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Frequently Asked Questions

Sampling and shipping of influenza clinical specimens and virus isolates

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A. REAGENTS AND KITS FOR SEASONAL AND AVIAN INFLUENZA

How can we obtain a WHO influenza reagent kit for identification (typing and subtyping) of seasonal influenza?

Contact a WHO Collaborating Centres for Influenza (WHO CC) from the following list: www.who.int/csr/disease/influenza/collabcentres/en/index.html

WHO recognized National Influenza Centres (NIC) can obtain a WHO kit free of charge.

You may also contact WHO Global Influenza Programme at GISN@who.int

What does the WHO influenza reagent kit contain?

It contains:

i. Reagents for Hemagglutination Inhibition assay (HI):
   - control antigens (A/H1, A/H3, B/Yamagata-like, B/Victoria-like),
   - reference sheep antisera , (A/H1, A/H3, B/Yamagata-like, B/Victoria-like),
   - influenza negative control sheep antiserum,
   - receptor destroying enzyme (RDE).

ii. Reagents for direct immunofluorescence assay (IFA):
   - two type specific (influenza A, influenza B) monoclonal antibody pools,
   - two subtype specific antibodies (influenza A/H1, influenza A/H3).

Does the WHO influenza kit contain any infectious material?

No. The reagents do not contain live viruses.

How will the WHO influenza kit sent?

The kit will be sent by regular postal service at room temperature (not exceeding 25°C). It does not require cold chain. There are no specific requirements for shipping of dangerous goods as the kits do not contain live viruses (see above).

For shipments during which extreme conditions (temperatures exceeding 25°C) are anticipated, ice packs (4°C) should be considered and arrangements made between the provider (the WHO CC) and the recipient laboratory. Likewise, if significant changes in temperature are anticipated (a variation of more than 15°C) during shipment or upon arrival, the provider and recipient should contact each other to ensure appropriate packaging.

Are PCR reagents available from WHO?

Upon special request and subject to availability, WHO CCs can assist with PCR diagnosis and providing specific reagents (primers) for the detection of influenza viruses other than seasonal influenza viruses.

Contact GISN@who.int or one of the following WHO CC for influenza:

www.who.int/csr/disease/influenza/collabcentres/en/index.html

Some PCR reagents and standard protocols require a Material Transfer Agreement (MTA) to be signed between the providing CC and the recipient.

In the event of an outbreak of avian influenza (AI) with suspected human cases, what reagents/materials can be obtained from WHO?

In the event of an outbreak of AI, WHO can provide various types of support. Please contact the WHO Representative or Liaison Office in your country to discuss your specific needs.

The following are examples of materials which can be purchased through the WHO GSM catalogue or provided by partner institutions. Please note that these items will soon be available as part of the standard WHO kit in the GSM catalogue:

- An AI investigation kit including - Personal Protective equipment (PPE) and respiratory specimen sampling kit (swab applicators for throat and naso-pharyngeal samples and virus transporting medium (VTM)) shipped at room temperature.
- RNA extraction kit - UN1760 [Corrosive liquid. n.o.s (Guanidiniumthiocyanate)] Class 8 - Dangerous Goods Declaration is required) shipped at room temperature.
- PCR kit - UN1845, no primers included, shipped with dry ice at a temperature not exceeding -20°C.

If the outbreak constitutes a public health event requiring the assistance of WHO Headquarters outbreak response teams, WHO may be able to cover the additional supplies to cover surge needs as part of the outbreak investigation. Other exceptional situations will be discussed on a case by case basis.

B. COMMERCIALLY AVAILABLE REAGENTS AND KITS

Are rapid tests for influenza commercially available?

Yes. Rapid tests for the detection of one or both seasonal influenza types (A and B) are commercially available. They are frequently referred to as "point-of-care" rapid diagnostic test kits.

Further information on obtaining and using rapid tests for influenza diagnosis is available at:

www.who.int/csr/disease/avian_influenza/guidelines/RapidTestInfluenza_web.pdf

In general, the sensitivity of rapid tests is variable (median 70-75%) and lower than that of cell culture, while their specificity is high (median 90-95%). Because of the low sensitivity, false negative results are a major concern with these tests.

It is important to note that rapid diagnostic test kits for influenza have very low sensitivity and specificity for diagnosing non-seasonal influenza, including H5N1 infection. If there is any indication of non-seasonal influenza, respiratory samples in VTM (Virus Transport Medium) should be sent to a qualified laboratory for analysis with proven methods.

Are kits for the detection of antibodies against A(H5N1) influenza viruses commercially available?

Some kits for the detection of antibodies against A(H5N1) influenza viruses are commercially available. However, there is no systematic assessment of the quality and reliability of these kits. WHO is not therefore in a position to recommend any of these commercially available products.

C. SHIPPING LOGISTICS AND DOCUMENTATION

Under what circumstances can materials be sent at room temperature (18 - 25°C)?

If the total travel time from sender to recipient does not exceed 24 hours, the following materials may be sent at room temperature:

- Lyophilized nucleic acids (RNA, DNA)
- Original respiratory specimens in nucleic acid stabilizing agent

Under what circumstances should materials be shipped with ice packs (0 - 4°C, not frozen)?

If the total travel time will exceed 24 hours and the material has been stored in a refrigerator prior to shipment and NOT FROZEN, the following materials should be sent in ice packs:

- Original respiratory specimens, sera and virus isolates - when the combined time for storage and transportation to recipient together will not exceed 2 days.
- Lyophilized nucleic acids (RNA, DNA)
- Original respiratory specimens in nucleic acid stabilizing agent - when combined time for storage and transportation to recipient together will not exceed 14 days.

