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**British Columbia's
Pandemic Influenza Response Plan (2012)**

**Pandemic Plan for British Columbia Public
Health Microbiology & Reference
Laboratory & Networks**

September 2012

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Outbreak Coordinator, technical staff and others in the Public Health Microbiology & Reference Laboratory, PHSA Laboratories.

This document will be reviewed annually by the Public Health Laboratory Director or designates, to meet our ongoing international (College of American Pathologists) and provincial (Diagnostic Accreditation Program) accreditation requirements.

1. GENERAL

1.1 Purpose

The purpose of this document is:

- To provide a framework and guidance for planning of a response to pandemic Influenza A for the Public Health Microbiology & Reference Laboratory (BCPHL), Provincial Health Services Authority (PHSA) Laboratories, as well as its public health laboratory partners in all other Health Authorities (HA) in British Columbia (BC).
- To identify laboratory services required to meet national laboratory standards for a pandemic response.
- To provide readily accessible general, laboratory related sources of information that will assist in implementing optimal and safe laboratory practices for pandemic response.
- To provide alignment for other related BCPHL plans such as the BCPHL Pandemic Plan, and the BCPHL Business Continuity Plan.

1.2. Background

Influenza A, a seasonal, respiratory communicable disease, appears in a pandemic form every few decades. The potential impact of global pandemic influenza ranges from relatively mild, such as in 2009, to devastating, such as in 1918-19.

Although most uncomplicated influenza presents as a self-limiting disease, severe cases, atypical presentations and epidemics occur, requiring definitive, rapid laboratory diagnosis. Laboratory surveillance testing is also required; testing for surveillance purposes will change with the public health needs.

Laboratories play a significant role not only in patient diagnosis and management of all communicable diseases but also in public health Core Functions such as surveillance and outbreak investigation. Laboratory outputs impact on the management of patients, support infection control decisions, and partner in public health interventions.

Principles for provincial public health laboratories testing during a pandemic were developed by the Canadian Public Health Laboratory Network (CPHLN) Pandemic Preparedness Group (www.phac-aspc.gc.ca/cpip-pclcpi/ann-c-eng.php).

National standards, based on these nucleic acid-based methods, are briefly described in this document.

This Pandemic Plan for BCPHL, and its partners in the BC laboratory network, provides a framework with overarching principles, including roles and responsibilities, for different types of laboratories.

Each laboratory will be responsible for their respective pandemic plan in the context of their specific laboratory agency/facility plans. The intent of this document is simply to provide a framework.

This framework document will be reviewed regularly by laboratories and the Ministry of Health.

The mild to moderate 2009 pandemic provided the health care system of BC with valuable experience as to how to plan for future pandemics. Based on historical precedent, it is plausible that such a pandemic will occur within

1.3. Assumptions

The following assumptions were agreed on for planning purposes, by the Canadian Public Health Laboratory Network (CPHLN) members, its experts in PILPN (Pandemic Influenza Laboratory Preparedness Network), and the Public Health Agency of Canada (PHAC).

While the following assumptions were used for planning purposes, pandemics and their viruses (including the 2009 event which did occur as assumed), are somewhat unpredictable. Preparedness as well as flexibility, while not foreign to microbiologists who work on constantly evolving microbes, are both needed in a response. Delineated below is a list of the assumptions made before the 2009 pandemic together with a comment, where appropriate, as how accurate they were in the 2009 pandemic.

CPHLN/PHAC assumed that:

- Pandemic would be of intermediate severity. (Pandemic was of mild to moderate severity)
- Severity would be impacted both by virus transmissibility and virulence.
- Pandemic would originate outside Canada, taking 1-3 months before reaching BC. (Pandemic originated in Mexico and reached Canada with a week of its identification)
- Second pandemic wave would occur 6-9 months after the first. (The major wave occurred within 5 months of the virus first being recognized.)

the next decade. It is anticipated that during this period diagnostics and management of influenza will continue to advance rapidly. Accordingly, the present plan must be reviewed every year or so to stay current.

Consultation, questions and suggestions for an improved plan are always appreciated (email: Kitty.Liu@bccdc.ca).

- Duration of each pandemic wave within BC would be up to 12 weeks. (When the pandemic influenza H1N1 was first recognized, the increase in laboratory testing was exaggerated by an actual encouragement for testing especially of returned travellers from Mexico. The overall demand for testing remained high throughout the summer at least in part because physicians were sensitive to the presence of the pandemic virus. This oversensitivity is supported by the fact that rhinovirus, which is generally associated with the common cold, was very often diagnosed in submitted specimens. In essence the pandemic had only one true wave which began in mid-September and ended at the end of December.)
- Waves would include build-up (pandemic virus spreading at an increasing rate resulting in an increasing incidence of infection); saturation of susceptible hosts (up to 30-40% of the BC population infected); then decline (decreasing incidence of infection in the BC population). (Saturation was achieved in early November with a prominent decline thereafter.)
- Planning would be done in the context of WHO Phases (Appendix A) and the scale-up/scale-down for each pandemic wave. (The speed with which the pandemic appeared in our setting made the WHO phases redundant. The phases need reformatting in light of present experience.)

- Pandemic strain of virus would start off co-circulating with non-pandemic, seasonal Influenza (and other respiratory viruses), but would eventually become the predominant virus. (This assumption was accurate)
- Reverse Transcriptase Polymerase Chain Reaction-based testing (RT-PCR) is the national and international gold standard for identifying and subtyping Influenza A.
- Volumes submitted to BCPHL could increase up to ten-fold during a pandemic wave. (Assumption was accurate)
- Pandemic strains of virus could develop resistance to Oseltamivir and testing for resistance in the BCPHL is essential. (Very limited resistance noted. BCCDC implemented a SNP assay which NML adapted and circulated across Canada)
- Laboratories will experience staffing shortages; some estimates up to one quarter to one third may become ill or be unable to work. (Minimal absenteeism was noted)
- Influenza serology testing (to identify individuals who are susceptible to infections of the second wave) will be required between waves. (Accurate assumption)
- Vaccines may not be available or recommended, to immunize the entire population in BC. (Vaccine became available for most of Canada before second wave except in BC where second wave preceded vaccine).
- Between waves, laboratories will review their patterns of practice, and make needed improvements or adjustments. (Accurate assumption, See PILPN Best Practices document)
- All BC laboratories will attempt to assist one another, as much as possible, in the event of one being temporarily overwhelmed by specimens or incapacitated by staffing shortages. (Did not happen. In general laboratories coped well)
- Each laboratory, however, is responsible for their own business continuity plan and their own response plan.

