World Health Organization

INTERGOVERNMENTAL MEETING ON PANDEMIC INFLUENZA PREPAREDNESS: SHARING OF INFLUENZA VIRUSES AND ACCESS TO VACCINES AND OTHER BENEFITS
Provisional agenda item 2

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Reports by the Director-General

Glossary of selected influenza-related terms to facilitate discussions in the intergovernmental meeting

1. This glossary of selected terms is intended to aid discussions during the Intergovernmental Meeting. An attempt has been made to keep the explanations as non-technical as possible.

VIRUSES

Candidate influenza vaccine viruses. These are influenza viruses that have been selected by WHO as viruses that potentially could be used as the basis for making influenza vaccine and that usually have been modified through laboratory techniques. Modifications are made to improve certain characteristics, for example, better growth properties in eggs, or, possibly to make a virus less dangerous. Depending on whether the candidate virus is for a seasonal or H5N1 vaccine, different laboratories, laboratory techniques, and levels of biocontainment may be used or required to perform the modifications. Candidate influenza vaccine viruses normally must be tested further by vaccine producers for their suitability for vaccine manufacturing and by WHO to see if essential features of the candidate virus have been retained through all the modifications.

High-growth reassortant. These are influenza viruses that have been modified by laboratory techniques to grow better in eggs so that more vaccine can be made. These viruses have two specifically selected genes for the proteins on the virus surface (typically from the **wild-type influenza** virus of concern) and six other internal "backbone" genes from another influenza virus (typically A/Puerto Rico/8/34). **Candidate influenza vaccine viruses** are often (but not always) high-growth reassortant viruses.

Influenza reference viruses. These are influenza viruses that have been found to infect people (and sometimes animals) in nature (i.e. **wild-type influenza viruses)** and that WHO has selected as representative of important groups of influenza viruses on the basis of extensive antigenic and genetic studies and comparisons with viruses from many countries. There are reference viruses for seasonal, H5N1 and other influenza viruses. As the **wild-type influenza viruses** evolve in nature, new reference viruses must be selected. Influenza reference viruses are used to make antibodies, which are used by national and other laboratories to identify recent influenza viruses.

New subtype of influenza virus. This term refers to influenza viruses that have surface proteins (haemaggluttinin alone or haemaggluttinin and neuraminidase together) that are very different from those found on existing human influenza viruses. This difference is large enough to define a new group (i.e. subtype) of influenza viruses. There are many influenza virus subtypes that naturally infect animals but usually do not infect people. However, some of these subtypes can infect people and when this is found, the subtype is considered "new" for humans. Any human infection by such a virus is a **novel influenza virus** infection that has the potential to cause a pandemic.

Novel influenza viruses. These are influenza viruses, which most often will be animal or partly animal influenza viruses, that have infected some people, but the vast majority of people in the world will never have been exposed to them and will have no pre-existing immunity to them. Novel influenza viruses have the potential to evolve and gain the ability to spread easily among people and possibly cause a pandemic. Novel influenza viruses are not variants of existing human influenza viruses.

Seed viruses. These are influenza viruses prepared from **candidate influenza vaccine viruses** by individual manufacturers for the manufacturer's specific vaccine-production process. Since vaccine processes differ among companies, different manufacturers may use differently prepared seed viruses.

Variant influenza viruses. This term refers to viruses that are related but are not identical to each other. As influenza viruses evolve, the more recent viruses can be considered variants of older related influenza viruses.

Wild-type influenza viruses. These are influenza viruses that have been cultured (i.e. isolated) directly from **clinical specimens** and have not been purposefully modified.

WHO-recommended viruses for vaccine use. These are **wild-type influenza viruses** that are recommended by WHO as the basis for an influenza vaccine. Often, recommended viruses in their original form are not optimal for manufacturing and therefore are modified using laboratory techniques**.**

REAGENTS AND SPECIMENS

Clinical specimens. These are materials collected from humans (or animals), generally in order to confirm a diagnosis. For influenza, most commonly, clinical specimens are taken from the respiratory tract (for example, swabs and aspirated fluid) but they can be from other locations. Clinical specimens can be frozen and stored for later use.

