

## Influenza

# Laboratory case definition

The Public Health Laboratory Network (PHLN) has developed standard case definitions to inform the diagnosis of key diseases in Australia. This document contains the laboratory case definition (LCD) for influenza.

Version	Status	Authorisation	Consensus Date
1.1	Update to new template and content to ensure gold standards of practice have been incorporated.	PHLN	24 July 2024
1.0	Initial PHLN Laboratory Case Definition	PHLN	26 November 2020

## 1 PHLN summary laboratory definition

#### 1.1. Condition

Influenza due to infection with influenza viruses.

#### 1.1.1. Definitive criteria

- Detection of influenza viruses by nucleic acid testing (NAT) from appropriate respiratory tract specimens (or in some situations specimens from other sites such as the eye); or
- Isolation of influenza viruses by culture from appropriate respiratory tract specimens (or in some situations specimens from other sites such as the eye); or
- Detection of influenza virus antigen using a TGA approved influenza virus antigen assay (such as rapid antigen tests (RATs) or Lateral Flow tests or immunochromatographic tests)<sup>1</sup> from appropriate respiratory tract specimens; or
- Seroconversion or a significant increase in antibody levels such as a fourfold or greater rise in antibody titre to influenza virus.

#### 1.1.2. Suggestive criteria

• a single high anti-influenza virus-specific antibody titre

#### 1.1.3. Special Considerations / Guide for Use

There are now a variety of 'Point of Care' (POC) tests for detecting influenza. These tests include the detection of viral antigens based on immunoassay technology, commonly referred to as RATs. Negative results from these assays should be treated with caution due to their relatively low sensitivity compared to NAT. Further laboratory-based testing should be sought if influenza is suspected in the presence of a negative RAT test result. Other POC tests are now available that are based on NAT (e.g. GeneXpert, Cobas Liat) and their analytical performance (sensitivity/specificity) are equivalent to other high throughput NAT tests.

All samples where influenza is detected should be typed (e.g. influenza A and/or B) and where possible influenza A positive samples should be subtyped. Most commercial tests detect influenza A or B viruses but do not subtype the influenza A virus. If influenza A virus subtyping is performed and no result is obtained (and there is a sufficient viral load in the

<sup>&</sup>lt;sup>1</sup> Note this only applies to testing performed in an accredited laboratory and excludes self-testing.

sample – such as a  $C_t$ <30 with a pan-influenza A real time reverse-transcriptase PCR (RT-PCR) assay) then this sample should be re-tested (for A(H3) and A(H1N1)pdm09 subtypes). If it fails to subtype then it should also be tested for other influenza A subtypes (if this testing is available) or referred to the WHO Collaborating Centre for Reference and Research on Influenza (WHOCCRRI) in Melbourne as soon as possible, as this may represent a human infection with a novel influenza virus.

#### 1.1.4. Links to related documents and websites

#### Pandemic influenza

• Australian Health Management Plan for Pandemic Influenza (AHMPPI)

#### Seasonal influenza

- NCIRS Fact Sheet on influenza
- Australian Government Department of Health and Aged Care influenza page
- <u>Australian Respiratory Surveillance Reports (ARSR) published fortnightly</u>
- WHO Collaborating Centre for Reference and Research on Influenza, VIDRL, Melbourne

#### Avian influenza

Australian Government Department of Health and Aged Care Avian Influenza landing page

## 2 Introduction

Influenza in humans is an acute, usually self-limited, febrile respiratory illness caused (in most instances) by infection with influenza A virus or influenza B virus, which in temperate climates occurs in outbreaks of varying severity almost every winter. Influenza may occur throughout the year in tropical climates, although there are typically one or two main peaks, often during the wet season. In pandemics, outbreaks may be seen outside the usual influenza season.