2. LABORATORY TESTING

2.1 General Roles and Responsibilities for BC Laboratories

Pandemic Influenza will involve different BC laboratory settings. All medical microbiology laboratories will contribute to the pandemic response.

Partners in a public health laboratory response include:

- Community laboratories (BC Biomedical Laboratories, LifeLabs)
- Acute care hospital laboratories (where no virology services are provided)
- Laboratories at St. Paul's Hospital, BC Childrens & Womens Hospital, Victoria General Hospital, Prince George Regional Hospital and possibly others (where some virology services are provided)

2.2 Types of Tests Used

The RT-PCR assay is the national and international standard for provincial public health laboratory testing for pandemic influenza as it:

- Is rapidly customized and can be developed further to detect whatever virus is causing the pandemic (subtype level)
- Provides the basis for further molecular subtyping and resistance testing
- Has the highest analytical sensitivity
- Produces minimal bio-safety hazards
- Is amenable to some stockpiling of reagents
- Is amenable to economies of scale

While RT-PCR for Influenza A is the foundational test, all contributions to testing, including specimen collection and transport are important and, must be carried out in a coordinated manner. This plan builds on an

- BCPHL

All laboratories have the responsibility to have specific plans, including business continuity plans, in place. Their plans, whilst consistent with the standards and information within this document, will also align with their own institution's /organizations' requirements. BCPHL, a member of the Canadian Public Health Laboratory Network (CPHLN), will be the provincial contact for the pan-Canadian laboratory response plan, including the provincial link with the National Microbiology Laboratory (NML). BCPHL will provide leaderships and assistance to other laboratories where possible, as well as providing core public health functions (www.phac-aspc.gc.ca/cpip-pclcpi/ann-c-eng.php) and specialized testing.

excellent, informal network of microbiology partnerships already in place.

Super-infection of the airway after a severe influenza illness is a major cause of mortality and severe morbidity. In addition to microbiology testing for viruses there will be increased demand for testing for respiratory bacterial pathogens such as *S. pneumoniae* and *H. influenzae*. The burden of this additional work is expected to be in the acute care hospital laboratories.

Point-of-Care (POC) testing was not originally recommended by the WHO or the CPHLN. Subsequently its use in very limited defined circumstances is being carefully considered (remote communities) by some agencies. BCPHL is not responsible for Quality Management oversight at this time, for POC. Its widespread use is not recommended at this time.

2.3 Roles & Responsibilities by Laboratory Type

- Community laboratories and acute care hospitals laboratories with no virology services, will work with their clinicians, infection control and public health colleagues, to follow information available through the Provincial Health Officer's website (<http://www.hls.gov.bc.ca/pho/>) Pandemic Steering Committee, on test utilization (who to test, when).
- Community laboratories and acute care hospitals laboratories with no virology services, will work on optimal collection and transport of samples.
- Some tertiary/quaternary acute care hospitals (ACH) laboratories (who are already providing virology services), will also, using RT-PCR detection methods, provide testing for their own patients.
- Samples will be shipped, along with the designated BCPHL requisition (Appendix C), in a conventional manner, using the usual system of laboratory transportation.
- BCPHL will undertake primary and secondary nucleic acid-based testing to detect and subtype Influenza A virus by assays defined by national standards (RT-PCR).
- BCPHL will undertake testing for laboratory surveillance using RT-PCR as well as other appropriate tests such as DNA sequencing.
- BCPHL will carry out anti-viral drug resistance testing as required.
- BCPHL will carry out serology testing as required for vaccine and population susceptibility assessment.
- BCPHL, under the guidance of the Public Health Agency of Canada (PHAC) Office of Laboratory Safety, and with the Provincial Infection Control Network (PICNet), will provide information on laboratory worker safety.
- BCPHL will be the provincial liaison as a member of the Canadian Public Health Lab Network (CPHLN), with the National Microbiology Laboratory (NML).
- National Microbiology Laboratory (NML) will serve as a reference laboratory for further characterization of the virus and for confirmation of anti-viral resistance testing, as required.
- BCPHL will be responsible for the review and updating of this plan, annually or as needed.

2.4 Specific Roles by BC Laboratory Type

Table 1 summarizes the type of testing done in t labs in BC by type of test.

Table 1. Influenza Testing in BC Laboratories

	Sample Collection and/or Transport	RT-PCR Detection	Nucleic acid-based Subtyping	Nucleic acid based-Resistance Testing	Serology Assays
Community Labs	YES	NO	NO	NO	NO
Acute Care Hospital Labs (With No Previous Virology Services)	YES	NO	NO	NO	NO
Acute Care Hospital Labs (With Previous Virology Services)	YES	YES	NO	NO	NO
BCPHL	Transport (From Health Units)	YES	YES	YES	YES
National Microbiology Laboratory	NO	NO	NO	YES (Confirmatory Only)	YES (National Studies Only)

2.5 Laboratory Roles and Responsibilities During WHO Pandemic Phases

Tables 2 (A-D) summarize the roles and responsibilities of BC laboratories during each WHO Pandemic Phase. Further development of the WHO Phases document is underway and this plan will be updated, accordingly.

Further information regarding testing is also captured in Section 2.6 below and in the appendices.

