

Request for Proposals: National Influenza Surveillance Reference Centers

Application Due Date: August 14, 2015

Submit to: Stephanie Chester, Manager of Influenza Programs
(Stephanie.chester@aphl.org)

Summary

The Association of Public Health Laboratories (APHL), in cooperation with the U.S. Centers for Disease Control and Prevention (CDC) Influenza Division (ID), is seeking to identify three (3) state or local public health laboratories (PHLs) that will serve as national influenza surveillance reference centers to provide testing on viruses submitted by other public health laboratories and vaccine effectiveness study sites to support national influenza surveillance initiatives. The Reference Centers will serve as an extension of the CDC ID Virus Surveillance and Diagnosis Branch (VSDB) and will provide services that are complementary to those at CDC based on methods and protocols that will be provided by APHL and CDC. Services provided by the reference centers will include: 1) influenza virus isolation and propagation; 2) neuraminidase inhibition testing; and 3) whole genome sequencing. Virus isolation and neuraminidase inhibition testing will be initiated immediately upon award at all three selected reference centers. Whole genome sequencing will be introduced in a phased approach one reference center at a time. Specifically, this Request for Proposals (RFP) seeks to identify one reference center that can start whole genome sequencing on surveillance specimens immediately at the start of the 2015-16 influenza season (approximately October 1, 2015). The other two selected reference centers will be given some funding and technical support to bring on influenza virus whole genome sequencing at a later date to be determined. Please see Figure 1 for a summary of the whole genome sequencing implementation process. Services will be provided at no cost to the submitting laboratories. Funding will be awarded via a contract with APHL.

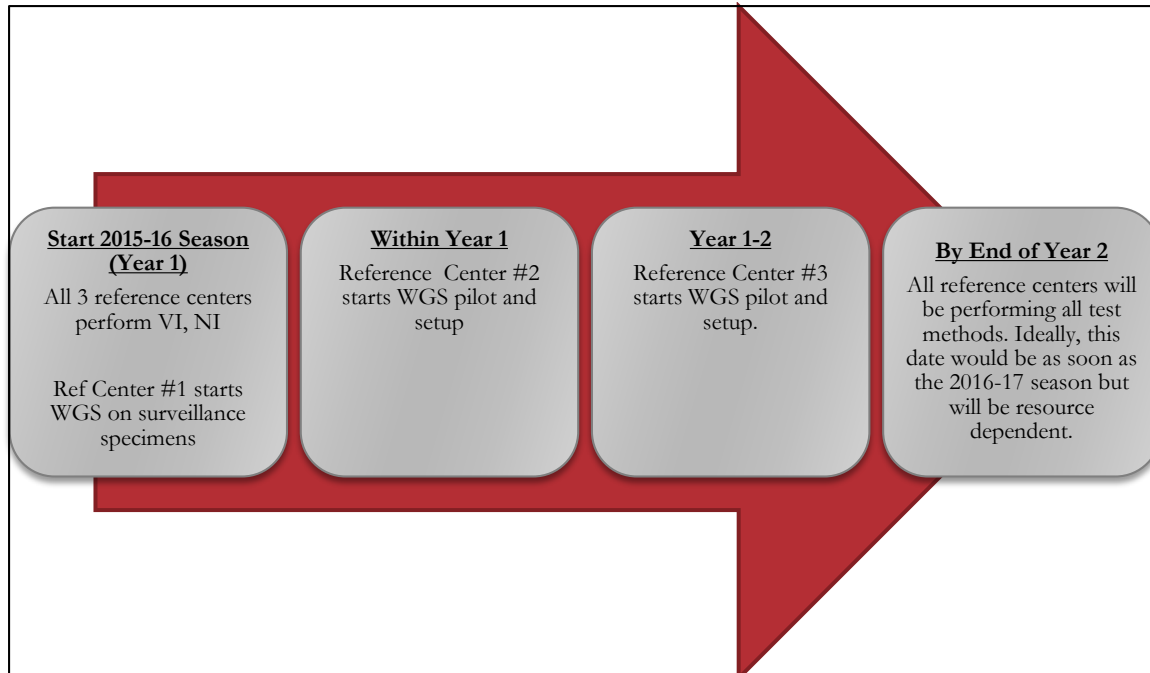


Figure 1

Background

State and local public health laboratories are the foundation of the US influenza surveillance system. Specimens collected and tested by PHLs are reported to CDC and included in [national surveillance data](#) to describe which viruses are circulating and at what prevalence. Furthermore, PHLs play a critical role in the vaccine strain selection process by providing specimens to CDC for further antigenic and genetic characterization. Data from PHLs and the viruses submitted to CDC are compiled and shared with the international community to help determine vaccine compositions for future seasons.