Influenza viruses are enveloped viruses of the family *Orthomyxoviridae* and contain segmented negative-sense single-stranded RNA genomes. The influenza virus types A, B, C and D can be distinguished on the basis of antigenic differences between their nucleocapsid and matrix proteins; influenza A viruses can be further subtyped based on the genetic sequence of their haemagglutinin (HA) and neuraminidase (NA) surface glycoproteins which can also be differentiated antigenically with the appropriate antisera. They replicate in the

columnar epithelial cells of the respiratory tract, and the primary mode of transmission is via respiratory droplets.

Influenza C causes very mild illness occurring mainly in children and has little clinical or public health implications compared to influenza A and B. Influenza D is a new classification that was included with influenza C and to date has only been detected in cattle. Influenza B *undergoes antigenic drift but not shift as it is a human virus with a single HA subtype, and* C and D viruses do not undergo antigenic shift or drift and they are not vaccine preventable. Standard laboratory tests do not detect influenza C or D. As only a few reference laboratories carry out influenza C testing (and very few influenza D), these influenza types are not covered further in this document.

In Australia, seasonal influenza (influenza A and B) is notifiable only with laboratory confirmation. Pandemic influenza is notifiable in Australia and New Zealand. Human cases of highly pathogenic avian influenza (HPAI) viruses are subject to quarantine regulations Australia-wide. Human HPAI (A(H5N1) viruses are also considered security sensitive biological agents (SSBA) in Australia and are regulated under the SSBA Regulatory Scheme. Surveillance programs for influenza are based upon laboratory, clinical or a combination of laboratory and clinical reporting schemes. Clinically based surveillance programs include one run through a GP network (Australian Sentinel Practice Research Network (ASPREN)) and there is also a hospital surveillance program (FluCAN), while Australian National Influenza Centres (NICs) also report laboratory data to the WHO Global Influenza Surveillance and Response System (GISRS) and Flutracking is an online self-reporting system.

Many large laboratories that perform influenza virus testing send a selection of influenza positive clinical samples and isolates to the WHOCCRRI either directly, or via one of the three Australian WHO NICs. Only the NIC laboratories and a few other laboratories isolate influenza viruses from clinical samples. Clinical samples and isolates are used to help monitor and identify the specific types of circulating viruses and also to select strains to be incorporated into the following season's influenza vaccines based on inactivated viruses. Selection of influenza strains for vaccines is based on the monitoring of antigenic and genetic changes and antiviral resistance at the WHOCCRRI. Clinical samples (only) are used to recover virus isolates in suitable embryonated hens' eggs or suitable cell lines as potential human vaccine seed viruses. These latter procedures can only be performed at the WHOCCRRI in Melbourne or at one of the other four global WHOCCRRIs.

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This document outlines methods for the laboratory diagnosis of influenza to confirm influenza as the cause of clinical influenza-like illness (ILI). Accurate laboratory and clinical diagnosis (or surveillance) of influenza is required for the annual winter epidemics (influenza activity is generally concentrated between May 1 and September 30 in temperate zones of Australia and New Zealand, and throughout the year in tropical zones of Australia with peaks around February-March and July-August). Occasionally imported or other cases of novel influenza infections that may have pandemic potential may be detected. The role of laboratory surveillance in influenza pandemic planning is discussed in the AHMPPI.

## 3 Laboratory diagnosis

#### 3.1. Clinical specimens

#### 3.1.1. Sample types

Nasopharyngeal swabs (NPS) or aspirates (NPA) are the optimal sample types because they contain the highest number of potentially influenza infected respiratory epithelial cells. NPAs are usually only available from children because of the difficulty in collecting NPAs from adults. NPS are the routine sample taken for most adults and are also acceptable samples from children. Combined swabs collected from the throat and from the anterior ends of the nasal turbinates can also be combined into a single specimen. This is better than separate swabs from either of these sites. Isolated throat swabs or throat gargles are less useful as most cells captured are squamous epithelial cells. Nasal washes can also be used although these are less popular in Australia than other countries such as the USA. Sputum is a poor sample for influenza virus detection or isolation due to bacterial contamination and the presence of mucus. In practice, lower respiratory tract specimens (e.g. bronchoalveolar lavage fluid) are indicated where lower respiratory involvement is clinically suspected. In some cases of influenza pneumonia, influenza virus may be detected from lower, but not upper respiratory tract specimens. Conjunctival swabs should be considered if conjunctivitis is present. Appropriate personal protective equipment should be worn during sample collection. Ideally, all samples should be collected within 96 hours of symptom onset.