Activation of BC plans in WHO Phases 4-6 will be confirmed to BC laboratories by Public Health Laboratory Director or medical designate, although it is anticipated that most laboratories will be aware of these developments.

Table 2A: Laboratory Roles & Responsibilities – Interpandemic Period (WHO Phase 1)

All B.C. Labs	<ul style="list-style-type: none"> Develop pandemic preparedness plans (testing capacity, supplies, equipment, human resources). Promote vaccination for influenza for laboratory staff.
BCPHL	<ul style="list-style-type: none"> Provide RT-PCR testing for Influenza A Provide RT-PCR and genome sequence-based influenza sub-typing Implement Oseltamivir/Amantadine resistance assays Participate in proficiency testing programs with NML Assist BC PHLN (remote Health Authority labs), as needed Implement protocols for rapid communication with health care workers submitting specimens Implement protocols for surveillance and assist in the analysis of information, in alignment with public health needs Carry out research related to better diagnosis, genomics and vaccines.
National Microbiology Laboratory	<ul style="list-style-type: none"> Provide anti-viral resistance testing methodologies Transfer required diagnostic technology to provincial public health laboratories Provide proficiency testing for introduced nucleic acid based technology. Provide regular, timely information on the pandemic virus from a global perspective Provide regular national and international information related to laboratory-based surveillance

Table 2B: Laboratory Roles & Responsibilities – Pandemic Alert Period (WHO Phases 2-3)

All B.C. Labs	<ul style="list-style-type: none"> Review their operational plans for surge capacity including review of priorities for testing to meet surge, as required Use guidelines for appropriate specimen collection and transport from BCPHL Submit specimens from suspected pandemic influenza cases to BCPHL Implement pandemic plans when pandemic reaches Phase 4
BCPHL	<ul style="list-style-type: none"> All responsibilities noted under Inter-pandemic Period Step-up surveillance for subtyping of influenza viruses (100% of all Influenza A) Ensure adequate quantities of supplies, equipment and trained personnel are in place Step-up antiviral resistance testing (10% of all Influenza A, or as required) Step-up viral genomic surveillance Send first specimens (highest priority) in which a new subtype is identified to the NML Ensure protocols are communicated to virology testing laboratories/ members of the BC Public Health Laboratory Network
National Microbiology Laboratory	<ul style="list-style-type: none"> Provide technical support as requested to BCPHL Provide confirmatory testing as required Provide further strain characterization including phenotypic antiviral resistance testing Advise BCPHL of any changes to testing protocols Lead in required proficiency testing Update BCPHL international surveillance issues

Table 2C: Laboratory Roles & Responsibilities – Pandemic (WHO Phases 4-6)

All B.C. Labs	<ul style="list-style-type: none"> • Confirm operational plans for surge capacity • Submit specimens from suspected pandemic influenza cases to BCPHL as required • Use guidelines for appropriate specimen collection and transport from BCPHL • Review priorities for testing to meet surge, as required • Implement individual pandemic plans when Pandemic reaches WHO Phase 4
BCPHL	<ul style="list-style-type: none"> • Deploy Pandemic Plan to meet diagnostic and surveillance needs • Provide pandemic and other public health labs functions giving priority to Tier 1 and 2 testing (BC) • Forward subset (5-10%) of isolates to NML for confirmatory testing • Communicate most recent diagnostic, biosafety and other guidelines to BC lab network • Communicate regularly with NML and CPHLN • Communicate with BCCDC staff, medical health officers, provincial health officers and others as needed
National Microbiology Laboratory	<ul style="list-style-type: none"> • Perform reference confirmatory characterization as needed • Collaborate with CPHLN Provincial Health Labs to undertake necessary research • Communicate with CPHLN Provincial Health Labs on any changes in antiviral resistance, novel RT-PCR primers, probes or other technical needs • Provide international lab surveillance technical guidelines

Table 2D: Laboratory Roles & Responsibilities – Post Pandemic Period

All B.C. Labs	<ul style="list-style-type: none"> • Evaluate pandemic response and make necessary changes
BCPHL	<ul style="list-style-type: none"> • Evaluate pandemic response and make necessary changes • Conduct post pandemic testing, such as serology testing to establish evidence of infection/immunity/vaccine efficacy.

2.6 Information on All Stages of Laboratory Testing

Specimen Collection and/or Transport Information (Pre-Analytical Stage)

BC Pandemic Steering Committee, along with Clinical Care and Public Health Advisory Group, will advise on who to test and where for both clinical diagnostic purposes and public health surveillance purposes. Current guidelines are available on the Provincial Health Officer’s website.

- Appropriate specimens for pandemic testing include:
- Nasopharyngeal swabs/washes (OPTIMAL)
- High nasal swabs/washes,
- Nasopharyngeal suction and aspirates

- Sputum, as well as lower respiratory specimens (endotracheal secretions and broncho-alveolar washes (BAL)).

Please note that:

- Nasopharyngeal swabs/washes are OPTIMAL specimens.
- Nasal swabs and washes are not optimal specimens but may be submitted.
- Throat swabs are suboptimal but may be submitted under some extenuating circumstances (consultation).
- Bacterial swabs (e.g. metal shaft swabs used for pertussis testing) are NOT acceptable.

All specimens for RT-PCR testing at BCCDC Site, PHSA Laboratories, must be submitted with an appropriately completed BCPHL Virology requisition (Appendix C). Further details regarding specimen collection and transport are found in Appendix D.

