World Health Organization

Operational Guidance on Sharing Influenza Viruses with Human Pandemic Potential (IVPP) under the Pandemic Influenza Preparedness (PIP) Framework

30 JUNE 2017

WHO/WHE/IHM/GIP/2017.3

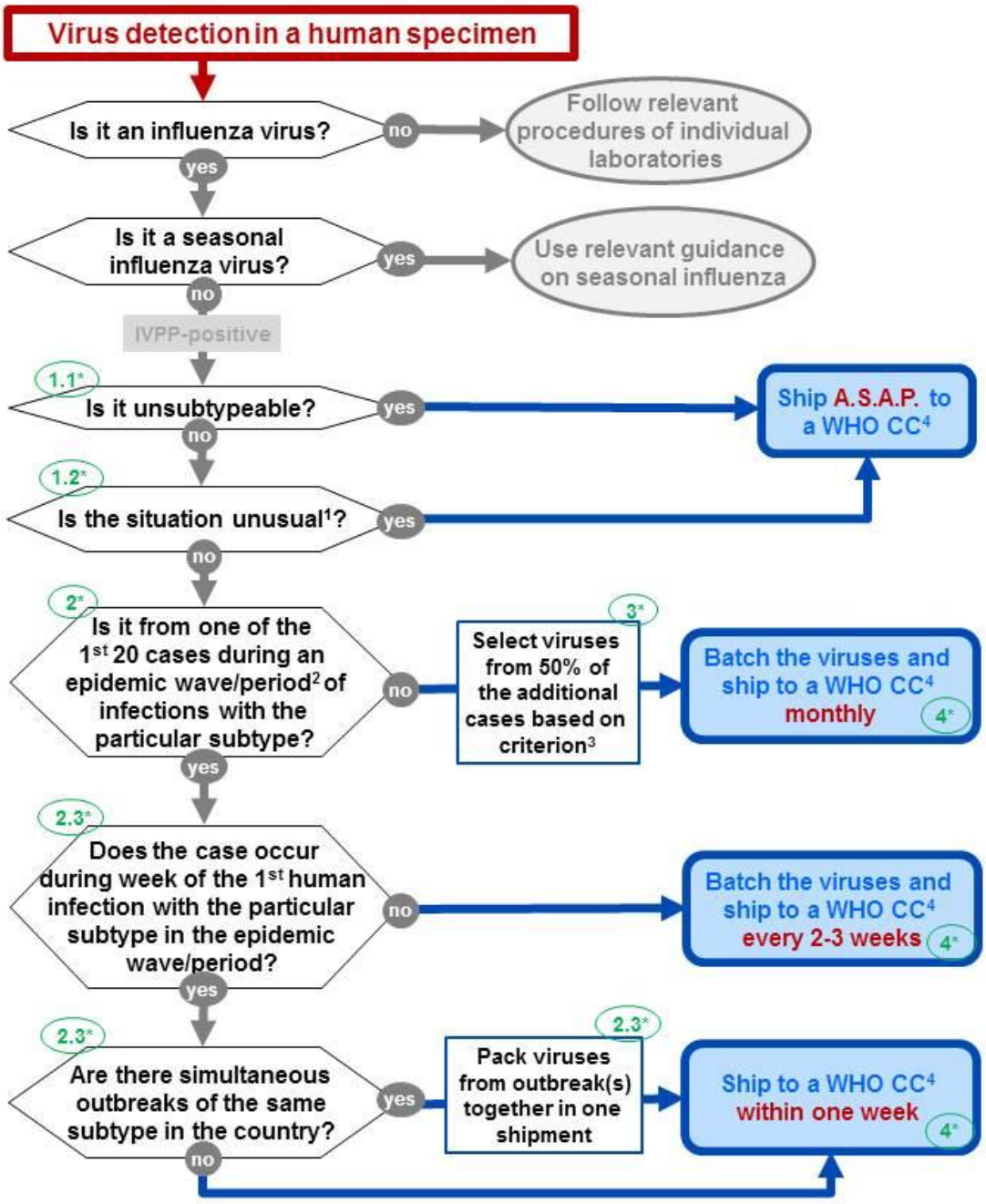
ACKNOWLEDGEMENTS

The World Health Organization (WHO) wishes to acknowledge the contributions of experts from WHO Collaborating Centres of the Global Influenza Surveillance and Response System (GISRS) and Dr Nancy Cox, independent consultant, who participated in the peer review of this Guidance.