Swabs may be flocked (nylon), cotton, rayon or dacron-tipped, plastic-coated or aluminium shafted. They either contain their own viral transport media (VTM), Universal Transport Medium (UTM) or can be placed into a vial of VTM/UTM immediately after collection. Other specimens should be placed in a sterile container. Specimens should ideally be stored and transported at 4 °C (according to the appropriate IATA standards) or, if they cannot be processed within 72 hours, they should be frozen at -70 °C. However, previous experiments have suggested that influenza virus may also be detected from swab samples stored and

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transported at room temperature for up to 5 days (Druce *et al* J Clin Microbiol 2012). Samples should never be frozen at –20 °C. If samples are not to be used for virus isolation, then dry flocked swabs are the best choice of swab to use, preferably as a nasopharyngeal swab. Note that some molecular transport media are specifically designed to INACTIVATE viral and bacterial pathogens (e.g., PrimeStore MTM, EKF Diagnostics) and so should be avoided if virus isolation is going to be performed.

#### 3.1.2. Serum samples

Serological diagnosis of influenza may be useful for surveillance and epidemiological purposes, and in specific cases of suspected post-influenza complications, such as myocarditis, acute disseminated encephalomyelitis (ADEM), and encephalitis, but NAT is the preferred method for rapid diagnosis of acute influenza for clinical purposes.

For serological investigations, serum samples should be taken during the acute phase (within 1–7 days of ILI onset) and during the convalescent phase ILI (14–28 days after ILI onset) and tested in parallel. The sensitivity of laboratory diagnosis of influenza is increased by using a combination of virus detection by NAT early in the illness and serology on acute and convalescent blood samples.

#### 3.2. Detection of influenza virus antigen or viral genome

Virus antigen (protein) detection assays are typically directed towards circulating epidemic viruses. They are usually less sensitive in the detection of novel strains, e.g., new pandemic strains or those with a different HA subtype such as A(H5N1) (HPAI) or A(H7N9) (HPAI or LPAI) or A(H9N2) (LPAI) or swine derived viruses.

#### 3.2.1. Antigen detection

Methods using monoclonal antibody (Mab)-based assays, with detection of the product by direct fluorescence (DFA) or enzyme immunoassay (EIA), using fluorescein/enzyme/gold-labelled secondary antibodies have largely been replaced by NAT testing in Australia. Point of cared tests (POC) based on immunochromatograhy (also known as ICT's or RATs or Lateral flow devices) also rely on viral antigen detection and are covered in section 3.3.3.

#### 3.2.2. Nucleic acid detection tests (NAT)

Influenza RNA in samples can be detected by NAT such as RT-PCR which requires thermal cycling, or other related assays such as loop-mediated isothermal amplification (LAMP) that are isothermal-based. NAT are the most sensitive test for influenza virus detection and also has extremely high specificity and a much more rapid turnaround time than virus culture

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(3,4). NAT increases detection rates of influenza viruses in clinical specimens compared with virus culture or other non-molecular tests. NAT are more tolerant of samples that have been improperly stored, transported, or excessively delayed, as NAT can detect non-viable (non-competent) virus. The sensitivity (depending on the primers/probes used) is approximately 90–100% compared with other direct detection tests, and the specificity approaches 100%. Primers/probes can be combined in a nested PCR to increase sensitivity or in a multiplex PCR to detect other respiratory pathogens. NAT primers should be reviewed annually (or as required) to ensure that influenza virus genetic drift has not affected assay sensitivity (especially if the target gene is the HA). In addition, the sensitivity will be affected by the adequacy of the specimen collection.