Antigenic characterization of viruses for vaccine composition meetings is a demanding and time sensitive process that requires large volumes of high titer viral isolates. Data from an APHL [survey](#) in 2012 indicate that few PHLs are still performing virus isolation for influenza viruses and many no longer have staff with sufficient experience in this traditional method. To meet national surveillance goals, APHL and CDC have supported three (3) national influenza surveillance reference centers to culture and isolate influenza viruses since 2009. Additionally, since 2011, these reference centers have also performed neuraminidase inhibition testing on viral isolates to detect phenotypic changes in viruses that indicate reduced inhibition of antiviral therapeutics.

Much value has been realized both at the PHL level and at the national level for maintaining these reference centers. Namely, these reference centers serve as a source of expertise for virus culture in the PHL community. They have served as an extension of CDC, increasing the overall national capacity for processing specimens for vaccine strain selection and detecting antiviral resistant viruses. In recent years, the reference centers have also proved valuable with respect to preparedness planning and continuity of operations plans. When the federal government shut down in October 2013, the reference centers started their services a month early so critical early season specimens that would usually be sent directly

to CDC were processed and ready for further testing at CDC as soon as the government reopened. Thirty-eight (38) resistant and potentially resistant viruses have been detected through the reference centers leading to important epidemiologic investigations and genetic analyses.

The ability of influenza viruses to reassort and mutate also requires the use of genetic test methods to monitor and analyze these changes. The 2014-15 influenza season proved to be a challenging season with drift of circulating H3 viruses leading to difficulties with antigenic characterization methods. To provide critical analysis of these drifted viruses, CDC performed genetic analysis using next generation sequencing (NGS) on more viruses than any previous season. In light of this and in an effort to shorten the lag time between collection and full characterization of influenza viruses, CDC and APHL want to establish NGS capacity in the PHL community. Although NGS is very informative, the time and expense in generating the data is considerable and can be hard to maintain for influenza surveillance. APHL and CDC also recognize that this technology and expertise is not readily available at many PHLs at the current time. Therefore, until the expertise is more readily available and test methods are less costly, there are only sufficient federal funds to support a limited number of laboratories for influenza NGS.

To address this, APHL and CDC are seeking to identify one (1) reference center (herein, referred to as “Reference Center #1”) to perform whole genome sequencing on surveillance specimens starting with the 2015-16 influenza season in addition to the other reference center testing services described above. The other two (2) selected reference centers (herein, referred to as “Reference Centers #2-3”) will be given some funding and technical support to bring on influenza whole genome sequencing in a gradual, phased approach over the latter portion of Year 1 and through Year 2 of this project.

Eligibility

Eligible laboratories include all public health laboratories with the following capabilities and facilities in place. Specific expectations regarding the methodologies to be used by the reference centers are outlined in Appendix A. All applicants are required to agree to the minimum requirements outlined in Appendix B.

- Infrastructure (e.g., equipment and laboratory space) for maintaining cell culture, virus isolation and neuraminidase inhibition services
- Established cell culture and influenza virus isolation and propagation capacity, preferably with MDCK and MDCK SIAT 1 cells
- Availability of adequate laboratory space and basic laboratory equipment to conduct whole genome sequencing
 - To be eligible as Reference Center #1 to perform all three (3) test methods in Year 1 at the start of the 2015-16 influenza season, the laboratory must have all equipment, protocols and personnel in place to perform influenza whole genome sequencing and transmit data to CDC via the APHL Informatics Messaging Services (AIMS) environment as described further in Appendix A.
 - To be eligible as Reference Centers #2-3, it is **not** a prerequisite to have a next generation sequencer for whole genome sequencing, but the laboratory should have

thermal cyclers and adequate space for an Illumina MiSeq, Qiagen QIAxcel, and a few other items of smaller footprint.

- Sufficient workforce capacity for expanded testing volume or the ability to hire additional qualified staff
- Willingness to alter or amend existing testing protocols and adhere to CDC-provided protocols

Anticipated RFP Schedule

At this time, APHL anticipates the following schedule:

July 15, 2015	– RFP issued
July 23, 2015, 2pm ET	– Informational teleconference for RFP questions and answers
August 14, 2015	– RFP responses due
August 21, 2015	– Proposal review completed
August 24-27, 2015	– If needed, follow-up interviews and updated proposals due
August 28, 2015	– Final review completed and reference center selection
September 1, 2015	– Begin training and season preparations
October 1, 2015	– Contracts finalized and surveillance testing begins

Any modification to this anticipated schedule will be communicated on APHL’s procurement website and via an email blast to the PHLs.