ABBREVIATIONS

ARI	Acute Respiratory Infections
BM	Biological Materials
CC	Collaborating Centre of GISRS
CDC	Centers for Disease Control and Prevention
Ct	Cycle Threshold
CVV	Candidate Vaccine Virus
ERL	Essential Regulatory Laboratory of GISRS
FAO	Food and Agriculture Organization of the United Nations
GIP	WHO Global Influenza Programme
GISRS	Global Influenza Surveillance and Response System
GSD	Genetic Sequence Data
IHR (2005)	International Health Regulations (2005)
ILI	Influenza-Like Illness
INSDC	International Nucleotide Sequence Database Collaboration
IVPP	Influenza Viruses with Human Pandemic Potential
IVTM	Influenza Virus Traceability Mechanism
MAARI	Medically Attended Acute Respiratory Illness
NIC	National Influenza Centre of GISRS
(PIP) Framework	Pandemic Influenza Preparedness Framework for the sharing of influenza viruses and access to vaccines and other benefits
RT-PCR	Reverse Transcription Polymerase Chain Reaction
SARI	Severe Acute Respiratory Infection
SMTA 1	Standard Material Transfer Agreement 1
UN	United Nations
VTM	Virus Transport Medium
WHO	World Health Organization

Step-wise Guidance at a Glance
Selection and Shipping of IVPP to WHO CCs of GISRS under PIP Framework



* More information can be found in the corresponding numbered chapters under the section "Guidance on which and when IVPP samples should be shipped to WHO CCs" of the "Operational Guidance on Sharing Influenza Virus of Human Pandemic Potential (IVPP) under the Pandemic Influenza Preparedness (PIP) Framework".

[1] Unusual situation of IVPP: includes cluster of 3 or more people infected, cluster involving healthcare worker(s) infected, first human infection(s) in a country with a novel subtype which may/may not exist or infect people in other countries, increasing proportion of cases with no known animal contact, and any other situations as a advised by WHO.

[2] Epidemic period: A period of no more than 12 months, e.g. 1 October - 30 September, 1 January – 30 December or another period of 12 months or less depending on seasonal patterns of circulation.

[3] Criteria for selection: different age groups, males and females, different geographic locations within the country, different months over the course of outbreak, before and after antiviral treatment, select clinical samples with real-time RT-PCR cycle-threshold (Ct) value of <30.

[4] WHO CC of the country's choice (see list: http://www.who.int/influenza/gisrs_laboratory/collaborating_centres/list/)

Purpose

This guidance is intended to help National Influenza Centres (NICs) and H5 Reference Laboratories of the Global Influenza Surveillance and Response System (GISRS) and other Nationally Authorized Laboratories to select and ship IVPP to WHO Collaborating Centres of GISRS under the Pandemic Influenza Preparedness (PIP) Framework.

Background and introduction

In May 2011, the Sixty-fourth World Health Assembly adopted the Pandemic Influenza Preparedness (PIP) Framework for the sharing of influenza viruses with pandemic potential and access to vaccines and other benefits (the "Framework")[1]. Section 5.1.1 of the Framework states that "Member States, through their National Influenza Centres (NICs) and other authorized laboratories, should in a rapid, systematic and timely manner provide PIP biological materials (PIP BM) from all cases of H5N1 and other influenza viruses with human pandemic potential (IVPP)[2], as feasible, to the WHO Collaborating Centre (WHO CC) or WHO H5 Reference Laboratory of the originating Member State's choice".

While this section of the Framework has provided general guidance for the sharing of IVPP, a need was identified by the PIP Review Group[3] to develop more precise and specific virus sharing guidance for NICs and other authorized laboratories that identify IVPP during the course of their ongoing surveillance activities. This document operationalizes the general guidance contained in the Framework for WHO Global Influenza Surveillance and Response System (GISRS) laboratories for the rapid sharing and shipment of IVPP. The document will be reviewed and revised periodically based on the characteristics of future IVPP outbreaks and the collective experience gained through its implementation. It also should be noted that this document covers IVPP and is complementary to other WHO guidance that pertains to sharing seasonal influenza viruses and non-IVPP zoonotic influenza viruses, such as those from animal and environmental samples, of public health importance.