There are two major classes of influenza NAT,

- Those directed at targets that are common to a specific influenza type, e.g. matrix or nucleoprotein or NS genes common to all influenza A virus strains or to all influenza B virus strains.
- Those that are specific to an influenza A virus subtypes, i.e., primers/probes are directed at targets in the HA gene that are specific for seasonal A(H3N2) or A(H1N1)pdm09 or other potentially zoonotic influenza viruses for example A(H5) or possibly the NA gene of seasonal A(HN1)pdm09 N1 or A(H3N2) N2 or influenza B NA.

Nucleic acid testing is the test of choice for definitive identification of human infection with influenza A viruses A(H5N1) or A(H5Nx) or A(H7N9), either of HPAI and LPAI-types and other zoonotic viruses that have infected humans overseas in the past.

A subset of positive samples should be referred to the WHOCCRRI or other reference laboratory in a timely manner for virus isolation, vaccine seed preparation, antiviral resistance monitoring and antigenic analysis. Laboratories performing NAT detection of influenza should participate in recognised testing quality assurance (QA) Programs (e.g., those run by the Australian RCPAQAP or alternative programs such as the Quality Control for Molecular Diagnostics (QCMD) or run by WHO for seasonal influenza viruses (A(H1N1)pdm09, A(H3N2), B viruses) as well as other zoonotic and potentially zoonotic influenza viruses (e.g. A(H5N6), A(H7N9), A(H9N2)).

#### 3.3. Detection of the virus – virus isolation

Isolation of influenza A or B virus in cell lines such as Madin-Darby canine kidney (MDCK) or other permissive cell lines, provides a definitive diagnosis of influenza, though it is slower and less sensitive than NAT and requires the virus to remain viable during storage and transport. However, cell culture does provide virus stocks for the more detailed antigenic analyses needed for strain identification and to assist vaccine selection, as well as the potential capacity to detect new influenza types that may not be detected by other methods. Propagated influenza virus isolates play an important role in the generation of collections of historical and reference isolates essential for future influenza research, molecular assay controls and development of more efficacious therapeutics. It is important that appropriate biosafety and SSBA guidelines are followed when culturing and processing influenza positive samples (See: <u>Australian/New Zealand Standard, Safety in laboratories Part 3:</u> <u>Microbiological aspects and containment facilities</u>).</u>

#### 3.3.1. Conventional culture and typing

Influenza viruses are usually isolated using MDCK cells, SIAT-1 MDCK or other epithelial cell lines. Primary monkey kidney cells are difficult to obtain and problematic to work with, so they are now rarely used. Influenza virus growth is suggested by haemadsorption or observation of typical cytopathic effect at 4–5 days post-inoculation. Confirmation is usually achieved by NAT or immunofluorescent antibody (IFA) testing using influenza type or subtype-specific monoclonal antibodies. Further strain typing can be carried out using the more time-consuming technique of haemagglutination inhibition (HAI).

All isolates should have preliminary typing and subtyping such as influenza A(H1N1)pdm09 or A(H3) (or other subtype), or influenza B, as quickly as possible, either in the laboratory carrying out the culture or in a reference laboratory. All influenza isolates (especially those that fail to type) should also be referred to the WHOCCRRI directly, via a local WHO NIC or local reference laboratory. Where a new or significantly different strain is suspected, then isolates should be referred urgently to the WHOCCRRI.

For egg-based influenza vaccines, influenza isolation is undertaken by inoculating cells lining the amniotic or allantoic cavity of embryonated chicken eggs, and this technique is still widely used for vaccine generation. This procedure is routinely performed using original clinical samples at the WHOCCRRI as well as the isolation of influenza viruses into suitable cell lines for cell-based influenza virus vaccines.