Principles for Laboratory Testing (Analytical Stage)

In general:

- Only methodologies and operating procedures approved and consistent with BCPHL and CPHLN, will be used when testing.
- Large laboratories already providing some virology services (BC Children's & Women's Hospitals, St. Paul's Hospitals, Victoria General Hospital) will do acute care patient testing for their respective hospitals. BCPHL will assist, as possible, in providing specialized technical and Quality support.
- All Laboratories doing testing for pandemic will be able to identify the novel virus as Influenza A or B.
- All Laboratories doing Influenza testing will participate in appropriate proficiency testing programs, as required by accreditation standards.
- All Laboratories doing Influenza testing will forward the first 10 specimens during the pandemic to the BCPHL for confirmation and further testing.
- Other Influenza positive samples will be submitted to BCPHL as requested.
- BCPHL will forward a subset of specimens to the NML.
- Guidelines or test utilization, from public health for both diagnostic and surveillance sampling, will be communicated to all lab users and all BC laboratories.

- Estimates of ramp-up/ramp-down sampling volumes, for both surveillance and diagnostic purposes, are summarized in Table 3 below.

Step-Up/Step-Down Diagnostic Sampling by Clinicians

Sampling is done by health care workers. Laboratory are not in a good position to control laboratory utilization and hence, the demand for testing. Laboratory utilization will be directed through the PHO website that will provide information from the Pandemic Steering Committee, including the Public Health Laboratory Director

It is important that all laboratory clients follow current directions for testing as noted on the Provincial Health Officer (PHO)'s website (<http://www.health.gov.bc.ca/pho/>). Inappropriate testing not only wastes resources, it impedes the expeditious testing of critical samples.

Sampling for diagnostic testing is for direct patient care and infection control purposes. Patterns of sampling need to remain flexible, depending on the actual circumstances in which the pandemic unfolds (other outbreaks occurring, emergency events, staff illness and availability, etc).

All services carried out by the BCPHL will be, managed according to the BCPHL Business Continuity Plan and if required, cross-trained staff will be reassigned to pandemic testing. Any changes in provision of services will be communicated to clients, according to CAP requirements, by the Public Health Laboratory Director, PHSA Laboratories.

Table 3 summarizes conceptually the Step-Up/Step-Down for diagnostic sampling.

Table 3: Conceptual Pattern for Diagnostic Sampling

	Proposed Samples To Be Tested (%)	Positive Influenza A Subtyped (%)
Week 1-2: Early Pandemic		
<ul style="list-style-type: none"> Patients with influenza-like illness who will be sampled. All specimens will be tested. Positives tested for drug resistance. Viruses sent to NML (national surveillance). 	100 N/A SN-P SN-P	100 N/A N/A N/A
Weeks 3-6: Peak Pandemic		
<ul style="list-style-type: none"> Demand for testing remains high but ceases to grow (physicians will rely more heavily on clinical diagnosis); testing focused on outbreaks, those with atypical presentations, and severely ill patients; staff illness 25-30 per cent. Positives tested for drug resistance. Selective use of cell culture. Viruses sent to NML. 	100 As clinically indicated 10 SN-P 10 SN-P	100 N/A N/A N/A
Weeks 6-8: Late Pandemic		
<ul style="list-style-type: none"> As the number of infections decreases, sampling should decrease; most testing will be to rule out influenza and to rule in other respiratory viruses; testing demands will be similar to that of pandemic peak but with decreased samples. Positive samples to be tested for drug resistance. 	10 As clinically indicated	100 N/A
Post-Pandemic		
<ul style="list-style-type: none"> Testing focuses on immune response (serology). Additional testing required for various applied research questions. 	As appropriate	As appropriate

Note: SN-P = Sentinel Network - Positives

(Note: In late pandemic the number of specimens decreased dramatically) (Number of drug resistant cases was low and testing for drug resistance was carried out if clinically indicated)(the assay adopted at BCCDC was able to identify influenza A and the pandemic subtype)

Step-Up/Step-Down Surveillance Sampling for Public Health

Sampling for surveillance purposes is directed by BC public health and will be directed from the PHO website (<http://www.hls.gov.bc.ca/pho/>).

Public health surveillance for outbreak investigation, management and disease surveillance as well as virus (genomic drift/shift/antiviral resistance patterns) characterization, are Core Public Health Laboratory Functions http://www.cphln.ca/pdf/2004-09-14_CPHLN_Core_Functions_eng.pdf

The table below summarizes conceptually how the BCPHL anticipates the Step-Up/Step-Down of sampling for public health surveillance.

Flexibility in surveillance sampling and testing is required and may change, depending on public health needs.

Utilization management for the BCPHL for surveillance purposes will be communicated through the PHO website (<http://www.hls.gov.bc.ca/pho/>) based on decisions of the Pandemic Steering Committee, including the Public Health Laboratory Director. All changes in plans (hence impacts on diagnostic and all other testing services, as well as impacts on BCPHL Core Functions) as well

as communications related to laboratory testing will be first discussed with the Public Health Laboratory Director (or medical designate)

before posting on PHO website or being communicated external to PHSA.

Table 4: Conceptual Patterns of Surveillance Sampling

	Proposed Samples To Be Tested (%)	Positive Influenza A Subtyped (%)
Week 1-2: Early Pandemic		
<ul style="list-style-type: none"> All specimens (100%) will be tested Specimens to test for drug resistance Viruses sent to NML (national surveillance) 	100 0 SN-P	100 N/A N/A
Weeks 3-6: Peak Pandemic		
<ul style="list-style-type: none"> Demand for testing remains high but cease to grow (physicians will rely more heavily on clinical diagnosis): Testing focused on outbreaks, those with atypical presentations, and severely ill patients Selective genomic characterization of virus (surveillance) 	SN-P plus 100 of Positive Diagnostic Samples SN-P (as appropriate)	100 100
Weeks 6-8: Late Pandemic		
<ul style="list-style-type: none"> Surveillance demands will be similar to that of pandemic peak but with probable decreasing volumes required 	As appropriate	100
Post-Pandemic		
<ul style="list-style-type: none"> Additional testing required for various applied surveillance related research questions 	As appropriate	As appropriate

Note: SN-P = Sentinel Network - Positives

3. OPERATIONS

The following general operational areas should be addressed in each laboratory's, specific pandemic plan.