Award

Funding will be distributed via an annual contract with APHL. See Term of Project below for details on the anticipated contract period.

Reference Center #1 will perform all three (3) test methods in Year 1 and will be awarded up to \$380,000.

Reference Centers #2-3 will be awarded up to \$230,000 in Year 1 for virus isolation and neuraminidase inhibition testing.

Reference Center #2 will be awarded up to \$300,000 depending on infrastructure and training needs for developing NGS capabilities and capacity.

Reference Center #3 will be funded to bring on NGS testing based on availability of funds in Year 1 or, more likely, Year 2 of this project. Funding amount will be dependent both on infrastructure and training needs for developing NGS capabilities and capacity, and on the funding that APHL receives in Year 2.

Laboratories selected to serve as a reference center will receive a notice of award from APHL. This notice of award will indicate the reference center “number” (i.e., 1-3), as described above, that was selected for that laboratory so as to indicate when whole genome sequencing will be incorporated into that laboratory’s project plan. The reference center number assigned to a selected laboratory will be determined by the evaluation team after taking into consideration overall scoring and whole genome specific question scoring. See Evaluation Process below for more details on the review scoring.

Use of funds: Recipient laboratories should use the funding for necessary equipment upgrades or expansions, validation of new testing services, testing of referred specimens beginning October 2015, and personnel time required to conduct these activities.

Term of Project

Year 1 of the project will run from October 1, 2015 to June 30, 2016. APHL anticipates the potential for annual renewals for a period of up to four (4) additional years (with each additional funding year running from July 1 to June 30) for a total of five (5) years. Each of the potential annual renewals will depend on the funding received by APHL and by CDC programmatic needs in that funding year.

Request for Proposals – Required Submissions

To submit a proposal to become a national influenza surveillance reference center, please respond to the following questions. Responses should be limited to no more than ten (10) single spaced pages (font size ≥ 11 pt. and page margins $\geq .5$ inches) and must comply with the submission requirements set out in Additional Information and Deadlines for Application Submission below.

1. Please describe the current methodology used in your laboratory for isolation of influenza viruses. Include information on how long the methodology has been in use, the cell lines used, how often it is performed, your annual and maximum volume, the amount of experience your laboratory staff has in using that methodology and any training your staff has received. If possible, please also include the nature of any experience your laboratory has with performing influenza virus isolation with MDCK and/or MDCK-SIAT 1 cells in particular. Please also describe any experience with hemagglutination titring.
2. What is the current average turnaround time (TAT) for influenza virus isolation? Please describe TAT from receipt to inoculation and from receipt to harvest.
3. Please describe the nature and extent of any experience with specimen accessioning for special projects outside of routine public health laboratory testing and with database data entry, queries, reports and management.
4. Please describe the current methodology, if any, used in your laboratory for phenotypic/functional influenza antiviral resistance testing, specifically neuraminidase inhibition assays. Include information on which assay is used, how long the methodology has been in use, how often it is performed, your annual and maximum volume, the amount of experience your laboratory staff has in using that methodology and any training your staff has received.
5. Please describe the nature and extent of any experience with whole genome sequencing in your laboratory (note, does not have to be influenza specific). Include information on which assay is used, how long the methodology has been in use, how often it is performed, your annual and

maximum volume, the amount of experience your laboratory staff has in using that methodology and any training your staff has received. Please also describe any existing infrastructure and personnel that could be utilized for this project including equipment, informatics and bioinformatics. For equipment and personnel availability, please note that the influenza assay requires about 3-5 days of run time on an Illumina MiSeq and the volume of specimens can be up to 96 per week. If your laboratory does not currently have whole genome sequencing available in-house, please specify the equipment and training needs your lab would have as well as the understanding of the commitment required to implement this assay.

6. If selected, would your laboratory be able to modify IT systems to transmit whole genome sequencing data via web services, direct secure messaging and APHL's AIMS S3 Utility/SDK? Please provide a letter of support signed by your IT Director or other similar IT authority stating they are in support of this project and are willing to work with APHL to establish connectivity to APHL's AIMS S3 Utility/SDK. Please indicate who would be the main IT point of contact for this project.
7. Does your laboratory have staff with the subject matter expertise to provide guidance and interpretation of hemagglutination (HA) titers, neuraminidase inhibition IC50 curves and basic quality control interpretation of whole genome sequencing results? Please describe the qualifications and experience of these staff members.
8. If selected, would your laboratory be willing to evaluate and incorporate additional new technologies as they become available? Please briefly describe your experience in participating in method or platform evaluation(s).
9. Briefly describe your laboratory's experience, if any, in providing reference testing (not limited to influenza testing) for other public health laboratories in a shared service model including but not limited to coverage for a limited period of time to assure continuity of operations. Include information on which reference center services you provide, how long you have served as a reference center, how your staffing been structured to support reference center testing volumes while balancing jurisdiction-specific testing priorities, your testing volume, and the nature of any issues or considerations, if any, for entering into a contract with APHL for reference center testing services.
10. Describe your laboratory's ability to absorb increased workload in performing all three test methods described here.
11. 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 and a proposed per specimen/isolate cost for each test method that includes reagents, staff time and any other charges and overhead. This budget may be forecasted based on an anticipated volume of 1000 specimens over the season for each test method for comparison purposes.
12. Include a signed copy of Appendix B as an attachment.