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Antiviral susceptibility testing using genotypic or phenotypic techniques is available at the WHOCCRRI and in some reference laboratories but is not currently part of routine testing. Antiviral susceptibility is monitored internationally via the WHO GISRS network<sup>6</sup>.

#### 3.3.2. Rapid culture assays

The time required for cell culture identification of influenza virus can be reduced to 1–3 days using shell-vial or multi-well plates (typically using MDCK cells) that can be stained after 48 hours culture using commercially available monoclonal antibodies. Sensitivity varies from 56–100% compared with conventional culture<sup>3,4</sup>, and is approximately 85% sensitive compared to PCR. Specificity of culture is 100%. Rapid culture positive samples should be subsequently re-cultured in the testing or a reference laboratory to provide an isolate for antigenic analyses as part of surveillance and vaccine development.

#### 3.3.3. Quality Assurance Programs

There is currently no quality assurance program (QAP) specifically for virus isolation, however the WHO does offer a QAP for influenza isolation for NIC's (performed by the WHOCCRRI) periodically.

#### 3.3.4. Point of Care Tests

As noted above, POC tests have traditionally been based on immunoassay technology using antibodies directed against conserved influenza proteins e.g. nucleoprotein; however, some of these tests are now being replaced by more sophisticated second-generation tests or molecular-based tests. The original antigen-based tests have been available for decades and may assist in the early management of suspected influenza cases. These may have a role in laboratories unable to perform NAT in outbreak situations, for doctors without reasonable laboratory access, or to guide the rapid use of influenza antiviral agents<sup>4</sup>. They are intended for use near the patient or at the bedside and the specificity has been shown to be generally high (90-95%). The earlier POCs are consistently less sensitive (60–85%) compared to NAT and culture. If a reliable negative result is required, or if the accuracy of a positive result is critical, then these samples should also be tested by NAT or another molecular-based POC test.

Improvements in the sensitivity of antigen-based POC tests have been made recently over the original visible immunoassay tests with the use of fluorescent labels and the use of a reader rather than relying on the naked eye to unequivocally determine positive or negative test results. In addition, POC tests based on NAT technologies have comparable analytical performance to laboratory-based NAT and results generated using these platforms should therefore be considered more reliable than the traditional immunoassay based POC tests.

Multiplex rapid POC NAT are able to simultaneously detect influenza A, influenza B, and other respiratory pathogens such as SARS-CoV-2 and RSV. These multiplex approaches have also been incorporated into RATs using antibody detection with tests capable of detecting influenza A, influenza B, RSV and SARS-Cov-2 on the one device and appear to have improved sensitivity over earlier devices.

#### 3.4. Serology

Detection of influenza-specific antibodies allows a retrospective diagnosis of influenza and is also a useful surveillance tool. As influenza is often a reinfection with pre-existing partial immunity present, recent infection can only be reliably diagnosed by demonstrating a significant increase in influenza-specific antibody levels (such as four-fold or greater rise in influenza-specific antibody titres). Single samples with a high titre are less reliable as they may reflect past infection or vaccination. However, a single high titre is suggestive of probable recent infection when the patient has had a consistent ILI occurring during the influenza season<sup>3,4</sup>. This is because neither vaccination nor infection in the previous season produces high antibody titres. Serological methods include complement fixation (CF), HAI, virus neutralisation (VNT) and enzyme immunoassays (EIA). Sensitivity varies from 80–50% (EIA>HAI>CF) as does specificity. Enzyme immunoassay-based IgM (and IgA) assays have not proved useful in routine laboratory diagnosis as most influenza is due to re-infection and patients will have pre-existing antibodies that may cross react.