Diagnostic reagents. These materials generally consist of killed reference viruses or purified surface proteins (i.e. antigens) from specific influenza viruses and antibodies to those viruses and surface proteins. Kits containing diagnostic reagents and instructions on their use are updated and produced every year by WHO and are used by laboratories around the world to identify influenza viruses. Diagnostic reagents for the detection and identification of influenza viruses by molecular techniques are also available.

Standardized reagents for inactivated influenza vaccines. Reagents are used to measure how much haemagglutinin – the main protein contained in influenza vaccines – is contained in batches of vaccine. Since the amount of haemagglutinin in vaccine is specified by regulations, the reagents must

be consistent (i.e. standardized) and must be produced in large quantities so all vaccine batches can be tested.

LABORATORY TECHNIQUES

Genetic reassortment. This is a process in which genes from two or more influenza viruses are separated from each other and then grouped together in different combinations resulting in a virus (or viruses) with characteristics of each of the parent virus. This process occurs in nature but can also be done in a laboratory using different techniques. The "classical" reassortment technique is a non-patented technology that is often used to make seasonal vaccine viruses but is not suitable for H5N1 viruses. In general, **reverse genetics** must be used for H5N1 viruses to make vaccine viruses that are safe for vaccine manufacturers to use.

Reverse genetics. This is a laboratory technology that has many different applications. For example, it can be used to reproduce influenza genes, to modify the genes, or to group genes together (i.e. gene reassortment). Reverse genetics can be used to construct influenza viruses from genetic sequence data and is protected by patents in several countries.

INSTITUTIONS AND SYSTEMS

"Essential" regulatory laboratories. The influenza laboratories at the Food and Drug Administration of the United States of America, the National Institute for Biological Standards and Control (United Kingdom of Great Britain and Northern Ireland) and the Australian Therapeutic Goods Administration have been termed "essential" because they have a unique and indispensable role in the process of developing (and regulating) influenza vaccines and in this capacity work closely with WHO and industry. These laboratories do not have formal Terms of Reference within WHO's **Global Influenza Surveillance Network.**

Global Influenza Surveillance Network. This is an international network of laboratories that is coordinated and maintained by WHO to facilitate global surveillance, risk assessment and risk response activities for influenza. This system is unique in terms of its infrastructure, capacity and combined pool of global influenza expertise.

National Influenza Centres. These are influenza laboratories designated by national authorities and recognized by WHO to perform certain roles within the **Global Influenza Surveillance Network.** National Influenza Centres have formal Terms of Reference with WHO.

WHO Collaborating Centres. Centres concerned with influenza generally are influenza laboratories designated by national authorities and recognized by WHO to perform certain roles within the **Global Influenza Surveillance Network**. In general, they differ from **National Influenza Centres** in having global responsibilities and greater technical capacities. Currently, there are four Collaborating Centres that focus primarily (but not exclusively) on human influenza viruses and vaccines (Centers for Disease Control and Prevention, Atlanta, Georgia, United States of America; National Institute for Medical Research, London; Victorian Infectious Diseases Reference Laboratory, Melbourne, Australia; and National Institute of Infectious Diseases, Tokyo) and one (St Jude Children's Research Hospital, Memphis, Tennessee, United States of America) that in its role as a WHO Collaborating Centre focuses primarily on animal viruses that threaten people and that can be used to make human vaccines.

WHO H5 Reference Laboratories. This is a group of influenza laboratories that have been designated by WHO as having the capacity to reliably diagnose H5 infection in humans. This group was created to strengthen national and regional capacities for reliably diagnosing H5 infection and will most likely be phased out once the capacity to test for H5 becomes more common among national laboratories.

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