Evaluation Team

APHL staff, led by the Influenza Program Manager, will conduct an initial review of all proposals for completeness. Any incomplete application on the proposal due date specified in 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 four (4) influenza subject matter experts (SMEs) from CDC ID and a panel of four (4) APHL members selected from non-applicant public health laboratories. SMEs from CDC will be identified and selected by the Director of CDC Influenza Division based on their familiarity with laboratory techniques and project requirements. APHL member experts will be identified from among the non-applicant PHLs by APHL's Influenza Program Manager and will have expertise in the laboratory testing methods described in this RFP and familiarity with APHL reference center structure. Once potential reviewers have been identified, APHL's Senior Director Public Health Systems will have final approval over the review team's composition.

Evaluation Criteria

Proposals will be evaluated based on responses to the questions above and will receive a numeric score of up to 100 maximum points based on the scorecard template in Appendix C. Laboratories will be given preference based on more extensive experience with the test methods, ability to handle increased volume, existing in-house subject matter expertise, experience and past performance serving as a reference center, ability to comply with expectations laid out in Appendix A and ability to meet the minimum expectations outlined in Appendix B.

The answers provided by a laboratory to items 8 through 12 in the Request for Proposals – Required Submissions section above may be utilized by the review committee to differentiate between proposals that otherwise have substantially similar evaluation criteria. If all other evaluation criteria are equivalent, preference will be given to applicants that would diversify APHL's funding allocation and provide geographical spread. The

Some of the ranking categories listed on the scorecard template in Appendix C require no explanation (such as “no experience” or the categories in item 4 on the scorecard). The remaining ranking categories noted on the scorecard template have the following meaning:

- “Excellent” – The laboratory exceeds expectations for capacity and has extensive experience performing the methods described.
- “High” – The laboratory meets or exceeds expectations for capacity and has extensive experience performing methods similar to the ones described and would easily be able to translate that experience to this project.
- “Moderate” – The laboratory has sufficient capacity and some experience with the methods described.
- “Low” – The laboratory may not have sufficient capacity and has little experience with the methods described.
- “Very experienced” – The laboratory has at least three (3) years of experience as a reference center, may provide more than one reference center service, demonstrates strong understanding of reference center requirements from an infrastructure and staffing perspective.
- “Some experience” – The laboratory has than three (3) years of experience as a reference center, may only provide one reference center service.

Evaluation Process

The entire review will be conducted via a combination of email communication between APHL's Influenza Program Manager and the members of the evaluation team or among the evaluation team members and teleconference and/or webinar evaluation sessions. APHL's Influenza 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. These interviews and any supplemental information would 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 diversity APHL's funding allocations. In addition, the evaluation team may receive documentation from APHL staff on an applicant's past performance as an influenza reference center or in other reference center capacities noted in this RFP as part of the evaluation criteria.

Post-Evaluation Procedures

The selected laboratories will be notified by APHL staff within ten (10) business days of the completion of the evaluation and the names of the three recipients will be posted 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 winning vendor 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 laboratories 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 reserve the right to tour the facilities to assess compliance with requirements for testing and/or have a teleconference with applicant laboratories. Post award, monitoring site visits may be conducted to include an assessment of continued compliance.

Additional Information and Deadlines for Application Submission

All questions should be directed to Stephanie Chester at stephanie.chester@aphl.org. Questions received from interested PHLs, together with the answers provided by APHL or CDC staff will be posted to APHL's procurement website (www.aphl.org/rfp).

Applications should be submitted to Stephanie Chester at APHL (Stephanie.chester@aphl.org; 8515 Georgia Ave Suite 700, Silver Spring, MD, 20910; telephone: 240-485-2728; fax: 240-485-270T0). For electronic submission, copy Kelsey Vellente (Kelsey.vellente@aphl.org). Applications must be received at APHL, attention Stephanie Chester by close of business August 14, 2015. Either electronic or physical submission is acceptable. APHL will send an email acknowledging the receipt of your application; if you do not receive an acknowledgement within 48 hours, call 240-485-2740 to confirm receipt.