CF tests detect antibodies directed at the influenza virus nucleoprotein and can distinguish between influenza A (but not between subtypes) and influenza B. A fourfold rise in antibody titre is definitive evidence of acute infection. HAI and VNT are the gold standard assays that allow subtype reactivity to be determined. There are generally accepted criteria that correlate with post-vaccine "immunity". The technical difficulties associated with these tests mean that they are not in widespread diagnostic use. Also, they may not detect new influenza A subtypes due to antibody cross-reactivity with existing circulating influenza A subtypes. For CF, a four-fold rise in influenza-specific antibodies is the most reliable indicator of recent infection. Single high titres are suggestive of recent infection in the appropriate clinical situation. Due to differences in how these tests are performed in different laboratories, the definition of "positive titre" and a "high positive titre" will vary between laboratories.

EIA tests have not been widely used and the criteria for immunity and for significant or protective antibody levels are not well established.

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Laboratories performing serology testing for influenza should participate in the RCPA Serology QA Program: for further information please refer to RCPA, or a similar program or participate in an inter-laboratory exchange with a sister laboratory that performs the same assay(s).

#### 3.5. Quality Assurance

Test-specific QA considerations are described under the various testing procedures.

# 3.6. Diagnosis of Human Cases with novel influenza virus infections (e.g. viruses of avian, swine or other species origin)

Where there is a suspected case of human infection with novel influenza A virus such as highly pathogenic avian influenza (A(H5N1), A(H5N6), A(H7N9)) or another novel strain such as swine-origin variant virus A(H1N2)v or A(H3N2)v, or a virus from an unusual species such as A(H5N1) HPAI originating from dairy cows or cats or other mammalian species or in the event of a new pandemic influenza emerging, the laboratory case definition will be similar to that for seasonal influenza, but may include exposure history, travel history, etc. as outlined in the AHMPPI with updates as appropriate from the WHO, US CDC and other similar organizations.

Specimen collection for suspected novel influenza infections will be similar to that for seasonal influenza (combined NPS or nose and throat swabs are the recommended sample) except that additional non-respiratory specimens, (e.g. conjunctival swabs, serum, faeces, rectal swabs and cerebrospinal fluid) may be useful in diagnosing some cases where the spread of influenza is more systemic (e.g. A(H5N1)) or localised at a non-respiratory site. For example, a conjunctival swab should be taken if there is conjunctivitis present or evidence of an eye infection. Influenza A(H5N1), A(H7N7) and other influenza A subtypes may be detectable from eye swabs. Lower respiratory tract samples may also be tested in suspected cases of severe influenza virus infection (e.g. A(H5N1), A(H5N6), A(H7N9)) when testing of the upper respiratory tract returned a negative result.

The diagnostic test of choice is NAT with both influenza A-specific and novel strain-specific primers/probes. All NAT positive novel influenza viruses should be sequenced (minimum HA and NA genes and preferably whole genome sequencing). If this cannot be performed in a timely manner at the testing laboratory, an aliquot of the positive sample should be shipped as soon as possible to the WHOCCRRI for confirmation of the subtype (HA and NA), and where whole genome sequencing and a risk assessment can be performed. Serial sampling (e.g. daily swabs) may be useful to monitor virus kinetics and antiviral resistance, to detect

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the presence of other pathogens, and potentially confirm the diagnosis in persons that are asymptomatic, pre-symptomatic or pauci-symptomatic.

Influenza serology maybe useful to determine if the subject has been infected with a novel influenza virus especially if the subject is asymptomatic. If seroconversion is confirmed this is likely to indicate a true infection. Ideally specimens used for serology testing would involve a serum sample taken at the time of infection or at symptom presentation and then a second serum sample 4-6 weeks later. The second sample is needed to confirm that seroconversion has occurred but is not needed for patient treatment decisions. If the subject presents with respiratory symptoms, serology testing may not be needed. If a subject has a positive NAT for a novel influenza virus, is asymptomatic and does not seroconvert this may indicate environmental carriage of virus rather than a true infection and the positive NAT may have been due to high viral loads in the environment such as where poultry culls are occurring. Serology testing against a novel influenza virus is most likely to be performed initially by a specialist laboratory such as the WHOCCRRI or the Australian Centre for Disease Preparedness, Geelong, Victoria.

