proposal for consideration, please respond to the following questions using this table. Responses must use a font size ≥11 point and page margins of ≥1 inch) and a maximum of six (6) pages. A downloadable version will be available directly from the site for ease of use.

Applicant Name			
Topic	**Question**	**Response**	**Additional Comments**
Testing Algorithm	What is your annual volume of culture positive MTBC?		
	Briefly describe your laboratory's current mycobacteriology testing algorithm (e.g., AFB smear, nucleic acid amplification testing, culture, identification, DST)		
	Is the time to MGIT positivity tracked in your laboratory?		
	Are growth units recorded in your laboratory?		
	Briefly describe the protocol for setting up drug susceptibility testing in your laboratory (e.g. subculture from primary MGIT).		
Isolation of chromosomal DNA from MTBC	Does your laboratory currently isolate chromosomal DNA from MTBC?		
	Does your laboratory currently isolate chromosomal DNA from other bacterial pathogens?		

	What method/kit is currently used in your TB laboratory for isolation of chromosomal DNA from MTBC?		
	How long has your TB laboratory been using this method/kit for isolation of chromosomal DNA from MTBC?		
	How many times per month does your laboratory isolate chromosomal DNA from MTBC?		
	How many MTBC chromosomal DNA extractions are performed in your lab annually?		
	Has this method been used for existing WGS protocols in your laboratory and been shown to provide DNA of sufficient quality and quantity?		
	If your laboratory has no experience with MTBC, but does have experience with DNA isolation from other bacterial species, please describe this experience, including your annual specimen volume.		
	If your laboratory has no experience isolating chromosomal DNA, describe plans for DNA extraction and validation.		

WGS of MTBC or other bacterial pathogens	Are NGS libraries made in your TB laboratory or in a core facility?		
	Which kit is used for WGS library preparation?		
	How many times per month are libraries prepared for MTBC WGS? If none for MTBC, how many times per month for other bacterial pathogens?		
	Is WGS for MTBC performed in the TB laboratory? If not, where?		
	Which kit is used for MTBC WGS? If no MTBC WGS, which kits are used for other bacterial pathogens?		
	How many times per month is WGS performed for MTBC? If none for MTBC, how many times per month for other bacterial pathogens?		
	What is your annual volume for WGS of MTBC or other bacterial pathogens?		
Existing Infrastructure	Describe existing infrastructure that could be utilized for this project including equipment.		
Staff WGS Experience	Describe staff experience in WGS methods including isolation of chromosomal DNA and library preparation.		
Proposed Study Specimen Set	What is the total number of specimens		

	that will be sequenced for this project (see Appendix A for maximum numbers per run)? *Note that a minimum of 32 MTBC positive MGIT cultures is required to be considered for this award.*		
	Will specimens be from a single jurisdiction or multiple jurisdictions? If multiple, please list all contributors and how specimens will be shared (e.g., timeliness, volume).		
	How many MTBC positive MGIT cultures did each contributing jurisdiction have in 2018?		
Additional Comments			

Appendix D: Score Card

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

Category	Maximum Value	Score	Comments (REQUIRED)
1. Does the applicant have a minimum of 32 MTBC positive primary MGIT cultures/year (can partner with other jurisdictions to meet this requirement)? **Yes** (20 points), **No** (0 points); Has the applicant identified a jurisdiction, defined the number of culture positive cases in the jurisdiction, and defined a mechanism for obtaining the cultures? **Yes** (10 points), **No** (0 points)	30		Type comments here. (REQUIRED)
2. Does laboratory setup DST on all culture positive isolates? **Yes** (10 points), **No** (0 points)	10		Type comments here. (REQUIRED
3. Does the applicant have sufficient capacity and experience performing extraction of chromosomal DNA from MTBC to comply with the requirements described in Appendix A of the RFP? Does applicant have capacity to acquire these skills? 3a. Does staff have sufficient experience in extraction of chromosomal DNA for WGS? **Yes** (5 Points), **No** (0 Points); 3b. Is the current/proposed chromosomal DNA extraction method likely to yield DNA of sufficient quality for WGS? **Yes** (5 Points), **No** (0 Points); 3c. What is the experience with MTBC DNA extraction for WGS? **High:** routinely (>10 extractions per month) isolates chromosomal DNA from MTBC and DNA is of sufficient quality and quantity for the proposed sequencing method (15 points); **Moderate:** does not routinely isolate chromosomal DNA from MTBC but has a validated protocol in place or has extensive experience with isolating chromosomal DNA from other bacterial species (10 points); **No Experience:** does not have experience in or a validated protocol for isolating chromosomal DNA from MTBC or other bacterial species (0 points)	25		Type comments here. (REQUIRED)

4. Does the applicant have sufficient capacity and experience performing WGS of MTBC or other bacterial pathogens to yield high quality sequence data and comply with the requirements described in Appendix A of the RFP? 4a. Does staff preparing libraries have sufficient experience? **Yes** (5 Points), **No** (0 Points); 4b. Does staff have sufficient experience in WGS methods? **Yes** (10 Points), **No** (0 Points); 4d. What is the applicants' monthly volume of WGS? **High:** routinely sequences >50 MTBC isolates or other bacterial pathogens per month (20 Points); **Moderate**: routinely sequences 10-50 MTBC isolates or other bacterial pathogens per month (15 Points); **Limited:** has some experience, but does not routinely sequence MTBC or other bacterial pathogens (10 points); **No experience**; (0 points)	35		Type comments here. (REQUIRED)
TOTAL SCORE	**100**	**____**	

Appendix E: 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.

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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).

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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.

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_____

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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.