An optional informational teleconference will be held Thursday, July 23, 2015 at 2:00 pm 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.

For the teleconference there are a limited number of lines, please use only one (1) line per laboratory.

Phone: 877-915-4937 Passcode: 1911175#

Appendix A: Expectations for National Influenza Surveillance Reference Center Testing

Cell Culture

- **Methods:** Currently, MDCK and MDCK-SIAT 1 cells are the selected method for performing influenza virus isolation due to the availability of SOPs and ID/VSDB experience with the method. The reference center must be able to grow and maintain both cell lines at sufficient volume to inoculate up to 100 viruses per week into T75 flasks. Both cell lines must be maintained at all times in order to process all submissions in a timely manner. Currently MDCK cells are used for influenza A/H1N1pdm09 and B viruses; MDCK-SIAT 1 cells are used for influenza A/H3 viruses. SOPs used will be identical to those used by the ID/VSDB virus isolation laboratory.
- **Procurement:**
 - Cell lines and reagents used will be identical to those used by the ID/VSDB virus isolation laboratory or CDC-approved equivalents.
 - The laboratory must be able to enter into a material transfer agreement (MTA) to acquire MDCK-SIAT 1 cells. CDC will provide both cell lines free of charge but the MTA is required.
 - The laboratory must be able and willing to adopt a new cell culture line if CDC determines that a different cell line will produce better antigenic characterization results for vaccine strain selection for a specific influenza type and/or subtype.
- **Volume/Capacity:** Influenza activity will impact volume demands for both cell lines. Throughout the season, the laboratory must be able to monitor and predict the number of T75 cell culture flasks needed based on submission schedules and influenza activity. The reference center must be able to grow and maintain both cell lines at sufficient volume to inoculate up to 100 viruses per week.
- **Turnaround Time:** Cell culture stocks must be propagated and maintained to support virus inoculation once per week.

Virus Isolation

- **Methods:** SOPs used will be identical to those used by the ID/VSDB virus isolation laboratory.
 - The laboratory will be available to perform daily checks of CPE and HA titration and will schedule virus inoculations to ensure critical CPE checking and HA titration days fall on days with staff availability. The laboratory must be able to still perform CPE checks and HA titration on weeks with holidays but inoculation schedules can be adjusted slightly to avoid coming in on actual holidays whenever possible. The laboratory will notify CDC and APHL of holiday week schedules/change in procedures on the monthly teleconference the prior month or by email at least 3 weeks in advance.
 - The reference center will follow-up with submitters if information on a specimen is incomplete or seems incorrect. The laboratory will never inoculate a virus for which the subtype is unknown or inconclusive, a suspect novel virus or co-infections. The laboratory will forward these specimens to CDC within 48 hours, preferable 24 hours for diagnostic testing.
- **Procurement:** Cell lines and reagents used will be identical to those used by the ID/VSDB virus isolation laboratory. The laboratory must have reliable access to timely shipments of guinea pig and turkey blood for HA titration.

- **Volume/Capacity:** The reference center must be able to inoculate up to 100 viruses using T75 flasks per week.
- **Turnaround Time:** The reference center must inoculate all viruses received within a week of specimen receipt. Specimens received after the day of inoculation should be inoculated in the following week. If a backlog occurs, the reference center will notify CDC and APHL immediately and prior to inoculation so feedback can be provided regarding prioritization of specimens based on CDC needs. Specimens and virus isolates with sufficient titers (as defined by CDC protocols) will be shipped to CDC once per week.
- **Data Management:**
 - Laboratory must have proficiency using databases and will enter specimens received into the CDC provided virus isolation database upon receipt (< 48 hours after receipt). Once released, the laboratory must adapt a newly implemented FluLIMS system for specimens accessioning. ID/CDC will provide necessary training for the new specimen management system and only basic internet requirements are needed (i.e., Internet Explorer 11).
 - The reference center will electronically transmit the database to CDC via FTP on a weekly basis and make weekly shipments of specimens to CDC using proper IATA shipping regulations.
 - The laboratory will maintain cell culture passage worksheets and submit copies of these to CDC with shipments.
 - Staff must demonstrate ability to perform accessioning and database entry.
 - The reference center must submit electronic weekly reports and a more comprehensive monthly report to APHL and CDC. The laboratory will monitor harvest rates, titers and turnaround times.
 - The reference center will work with CDC on troubleshooting if any issues occur.