At a minimum, laboratories must meet basic PC2 standards and use PC3 work practices to handle specimens that are suspected to contain novel or potentially pandemic influenza viruses and use a PC3 facility wherever possible. Appropriately equipped and accredited laboratories may also perform virus isolation under PC3 conditions.

The reliability of non-NAT based POC tests for detection of novel or potential pandemic influenza viruses (of avian or swine or other origin) are not well established and should not be used for diagnostic purposes.

## 4 Agreed Typing and Subtyping Methods

#### 4.1. Laboratory Nomenclature of National Database Dictionary

4.1.1. Organism Name(s) List

Influenza A virus, Influenza B virus, Influenza C virus, Influenza D virus

4.1.2. Typing/Subtyping Nomenclature List(s)

Types: influenza A, *or* influenza B (influenza C is rarely tested diagnostically nor is Influenza D).

Influenza A Subtypes: Currently there are two influenza A viruses that are circulating in humans, A(H3N2) and A(H1N1)pdm09. The H refers to the haemagglutinin type of which

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there are 18, and the N refers to the neuraminidase type of which there are 11 subtypes. Most of these subtypes can be found in avian species but only a few of these HA and NA subtypes have been detected in humans (e.g. H1N1, H3N2 and in the past H2N2). There are two other subgroups of distantly related influenza A viruses included in this list that have recently been detected in certain bat species (H17N10 and H18N11).

#### 4.1.3. Influenza B-lineage determination

Two lineages of influenza B viruses (B/Victoria/2/87-like or B/Yamagata/16/89-like) that differ in their antigenic and molecular characteristics are circulating in the human population. These two lineages diverged in the 1990's and B-viruses are referred to as being either of B/Victoria/2/87-lineage (B/Victoria-lineage) or B/Yamagata/16/88-lineage (B/Yamagatalineage). However, following the COVID-19 pandemic, the vast majority of characterised influenza B viruses belong to the B/Victoria lineage. This raises the possibility that B/Yamagata viruses may become extinct (Paget *et al* Eurosurveill 2022), hence lineage determination of influenza B viruses may no longer be necessary in the future.

# 5 Laboratory nomenclature for national data dictionary

SNOMED CT code	Concept name	Description
6142004	Disorder	Influenza
95891005	Clinical finding	Influenza-like illness
442438000	Organism	Influenza A virus
24662006	Organism	Influenza B virus
81524006	Organism	Influenza C virus

## 6 References

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## 7 Glossary

- (US) CDC Centers for Disease Control and Prevention
- CSF Cerebrospinal fluid
- $\mathbf{C}_t$  Cycle threshold
- DFA Direct fluorescent antibody
- EIA Enzyme immunoassay
- ELISA Enzyme linked immunosorbent assay
- HAI Haemagglutination inhibition
- ICT Immunochromatographic test
- IFA Immunofluorescent antibody
- IgA Immunoglobulin A
- IgM Immunoglobulin M
- IVD (device) In vitro diagnostic medical device
- LAMP Loop-mediated isothermal amplification
- NAT Nucleic acid test/ing
- PCR Polymerase chain reaction
- PC2 laboratory Physical containment level 2 laboratory
- PC3 laboratory Physical containment level 3 laboratory
- **POC** Point-of-care
- **QAP** Quality assurance program
- QC Quality control
- **RNA** Ribonucleic acid
- RT Reverse transcriptase
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RT-PCR – Reverse transcription polymerase chain reaction

- SSBA Security sensitive biological agent
- Strain Variant that possesses unique and stable phenotypic characteristics
- Test sensitivity Ability of a test to correctly identify patients with a disease
- Test specificity Ability of a test to correctly identify people without the disease
- **TGA** Therapeutic Goods Administration
- UTM Universal transport medium
- **VTM** Viral transport media
- WGS Whole genome sequencing
- **WHO** World Health Organization
- WHOCCRRI WHO Collaborating Centre for Reference and Research on Influenza