3.1 Human Resources

The following principles should be considered by all laboratories:

- During a pandemic, up to one third of the staff may be unavailable (personal illness or family illness); each laboratory should have its own business continuity plans in place including consideration of test deferrals.
- Laboratories must have plans to increase the capacity for specimen reception and accessioning unless these functions are redesigned to be scalable.
- When trained staff members are fully occupied with testing for influenza, laboratories will have to back-fill for staff performing other critical testing and reporting of results (performing essential pre- and post-analytical functions).
- Laboratories must have an adequate number of trained staff to perform testing and to maintain competency for their priority testing (as determined by their business continuity plan).
- Laboratories doing influenza testing should be performing acceptable RT-PCR on a routine basis to ensure that their staff are familiar with the standard operating procedures, should participate in proficiency testing, and have appropriate Quality Management Systems elements in place.
- Immunization of laboratory staff, as key health care workers, must be planned, and promoted for all laboratory staff.
- Personal Protective Equipment (PPE) must be available for all laboratory staff, as required.
- Fit-testing for N95 respirators must be carried out and documented annually for all designated laboratory staff.

3.2 Equipment

The following information may apply to BC laboratories that routinely perform influenza testing:

- Real-time polymerase chain reaction (RT-PCR) assays require equipment and appropriate facilities for safe and accurate nucleic acid-based (RT-PCR) testing, including nucleic acid extraction, amplification and detection of PCR products.
- Additional RT-PCR related equipment that will be necessary include refrigerator/freezer capacity, and appropriate specimen handling capacity under bio-safety Containment Level 2+ for pandemic influenza.
- Each laboratory will be responsible for maintaining their business continuity for equipment, reagents and other consumables (source of which is described below).

3.3 Reagents and Supplies

The following information may be useful for some BC laboratories:

- RNA extraction reagents have a shelf-life of under one year. Stockpiling of these can be costly from wastage of expired reagents.
- RT-PCR reagents are readily available and can be stockpiled (stable for several years at -80°C). Primers and probes are generally stable for years and can be readily stockpiled.
- BCPHL will provide appropriate swabs and viral transport media for RT-PCR, as testing volumes change with Scaling-up/down phases.
- “COPAN Flocked swabs” to collect specimens are required and must be readily available to all labs in BC. Under circumstances where supplies are limited, triaging by BCPHL may occur.
- Viral transport medium is required in adequate volumes and, along with above swabs, must be readily available to all laboratories in BC. Triaging by BCPHL may occur.
- While the “COPAN Flocked Swabs” have a multi-year shelf life, viral transport medium expires within a year after production. Consideration should be given to stocking swabs separately from transport medium to avoid having to discard expired stocks or transport medium may be stored frozen to extend its shelf life and this approach should be validated.
- Each laboratory performing RT-PCR will be responsible for maintaining their specific business continuity based on appropriate volumes of reagents and supplies.

4. LABORATORY BIOSAFETY

4.1 Laboratory Bio-Safety & Bio-hazard Containment Guidelines

The following information should be considered by all BC laboratories:

- Bio-Safety regulations as developed by the PHAC Office of Laboratory Safety (OLS) will be followed.
- BCPHL Biosafety Biosecurity Biohazard Containment (BBBC) Program will work with OLS.
- BCPHL will communicate all changes to bio-safety requirements to all BC labs.
- Laboratory practices for working with influenza require Containment Level-2 (CL-2) containment, currently in practice in all virology laboratories.
- Growth of a new pandemic strain in cell culture under current guidelines will likely require CL-2+ (CL-3 personal protective equipment for the operator working in a CL-2 level) containment.
- Testing for pandemic virus by RT-PCR will be done under CL-2 containment except for procedures such as opening the transport containers and transferring the specimen into lysis buffer, procedures which are AGMP. For these procedures CL-2+ containment is recommended (CL-3 personal protective equipment for the operator working in a CL-2 level).
- CL-2 containment should be used by technologists processing respiratory specimens for bacteriological assays and those opening containers in which such specimens have been shipped.
- Appropriate personal protective equipment (PPE) is needed when handling such specimens. It is recommended that the equipment be at CL-2+. During the pandemic period it is expected that only the very ill patients will be admitted to acute care hospitals.
- Influenza, regardless of subtype, is readily inactivated by alcohol or chlorine based disinfectants.
- Bio-safety measures may be taken to minimize work related transmission of influenza.
- Infection control guidelines must be used as appropriate and directed through BCPHL from the OLS.
- Social distancing with the laboratory including dividing staff into smaller work units and maintaining minimal personal face-to-face contact throughout the pandemic, may be considered.

5. COMMUNICATIONS

The following principles of communications are noted:

- All laboratories will communicate their laboratory specific plans as well as their laboratory test results, within their own jurisdictions.
- All province-wide communications from BCCDC or public health pertaining to laboratory issues must be reviewed and approved by the Public Health Laboratory Director (BCPHL), or designate.
- Public Health Laboratory Director (BCPHL) or designate, will be responsible for leading communications along with Operations Director, Laboratory Surveillance Outbreak Coordinator, and other BCPHL staff.
- Communication between BCPHL and all other BC laboratories and physicians submitting specimens is expected to follow the current reporting format.
- BCPHL will communicate results to both PHSA Laboratories and BCCDC Executive, the BC Medical Health Officers and BCCDC Epidemiologists.
- BCPHL will communicate regularly with BCCDC Emergency Operations Centre (EOC).
- BCPHL will communicate regularly with Lower Mainland Laboratories/PHSA Laboratories EOC.
- BCPHL will communicate regularly with CPHLN/NML.

6. QUALITY & STANDARDIZATION

- All laboratories designated for influenza testing must have the RT-PCR assays validated to acceptable accreditation (provincial or international) standard in their setting with written records and documentation approved with date by their Laboratory Director.
- Minor alterations, such as changes of primers and probes may be validated expeditiously (Molecular Services in the BCPHL) using a limited number of specimens; consultation with BCPHL is available.