Neuraminidase Inhibition (NI) Testing

- **Methods:** The NA-Fluor™ Influenza Neuraminidase Inhibition Assay Kit is the selected method for NI reference center testing due to standardization of IC50 values that CDC and previous reference centers were able to achieve, making it a reliable assay to employ at multiple laboratories while combining and reporting results in one national report. Additionally, the CDC/ID/VISDB has extensive experience with this method.
 - SOPs used will be identical to those used by the CDC/ID/VISDB.
 - For the 2015-16 season, the reference centers will perform this assay against up to four (4) antiviral therapeutics: peramivir, zanamivir, oseltamivir and laninamivir.
 - The laboratory must successfully complete a proficiency test panel of reference viruses prior to starting testing on surveillance specimens.
 - The laboratory must prepare and test a large stock of two reference viruses provided by CDC (H1N1pdm09 with and without H275Y) to be included in each NI assay run for quality control.
 - The laboratory is responsible for repeat testing of viruses due to technical errors leading to unacceptable results and IC50 curves. If approved by APHL and CDC, the laboratory will be compensated for repeat testing for viruses that show reduced inhibition.
- **Procurement:**
 - NA-Fluor kits, equipment, reagents and reference viruses used will be identical to those used by the CDC/ID/VISDB or CDC-approved equivalents.
 - Laboratory must purchase the following antiviral drugs: peramivir, zanamivir, and oseltamivir from commercial sources (no MTA is required); laninamivir can be obtained via a MTA. CDC and APHL can provide contact information for laninamivir. During the first

year, CDC will be able to provide a small amount of laninamivir while an MTA's execution is pending.

- **Volume/Capacity:** The reference center must be able to test up to 100 viruses per week.
- **Turnaround Time:** The laboratory may batch samples on a weekly basis but samples should be tested within 7 business days of virus aliquoting for storage and shipment.
- **Data Management:** The laboratory must upload data on a weekly basis to an FTP site and notify CDC and APHL of the upload. In the email notification, the laboratory will notify CDC and APHL of any viruses exhibiting reduced inhibition or ones with abnormal curves that may be due to technical error.

Whole Genome Sequencing

For selection as a reference center the following items do not need to be in place currently, but the laboratory must be able to implement and maintain these requirements with some, but not necessarily full, financial support and technical assistance from CDC and APHL. Any proposal should clearly outline what is already in place or similar experiences that demonstrate the laboratories ability to implement these expectations as well as what support financial and technical would be needed from APHL and CDC to achieve the objectives. This is a time and financial resource intensive undertaking therefore labs without existing capacity should demonstrate understanding of what it will take to bring on board and what resources can be dedicated to this effort.

1. **Methods:** The Illumina MiSeq is the selected NGS platform for influenza reference center whole genome sequencing. The Qiagen QIAxcel Advanced System is the selected platform for gel analysis used in QC and normalization steps of the influenza whole genome sequencing protocol. Other methods, including bioinformatics software, are still under evaluation, but the reference centers will be expected to use standardized methodologies identical to those used by the CDC/ID. This is a new testing service for the national influenza surveillance reference centers and as such selected reference centers need to be flexible and willing to pilot new methodologies, equipment, reagents and software until an ideal solution is reached.
2. **Procurement:** Equipment and reagents will be identical to those used by the CDC/ID. Some financial support will be provided to initially procure equipment and reagents to establish capacity. Once established, the cost of reagents will be incorporated into per specimen reimbursement.
3. **Volume/Capacity:** The reference center must be able to test up to 94 samples plus 2 controls per week (i.e., a full sequencing run).
4. **Turnaround Time:** The laboratory may batch samples on a bi-weekly basis. The influenza assay requires about 3-5 days of run time on an Illumina MiSeq.
5. **Data Management:** The CDC/ID recently established a mechanism that allows the electronic sharing of influenza sequencing data, leveraging cloud-based computing (see Figure 2). Reference Centers will need to establish a connection to the APHL Informatics Messaging Services (AIMS) cloud-based environment and have adequate local server space for temporary storage of files to transmit sequence data to the CDC. Additionally centers will have open access to ClarityLIMS (a genomic focused LIMS) and a suite of bioinformatics analysis tools provided by APHL and CDC in the AIMS environment. The reference center must be prepared to appoint staff who will be trained to use these tools and perform quality control analysis, results interpretation and data transfer. Due to the complexity of transferring whole genome sequencing data and investment CDC and APHL have already put into the current CDC/ID model, selected

reference centers will need to be able to transmit sequencing data using the following mechanisms available via AIMS:

- Web Services,
- Direct Secure Messaging,
- And ultimately AIMS S3 Utility / SDK.

APHL and CDC will ensure the financial support for the electronic transmission of data to CDC, access to ClarityLIMS and the bioinformatics analysis tools. Ultimately, data will be transferred in real-time via AIMS, but until this capacity is established, the reference center is expected to transmit data via an interim solution (e.g., FTP) within 48 hours of completing a run.