Roles of NICs, H5 Reference Laboratories and other authorized laboratories under the PIP Framework

GISRS serves as a global alert and response mechanism for the emergence of influenza viruses, including those with pandemic potential. There are four categories of laboratories

[1] http://www.who.int/influenza/pip/en/
[2] Definition see article 4.2 of PIP FW http://www.who.int/influenza/pip/en/
[3] http://apps.who.int/gb/ebwha/pdf_files/EB140/B140_16-en.pdf

within GISRS that have roles related to surveillance and response: NICs, WHO CCs, WHO H5 Reference Laboratories and Essential Regulatory Laboratories (ERLs). Terms of reference related to work with PIP BM for each of these categories of laboratories are elaborated in Annex 5 of the Framework. NICs, which conduct surveillance related to seasonal and pandemic influenza, are designated by their national ministries of health and recognized by WHO. In contrast, H5 Reference Laboratories were designated by WHO on an ad hoc basis since 2004 to support GISRS, especially in countries without reliable laboratory detection capacity in place, in response to the emergence and spread of the highly pathogenic avian influenza viruses of H5N1 subtype. Within this context, a critical role for both NICs and H5 Reference Laboratories is to rapidly share influenza viruses and/or clinical specimens from human infections caused by IVPP with one of the WHO CCs of GISRS: Melbourne (Australia), Beijing (China), Tokyo (Japan), London (United Kingdom of Great Britain and Northern Ireland), Atlanta (United States of America) or Memphis (United States of America). Contact information for WHO CCs is contained in **Annex 1**.

NICs receive clinical specimens collected from patients with influenza-like illness (ILI), severe acute respiratory infections (SARI) or other respiratory syndromes and perform initial detection and identification of influenza viruses, if present. When NICs detect IVPP, they are expected to send IVPP-positive clinical specimens and/or IVPP isolates to WHO CCs. These Centres are responsible for conducting detailed antigenic, genetic and biological characterization of IVPP, and providing critical information for public health risk assessment and risk management, including the development of candidate vaccine viruses (CVVs), and other public health related purposes. Although NICs are encouraged to perform virus isolation for seasonal influenza viruses, they may not have access to appropriate biocontainment facilities or relevant experience of working with highly pathogenic avian influenza viruses such as H5N1, H5N6, H5N8 and other viruses with pandemic potential such as H7N9. Therefore, NICs should not delay shipping influenza virus-positive samples to a WHO CC in pursuit of virus isolation locally. To ensure rapid sharing, it is important that NICs prepare viral materials for shipment as soon as identification has taken place of an unsubtypeable influenza A virus or of an H5, H6, H7, H9, H10 or other non-seasonal influenza viruses including H1 and H3 variant viruses.

Originally, WHO H5 Reference Laboratories were designated to fill in surveillance gaps for countries that did not have the capability to perform laboratory detection of influenza H5N1 viruses. H5 Reference Laboratories and NICs share the same guiding principles and have similar core terms of reference under the Framework (Annex 5 of the Framework) and therefore must share identified IVPP with WHO CCs according to the guidance set out in this document.

The Framework aims to position virus-sharing and benefit-sharing on an equal footing as both are essential for implementing the principles embodied in the Framework. IVPP are

shared through WHO GISRS under the Standard Material Transfer Agreement 1 (SMTA 1) contained in Annex 1 of the Framework. The SMTA 1 is a binding contract that establishes the conditions under which GISRS laboratories exchange PIP BM with each other. Briefly, the NIC or H5 Reference Laboratory sending PIP BM to a WHO CC must:

1. comply with its respective terms of reference as outlined in Annex 5 of the Framework;
2. ensure that materials are handled according to applicable WHO and national biosafety standards;
3. consent to the onward transfer and use of the materials to all members of WHO GISRS according to the terms and conditions specified in SMTA 1;
4. consent to transfer the materials onward to entities outside GISRS, providing that the prospective recipient has concluded or agreed to conclude a Standard Material Transfer Agreement 2 (SMTA 2) with WHO;
5. inform WHO of shipments of materials to entities within and outside GISRS by recording transfer of the PIP BM in the Influenza Virus Traceability Mechanism (IVTM) (Questions regarding how to record the transfer of PIP BM in the IVTM should be addressed to gisrs-whohq@who.int and/or to staff in the WHO CC that will receive the shipment); and
6. comply with requirements of the International Health Regulations (IHR) 2005 according to the procedures established nationally.

Importance of Sharing Influenza Viruses with Pandemic Potential (IVPP)

The rationale for rapidly sharing IVPP-positive clinical specimens and/or IVPP isolates with the WHO CCs is to allow them to conduct required laboratory work:

- to inform public health risk assessments;
- to monitor virus evolution and antiviral susceptibility;
- to determine if current diagnostic tests are working well or if new ones must be