7. USEFUL WEBSITES

<http://www.bccdc.ca/default.htm>

<http://www.hls.gov.bc.ca/pho/>

<http://www.who.int/en/>

<http://www.phac-aspc.gc.ca/cpip-pclcpi/ann-c-eng.php>

<http://www.phsa.ca/default.htm>

GLOSSARY

Admin	- Administration
BAM	- Bacteriology and Mycology Program of BCPHL
BBBC	- Biosafety Biosecurity Biohazard Containment Program of BCPHL
BCCDC	- British Columbia Centre for Disease Control
BCPHL	- British Columbia Public Health & Microbiology Reference Laboratory, PHSA Laboratories
CPHLN	- Canadian Public Health Laboratory Network
CPRLLL-Pre	- Central Processing Receiving Lane Level Laboratory – Pre-Analytical
CPR-VS	- Central Processing Receiving Lane Level Laboratory – Viral Serology
EM	- Environmental Microbiology Program of BCPHL
Myco/TB	- TB/Mycobacteriology Program of BCPHL
NML	- National Microbiology Laboratory
Para	- Parasitology Program of BCPHL
PHLAC	- Public Health Laboratory Advisory Committee
PHLD	- Public Health Laboratory Director
PHSA	- Provincial Health Services Authority
MS	- Molecular Services of BCPHL
TS	- Tech Support of BCPHL
VI	- Virology Program of BCPHL
ZEP	- Zoonotic & Emerging Pathogens Program of BCPHL

APPENDICES

Appendix A: World Health Organization Pandemic Phases

BCPHL will scale up/scale down its testing in response to both the WHO Phases, the clinical severity of the pandemic, and in response to specific directions from the public health community.

The WHO currently has 6 Pandemic Phases:

- Interpandemic Alert Phase 1: No new influenza subtypes with pandemic potential identified
- Pandemic Alert Phase 2: Influenza subtype with pandemic potential circulating in animals
- Pandemic Alert Phase 3: Human infections with new subtype with no sustained human-to-human transmission
- Pandemic Phase 4 (Step-Up): Limited ongoing human-to-human transmission in small clusters
- Pandemic Phase 5 (Step-Up): Localized human-to-human transmission in defined geographic settings (institutional or defined community setting)
- Post Pandemic Phase 6 (Step-Down): Sustained transmission in the population.
- Post Pandemic: Pandemic is declared over.

The WHO is currently revising its approach to global monitoring (<http://www.who.int/en/>).

Appendix B: BCPHL Contact Information

Program	Name	Telephone	Fax	Email
Public Health Laboratory Director	Judith Isaac-Renton, MD	604-707-2619	604-707-2603	judy.isaac-renton@bccdc.ca
Assistant to the Director	Kitty Liu	604-707-2646	604-707-2603	kitty.liu@bccdc.ca
Associate Director	Mel Krajden, MD	604-707-2421	604-707-2603	mel.krajden@bccdc.ca
Director of Laboratory Operations	Kathy Kelemen	604-707-2634	604-707-2603	Kathy.kelemen@fraserhealth.ca
Chief Technologist, BCCDC and CPR-LL	Amelia Trinidad	604-707-2650	604-707-2603	amelia.trinidad@bccdc.ca
Lab Outbreak/Surveillance Coordinator	Yin Chang	604-707-2632	604-707-2603	yin.chang@bccdc.ca
Healthy Water Program/EWQA Coordinator	Cora Yee	604-707-2639	604-707-2603	cora.yee@bccdc.ca
Administrative Assistant	Yvonne Santa Cruz	604-707-2627	604-707-2603	yvonne.santacruz@bccdc.ca
Biosafety Biosecurity Biohazard Containment				
Public Health Lead	Neil Chin	604-707-2614	604-707-2603	neil.chin@bccdc.ca
Supplies Fax			604-707-2606	
Bacteriology/Mycology				
Program Head	Linda Hoang, MD	604-707-2618	604-707-2604	linda.hoang@bccdc.ca
Section Head	Ana Paccagnella	604-707-2610	604-707-2604	ana.paccagnella@bccdc.ca
Main Laboratory		604-707-2617	604-707-2604	
Mycology Laboratory		604-707-2621	604-707-2604	
Central Processing & Receiving/Lane Level Lab				
Public Health Program Head	Judith Isaac-Renton, MD	604-707-2619	604-707-2603	judy.isaac-renton@bccdc.ca
Director of Laboratory Operations	Kathy Kelemen	604-707-2634	604-707-2603	kathy.kelemen@fraserhealth.ca
Chief Technologist	Amelia Trinidad	604-707-2650	604-707-2603	amelia.trinidad@bccdc.ca
High Volume Virology	Mel Krajden, MD	604-707-2421	604-707-2603	mel.krajden@bccdc.ca
Section Head, High Volume Virology	Annie Mak	604-707-2828	604-707-2601	annie.mak@bccdc.ca
Section Head, CPR- Pre-Analytical	John Chan	604-707-2830	604-707-2601	john.chan@bccdc.ca
Fax/Results Line			604-707-2601	
Environmental Microbiology				
Program Head	Judith Isaac-Renton, MD	604-707-2619	604-707-2603	judy.isaac-renton@bccdc.ca
Section Head	Joe Fung	604-707-2608	604-707-2600	joe.fung@bccdc.ca
Water Laboratory		604-707-2620	604-707-2600	
Water Results Line		604-707-2665		
Foodborne Disease	Julie Wong	604-707-2611	604-707-2600	julie.wong@bccdc.ca
GI Outbreak Notification Fax			604-707-2607	
EWQA Provincial Coordinator	Shelley Tiffin	604-707-2633	604-707-2603	shelley.tiffin@bccdc.ca
Parasitology				
Program Head	Judith Isaac-Renton, MD	604-707-2619	604-707-2603	judy.isaac-renton@bccdc.ca
Clinical Microbiologist	Muhammad Morshed, PhD	604-707-2622	604-707-2654	muhammad.morshed@bccdc.ca
Section Head	Quantine Wong	604-707-2612	604-707-2654	quantine.wong@bccdc.ca
Laboratory		604-707-2629	604-707-2654	
Mycobacteriology/TB				
Program Head	Patrick Tang, MD, PhD	604-707-2616	604-707-2675	patrick.tang@bccdc.ca
Section Head	Mabel Rodrigues, PhD	604-707-2615	604-707-2672	mabel.rodrigues@bccdc.ca
Laboratory		604-707-2630	604-707-2672	
Translational Research in Microbiology				
Program Head	Patrick Tang, MD, PhD	604-707-2616	604-707-2675	patrick.tang@bccdc.ca
Section Head	Alan McNabb	604-707-2683	604-707-2603	alan.mcnabb@bccdc.ca
Laboratory		604-707-2680		
Virology Services				
Program Head	Mel Krajden, MD	604-707-2421	604-707-2603	mel.krajden@bccdc.ca
Clinical Virologist	Alan McNabb	604-707-2609	604-707-2675	alan.mcnabb@bccdc.ca
Section Head		604-707-2623	604-707-2605	
Laboratory (Virus Isolation)			604-707-2605	
Virus Isolation Outbreak Fax				
Zoonotic Diseases & Emerging Pathogens				
Program Head	Muhammad Morshed, PhD	604-707-2622	604-707-2602	muhammad.morshed@bccdc.ca
Section Head	Quantine Wong	604-707-2613	604-707-2602	quantine.wong@bccdc.ca
Laboratory (Serology)		604-707-2628	604-707-2602	
Laboratory (Molecular)		604-707-2626	604-707-2602	