It is important that the sender verifies with the shipper that the temperature in the parcel will stay below 4°C at all times during transportation. This may require changes of ice pack during the journey and storage in a refrigerated area.

It is important to ensure that the ice packs do not touch or get too close to the specimens in order to prevent freezing.

Under what circumstances should materials be sent on dry ice (- 78°C)?

If the materials have been frozen at - 78°C or lower prior to transportation and if the exact duration of travel is unknown, the following materials must be sent on dry ice:

- Original respiratory specimens, sera and virus isolates

The samples should be collected in suitable screw capped tubes, closed tightly and well sealed to avoid leakage of CO_2 inside the tube which inactivates influenza viruses.

The sender should verify with the shipper that the temperature in the parcel will stay below -78°C at all times during transportation. This may require supplementing the dry ice. Ensure that that all vials are well sealed to prevent CO_2 gas from entering the vials and damaging the material.

Under what circumstances should the materials be sent in liquid nitrogen (-210 to -195°C)?

If the materials have been frozen in liquid nitrogen prior to transportation, and the exact duration of travel will exceed seven days or is unknown, the following materials should be sent in liquid nitrogen:

- Original respiratory specimens, sera and isolates

The costs involved in shipping in these kinds of containers are high. It is therefore advisable to group a large number of specimens into one shipment. The sender should verify with the shipper that the required levels of liquid nitrogen will be maintained and supplemented as necessary throughout the shipment. Ensure that vials and labelling used are appropriate for storage in liquid nitrogen and that they are well sealed.

What is the WHO Shipment Fund Project and how does it work?

The Shipment Fund Project provides shipping services for all NICs who share their influenza specimens with the GISN. Other national influenza laboratories may also be eligible to benefit from the Project.

The Project covers the cost of shipping specimens from the national laboratory to a WHO CC or an H5 Reference Laboratory. It also allows for the simplification of certain aspects of shipping infectious substances - for example, procedures for requesting the shipment of influenza specimens. In addition, logistic and technical support for the shipment is available from WHO Headquarters for the sending laboratory.

For detailed information please contact WHO Headquarters.
GISN@who.int

Is an import permit required for shipments of respiratory samples that may contain influenza viruses to a WHO CC?

The import documentation required varies according to the country of destination. The sending laboratory should, in the first instance, contact the recipient laboratory in advance to ascertain what import documentation will be required and make the necessary arrangements for obtaining the relevant permits for the shipment.

Seasonal influenza viruses rarely require import permits. However, if the shipment includes an avian or novel influenza virus, an import permit will be required.

Is it possible to pack in the same triple system packaging both UN2814 and UN2900 material?

Yes. This is called an "all packed in one" parcel. It is, however subject to certain conditions and should be considered on a case by case basis. Please contact WHO Headquarters to discuss your shipment.
GISN@who.int

When is a Dangerous Goods Declaration required?

A Dangerous Goods Declaration is always required for any shipment containing Category A (UN2814, UN2900) Infectious Substances, whether it is in dry shipper (Liquid nitrogen), Frozen (-78°C), on ice packs (0-4°C) or at room temperature (18-25°C).

The outside of the package containing the Category A material must be clearly marked and labelled as follows:

- Proper Shipping Name:
  - If UN2814: **Infectious Substance, affecting humans**
  - If UN2900: **Infectious Substance, affecting animals** only
- Infectious substance label "division 6.2" affixed
- Full name and address of both the shipper and of the consignee
- Full name and telephone number of the responsible person (mandatory).

Is a Dangerous Goods Declaration (DGD) required when sending Category B material in liquid nitrogen?

Category B (UN3373) material does not require a Dangerous Goods Declaration (DGD) when it is sent using a dry shipper (in liquid nitrogen). When using a dry shipper, the liquid nitrogen is fully absorbed in a special sponge placed inside the container and therefore it is no longer dangerous.

The outside of the package containing Category B material must be clearly marked and labelled as follows:

- Proper Shipping Name: "Biological substance, Category B"
- The diamond mark affixed with "UN3373" written inside
- Full name and address of both the shipper and consignee
- Name and telephone number of the responsible person
  - if not indicated on the Air Waybill or
  - if other dangerous goods, such as dry ice (UN1945), are included in the package.

Is special training required for shipping infectious substances?

Yes if you intend to ship Category A material.

If, you are shipping only Category B or exempt human/animal specimens, there is no legal requirement to undertake special training in advance.

However, WHO recommends that anyone shipping these substances undertakes some basic training in dangerous goods to ensure awareness of regulations, packaging and classification of specimens.

What are the IATA Dangerous Goods Regulations (DGR)?

The IATA Dangerous Goods Regulations outlines the requirements for shipping dangerous goods by air in a user friendly, easy to understand format. It is a useful

"field manual" and is based on the agreed standards of the International Civil Aviation Organization. The DGR also includes additional information which can assist shippers in ensuring their consignments are fully in compliance with existing rules and will be quickly and easily accepted by the airlines.

We have correctly followed all the instructions but the airline has refused to carry our shipment. What can we do?

Talk to the airline to try to understand their objections in detail. Check that you are complying with any State or operator variations that may exist as outlined in Section 2 of the IATA DGR.

Is there any possibility that the shipment may have been damaged on its way to the airport?

Please bear in mind that airlines are not obliged to accept and transport a particular substance or product and can impose their own requirements above and beyond the regulations in force.

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