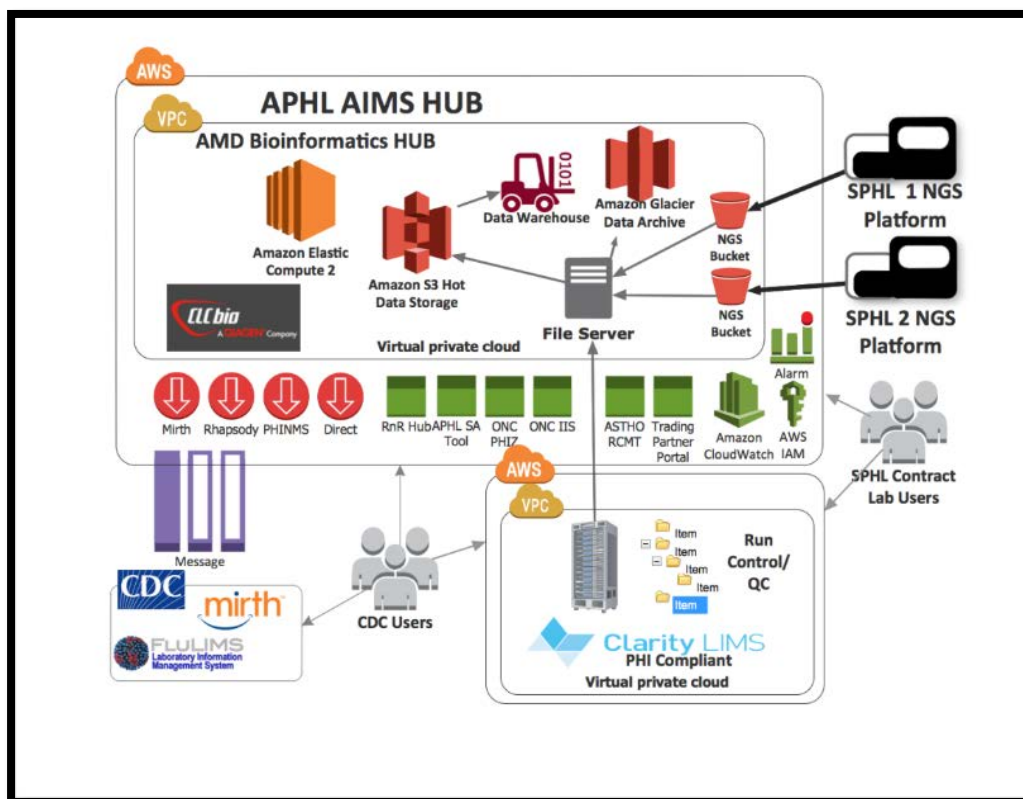


Figure 2. Data Transfer Architecture for Influenza Reference Center WGS Testing

Performance Monitoring and Evaluation

- Virus Isolation:** The reference center must submit electronic weekly reports and a more comprehensive monthly report to APHL and CDC. The laboratory will monitor and submit to APHL and CDC harvest rates, titers and turnaround times.
- Neuraminidase Inhibition:** The reference center must submit electronic notices of data upload and a more comprehensive monthly report to APHL and CDC. The laboratory will monitor and submit to APHL and CDC number and percent of viruses showing reduced inhibition, number of specimens tested and turnaround times. Prior to starting surveillance testing, the reference center must successfully complete a proficiency panel each year.
- Whole Genome Sequencing:** During pilot and setup phases, performance will be monitored by timeliness of responses to CDC and APHL requests, satisfactory results on a limit of detection panel and successful completion of a proficiency panel. Once active surveillance testing starts, the

reference center must submit electronic notices of data transfer and a more comprehensive monthly report to APHL and CDC. The laboratory will monitor and submit to APHL and CDC number of specimens tested and turnaround times.

Site visits and teleconferences

- As needed, CDC and APHL will conduct a site visit for training new laboratories on virus isolation and neuraminidase inhibition with CDC's protocols and to ensure surveillance testing is ready to start. 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 and review of worksheets and database.
- CDC and APHL will conduct a training site visit for each laboratory as whole genome sequencing capabilities are added. Additional site visits or training at CDC may be conducted depending on challenges that arise during the onboarding process for the new technology.
- APHL in collaboration with CDC will host a monthly teleconference for virus isolation and neuraminidase inhibition which must be attended by the reference centers to provide status updates and discuss any ongoing challenges and potential solutions.
- During implementation of whole genome sequencing, APHL and CDC will convene bi-weekly calls to work through challenges and keep project momentum going. Once testing is established, there will be separate monthly calls for sequencing until all three reference centers have this capability then it will be incorporated into the virus isolation and neuraminidase inhibition monthly calls.