Appendix C: BCPHL Pandemic Influenza Requisition

PHSA Laboratories

Public Health Microbiology & Reference Laboratory

Virology Requisition

BC Centre for Disease Control, 655 West 12th Avenue, Vancouver, BC V5Z 4R4 www.phsa.ca/bccdcpublichealthlab

Section 1 - Patient Information

PERSONAL HEALTH NUMBER (or out-of province Health Number and province)	DOB (DD/MMM/YYYY)	GENDER <input type="checkbox"/> M <input type="checkbox"/> F <input type="checkbox"/> UNK	DATE RECEIVED
PATIENT SURNAME	PATIENT FIRST AND MIDDLE NAME		
ADDRESS	CITY	POSTAL CODE	

PHSA LABORATORIES USE ONLY

Section 2 - Healthcare Provider Information

ORDERING PHYSICIAN (Provide MSC#) Name and address of report delivery	ADDITIONAL COPIES TO: (Address / MSC#) 1. 2. 3.	OUTBREAK ID
<input type="checkbox"/> I do not require a copy of the report		SAMPLE REF. NO.
CLINIC OR HOSPITAL Name and address of report delivery		DATE COLLECTED (DD/MMM/YYYY)
PHSA CLIENT NO.		TIME COLLECTED (H:MM)

Section 3 - Test(s) Requested

PATIENT STATUS <input type="checkbox"/> In patient at hospital <input type="checkbox"/> ER patient <input type="checkbox"/> History of contact with infection <input type="checkbox"/> Travel history _____	SIGNS / SYMPTOMS Date of Onset: _____ (DD/MMM/YYYY) <input type="checkbox"/> Asymptomatic <input type="checkbox"/> Cough <input type="checkbox"/> Fever <input type="checkbox"/> Rash <input type="checkbox"/> Upper Respiratory Infection <input type="checkbox"/> Lower Respiratory Infection <input type="checkbox"/> Other, specify: _____	
RESPIRATORY VIRUSES <input type="checkbox"/> Nasopharyngeal swab <input type="checkbox"/> Nasal swab <input type="checkbox"/> Bronchoalveolar lavage <input type="checkbox"/> Nasal wash <input type="checkbox"/> Other, specify: _____ <input type="checkbox"/> Previous POC test result <input type="radio"/> Influenza A <input type="radio"/> Influenza B <input type="radio"/> RSV	HERPES VIRUSES <input type="checkbox"/> Genital lesion for HSV <input type="checkbox"/> Non-genital lesion for HSV <input type="checkbox"/> Skin swab for Varicella-Zoster <input type="checkbox"/> Other, specify: _____ Urine for: <input type="checkbox"/> Cytomegalovirus	GASTROINTESTINAL VIRUSES Feces* for: <input type="checkbox"/> Rotavirus/Adenovirus <input type="checkbox"/> Norovirus <input type="checkbox"/> Other, specify: _____
HEPATITIS VIRUSES Blood for: <input type="checkbox"/> Qualitative HCV RNA (diagnosis) <input type="checkbox"/> Quantitative HCV RNA (treatment only) <input type="checkbox"/> Baseline <input type="checkbox"/> Week, specify: _____ <input type="checkbox"/> HCV Genotyping	ENCEPHALITIS / MENINGITIS Cerebrospinal Fluid for: <input type="checkbox"/> Encephalitis (e.g. HSV-1, West Nile Virus) <input type="checkbox"/> Meningitis (HSV-2, Enterovirus) <input type="checkbox"/> Other, specify: _____	MEASLES / RUBELLA VIRUSES <input type="checkbox"/> Measles <input type="checkbox"/> Rubella <input type="checkbox"/> Urine <input type="checkbox"/> Nasal / Nasopharyngeal swab <input type="checkbox"/> Other, specify: _____
For other available tests and additional information, consult the Public Health Microbiology & Reference Laboratory's Guide to Programs and Services at www.phsa.ca/bccdcpublichealthlab	MUMPS VIRUSES <input type="checkbox"/> Buccal swab <input type="checkbox"/> Urine	BIOPSY / AUTOPSY / OTHER TESTS <input type="checkbox"/> Specify: _____

PHSA LABORATORIES USE ONLY

DATE INOC.		TYPE OF SPECIMEN		LAB NO.	OTHER
DATE	DAY	AS49		MK	

*Infectious Diarrhea - Guideline for Ordering Stool Specimens http://www.bcguidelines.ca/gpac/guideline_diarrhea.html

Appendix D: Specimen Collection, Testing and Shipping for Virus Confirmation

Suggested Procedure:

Collect specimens, where appropriate, from patients presenting with clinically compatible history within **72 hours of onset** of symptoms.

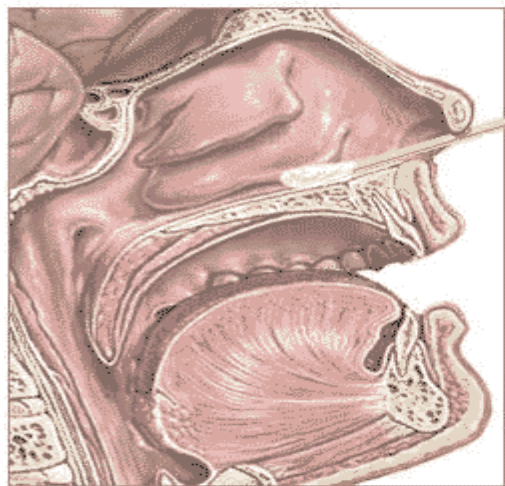
Personal protection during specimen collection: It is recommended that gloves and a facemask be worn by the health care worker when collecting specimens. Hands should be washed well if water and soap are available, or sanitized with a disinfecting wipe if not, and fresh gloves used for each new patient.

Patients with copious discharge should be requested to gently clean their nose by washing or with tissue.

Optimal Samples: Nasopharyngeal

These specimens are ideal. Use the provided flocced swab with nylon tip.

1. Facing the patient, gently push the patient's nose upward and insert the swab perpendicular to the face along the floor of the nasal cavity.
2. If the nasal mucosa is swollen, rotate the swab between finger and thumb while inserting it.
3. The swab should be inserted to the base of nasal cavity (this will be approximately half the distance from the nose to the ear).
4. Rotate swab to collect the cells in the mucus cavity and withdraw while rotating.
5. Place the swab into the accompanying vial of transport media, bending or cutting at the mark on the swab to seal the lid securely.
6. Label the container with the patient's full name and date of birth.



A sterile swab is passed gently through the nostril and into the nasopharynx

ADAM.

Submitting Specimens to BCPHL:

PLEASE ENSURE THE SPECIMENS/SAMPLES AND REQUISITION FORMS ARE CLEARLY LABELLED.

Please indicate if these are outbreak associated specimens or other agreed on highest priority specimens. BCPHL staff will triage based on requisition information prioritize testing.

Complete the Virology Services Requisition form (Appendix C) for each patient's swab to be submitted, providing:

- Accurate patient and health care provider information
- Patient Status
- Relevant clinical signs and symptoms and travel history
- Date and time of specimen collection
- Specimen type
- Travel history
- If the person is being treated with anti-virals, include this information on the requisition form in the Signs/Symptoms area. Specimens will not be routinely tested for resistance to antiviral drugs, but may be if there is evidence to suggest this is important.

Specimens/Samples Transport:

Assemble specimens and ship using provided specimen containers under Biological Substance, Category B and UN3373 specifications.

Use the labels provided and include an ice pack if possible.

Ordering Specimen/Samples Kits:

The *Specimen Container Order Form* can be found on our website at <http://www.phsa.ca/NR/rdonlyres/357FE8D0-2020-4A34-9416-8C3B12C4F2C3/0/SampleContainerOrderForm.pdf>

Contact: Nick Burnett, Procurement Team Lead, 604-875-2345x5467

Appendix E: BCPHL Antiviral Resistance Testing Program

Purpose:

- To provide a rapid (next day) diagnosis of antiviral resistant influenza A viruses from patient specimens.
- To implement testing of influenza A viruses for antiviral resistance mutations of in the NA and M2 genes by sequence analysis or SNP assays.

Background:

Antiviral drugs will be the mainstay of management of patients with pandemic influenza, until adequate quantities of vaccine are available. These include the neuraminidase inhibitors (Oseltamivir and Zanamivir) and ion channel blockers, (Amantadine). Both seasonal influenza and pandemic influenza have been shown to develop resistance to these agents. Of particular concern is the very high levels of resistance that have developed to Amantadine in the H3N2 strains and to Oseltamivir in the H1N1 strains of Influenza A. The fact that the H1N1 strain of seasonal influenza A shares antigenic identity with the H5N1 strain in terms of the neuraminidase component is of particular concern. In one report half of the patients hospitalized with avian influenza H5N1, the virus developed resistance to Oseltamivir with a fatal outcome for the patient. Development of resistance to this drug by the N1 viruses could seriously compromise the entire management strategy which is based on Oseltamivir therapy and prophylaxis

Conventionally, testing for antiviral resistance has been performed by the NML using a phenotypic assay platform. This testing is time consuming with a 1 week turn-around time. While phenotypic testing is comprehensive, most of the drug resistant mutant viruses can readily be identified by specific mutations in the neuraminidase gene or the M2 gene. This allows for the implementation of tests on the viral genome which can be performed by sequence analysis or single nucleotide polymorphism (SNP) assays that can readily be performed at the BCCDC. The BCCDC is in the process of implementing an SNP assay and performs a limited amount of sequence analysis on influenza A H1N1.

Assumptions:

- Because of the high prevalence of resistance to Oseltamivir in the currently circulating H1N1 influenza A viruses, testing for this marker will become of major importance. (Did not occur)
- Pandemic strains of influenza A virus will likely have a substantial degree of antiviral resistance. (Resistance occurred in treated patients but was uncommon)
- Reference laboratories will be required to test influenza virus from patient specimens for antiviral resistance markers.