Appendix B: National Influenza Surveillance Reference Center Minimum Requirements

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. If your laboratory cannot respond “yes” to one or more of the minimum requirements, your laboratory does not meet the minimum qualifications required to apply for this award.

YES	NO	MINIMUM REQUIREMENT
<input type="checkbox"/>	<input type="checkbox"/>	Does your laboratory currently perform in-house cell culture for the purposes of influenza virus isolation?
<input type="checkbox"/>	<input type="checkbox"/>	Does your laboratory have the infrastructure currently in place or the ability to adapt it to perform all three (3) test methods outlined in Appendix A?
<input type="checkbox"/>	<input type="checkbox"/>	Does your laboratory have sufficient space for expansion/purchase of additional equipment if necessary?
<input type="checkbox"/>	<input type="checkbox"/>	Does your laboratory have sufficient workforce capacity for expanded testing volume or the ability to hire additional qualified staff?
<input type="checkbox"/>	<input type="checkbox"/>	Would your laboratory be willing to alter or amend existing testing protocols at the request of APHL and CDC?
<input type="checkbox"/>	<input type="checkbox"/>	Would your laboratory be willing to accept at least annual site visits from APHL and/or CDC?
<input type="checkbox"/>	<input type="checkbox"/>	Would your laboratory be willing to increase the frequency with which certain methods are performed in your laboratory if required by APHL and CDC to meet expected turnaround times?
<input type="checkbox"/>	<input type="checkbox"/>	Does your laboratory have a letter of support from your IT department to establish connectivity to APHL's AIMS S3 Utility/SDK environment and a designated IT staff member to support this activity?
<input type="checkbox"/>	<input type="checkbox"/>	Does your laboratory have staff with classical virology expertise to help with troubleshooting and interpretation of atypical test results?
<input type="checkbox"/>	<input type="checkbox"/>	Is your laboratory able to enter into material transfer agreements in a timely manner?

Appendix C: National Influenza Surveillance Reference Center RFP 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)
<p>1. Does the applicant have sufficient capacity and experience performing cell culture to comply with the requirements described in Appendix A of the RFP? Consider experience with described cell lines, methods and experience of existing staff.</p> <p>Excellent = 13-15; High= 9-12; Moderate =5-8; Low =1-4; No experience = 0</p>	15		Type comments here. (REQUIRED)
<p>2. Does the applicant have sufficient capacity and experience performing influenza virus isolation to comply with the requirements described in Appendix A of the RFP? Consider experience with described method(s), experience of existing staff.</p> <p>Excellent = 13-15; High= 9-12; Moderate =5-8; Low =1-4; No experience = 0</p>	15		Type comments here. (REQUIRED)
<p>3. Does the applicant have sufficient capacity and experience performing neuraminidase inhibition to comply with the requirements described in Appendix A of the RFP? Consider experience with described method(s), experience of existing staff.</p> <p>Excellent = 13-15; High= 9-12; Moderate =5-8; Low =1-4; No experience = 0</p>	15		Type comments here. (REQUIRED)

Appendix C

<p>4. Does the applicant have sufficient capacity and experience performing influenza WGS to comply with the requirements described in Appendix A of the RFP? Consider experience with described method(s), experience of existing staff. If the applicant does not currently have influenza WGS, evaluate their experience with other pathogens and/or their understanding of what is required to bring the test service in-house.</p> <p>High/Has in-house influenza WGS capability and capacity = 11-15; Moderate/Has other (non-flu) in-house WGS capability and capacity 6-10; Low/Demonstrates Understanding of what is required to implement WGS and staff expertise and capacity to establish capacity =1-5; No experience = 0</p>	15	Type comments here. (REQUIRED)
<p>5. Does the applicant demonstrate the ability to increase testing capacity for all required methods? Consider the available of existing staff, equipment and space and the ability of the laboratory to purchase additional equipment or hire additional staff.</p> <p>Excellent = 13-15; High= 9-12; Moderate =5-8; Low =1-4; No experience = 0</p>	15	Type comments here. (REQUIRED)
<p>6. Does the applicant demonstrate the ability to regularly meet target turnaround times as listed in Appendix A?</p> <p>Excellent = 13-15; High= 9-12; Moderate =5-8; Low =1-4; No experience = 0</p>	15	Type comments here. (REQUIRED)
<p>7. Rate the applicant's level of experience in providing reference testing services for other public health laboratories.</p> <p>Very experienced = 7-10 points; Some experience = 3-6 points; No experience = 0-2 points.</p>	10	Type comments here. (REQUIRED)
TOTAL SCORE	100	