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## **Pandemic Influenza Preparedness: Sharing of influenza viruses and access to vaccines and other benefits**

### **Report by the Director-General**

1. In December 2008, the Intergovernmental Meeting on Pandemic Influenza Preparedness: Sharing of influenza viruses and access to vaccines and other benefits resumed its deliberations on the development of a framework for the sharing of influenza viruses and benefits. The basis for its work was the Chair's text,<sup>1</sup> which had been prepared in close consultation with Member States.
2. In suspending the session, the Intergovernmental Meeting requested the Director-General to undertake preparatory work in the four following areas:<sup>2</sup>
  - further development of the traceability mechanism;
  - preparation of detailed terms of reference for WHO Collaborating Centres on Influenza, the WHO H5 Reference Laboratories, essential regulatory laboratories, and the National Influenza Centres, following the guiding principles included in the Intergovernmental Meeting text;<sup>3</sup>
  - preparation of a revised version of the technical part of the Standard Material Transfer Agreement, following the agreed principles of the Intergovernmental Meeting text;
  - preparation of a report identifying the needs and priorities for each of the benefits listed in section 6 of the Intergovernmental Meeting text, in particular concerning the vaccine stockpile, as well as options for their financing.
3. Reports on this work, attached as Annexes 1–4, are submitted to the Intergovernmental Meeting for consideration.

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<sup>1</sup> Document A/PIP/IGM/WG/6.

<sup>2</sup> See document EB124/4 Add.1.

<sup>3</sup> See document EB124/4 Add.1, Annex 2.



ANNEX 1

**DEVELOPMENT OF THE INFLUENZA VIRUS TRACEABILITY MECHANISM**

1. In resolution WHA60.28 “Pandemic Influenza Preparedness: sharing of influenza viruses and access to vaccines and other benefits” the Health Assembly requested the Director-General, *inter alia*, to convene an Intergovernmental Meeting. During the session of the Intergovernmental Meeting held in Geneva in November 2007, Member States adopted an Interim Statement mandating WHO to “establish a technical and feasible traceability mechanism as soon as possible within WHO to track all shared H5N1 and other potentially pandemic human viruses and parts thereof.”

**Recent developments**

2. At the resumed session of the Intergovernmental Meeting in December 2008, the Director-General submitted a progress report on the establishment of the WHO influenza virus traceability mechanism.<sup>1</sup> The report provided details of recommendation on how the interim traceability system, launched in January 2008, could be made more efficient and user friendly in order to respond to Member States’ requirements.
3. Since the suspension of the session in December 2008, the Secretariat has taken the following steps in order to continue improving the influenza virus traceability mechanism.
4. Detailed technical specifications have been finalized through a broad consultative process.
5. Based on these detailed specifications, the Secretariat decided that internal development of the influenza virus traceability mechanism would yield a mechanism that most closely responded to the Intergovernmental Meeting’s request and the needs identified by stakeholders, all in the most efficient, cost-effective and sustainable manner.
6. In order to take advantage of possible contributions from other existing systems and potential contributions to the influenza virus traceability mechanism, the Secretariat issued a detailed Invitation for Contributions, encouraging interested parties to submit complete software systems or discrete components that could enhance the influenza virus traceability mechanism.
7. The terms and conditions for responding to the Invitation and those governing the acceptance of contributions by WHO were set out in the Invitation for Contributions.
8. Any contributions accepted by WHO will be integrated into the influenza virus traceability mechanism.
9. The expected launch date of the influenza virus traceability mechanism is late 2009.
10. Training in use of the system is planned and will be provided to [WHO Network] laboratories.

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<sup>1</sup> See document A/PIP/IGM/9.

## ANNEX 2

### WHO COLLABORATING CENTRES FOR INFLUENZA

#### TERMS OF REFERENCE RELATED TO WORK WITH PANDEMIC INFLUENZA PREPAREDNESS BIOLOGICAL MATERIALS

##### BACKGROUND

The [WHO Network] serves as a global alert mechanism for the emergence of influenza viruses with important features, including those with pandemic potential. For activities related to pandemic influenza, the [WHO Network] includes four complementary categories of institutions and laboratories: National Influenza Centres, WHO Collaborating Centres, WHO H5 Reference Laboratories and Essential Regulatory Laboratories. The [WHO Network] is coordinated by the WHO Global Influenza Programme. Within each category all institutions and laboratories perform functions defined by core Terms of Reference. The core Terms of Reference for WHO Collaborating Centres are the minimum requirements that must be met by each WHO Collaborating Centre and the capacity to fulfil these is a prerequisite to designation as a WHO Collaborating Centre. Each laboratory or institution that is formally recognized or designated as a part of the Network by WHO has accepted to be bound by the core Terms of Reference applicable to its category. The following are the core Terms of Reference applicable to the WHO Collaborating Centres.

In addition, individual WHO Collaborating Centres within the Network may have additional Specific Terms of Reference, where appropriate. The Specific Terms of Reference recognize that there are differences in expertise, capacities and interests among the WHO Collaborating Centres and provide for individual WHO Collaborating Centres to perform additional functions related to pandemic risk assessment and response. Specific Terms of Reference will be discussed with and agreed upon between the WHO Collaborating Centre and the WHO Global Influenza Programme before the WHO Collaborating Centre's designation and redesignation.

In general, the WHO Collaborating Centres conduct influenza pandemic risk assessment on an ongoing basis and provide advice, expertise and support to Member States and the Secretariat to facilitate activities in response to influenza risks. The WHO Collaborating Centres support outbreak investigation, conduct comprehensive virus analyses, and select and develop candidate influenza vaccine viruses with pandemic potential. The efficient implementation pandemic influenza risk assessment and risk response is based on the collective efforts of all [WHO Network] members and through the rapid sharing of biological materials, reference reagents, epidemiologic data and other information.

It is understood that the Guiding Principles, as agreed by the Intergovernmental Meeting and reproduced below, will guide all activities, specific Terms of Reference or associated functions of the [WHO Network] laboratories when they act in their capacity as a [WHO Network] laboratory. The Terms of Reference for all [WHO Network] laboratories have been developed under the following overarching Guiding Principles:

### **Guiding Principles for the development of Terms of Reference for current and potential future [WHO Network] laboratories for H5N1 and other human pandemic influenza viruses**

1. *All activities conducted by [WHO Network] laboratories under their WHO Terms of Reference will be consistent with the [Framework and the] Standard Material Transfer Agreement.*
2. *The [WHO Network] laboratories will be coordinated by, and provide support to, WHO.*
3. *The [WHO Network] laboratories will provide a timely summary report of laboratory analyses and on request any other available information on tests conducted, test results and associated risk assessment and risk response as is specified in their Terms of Reference.*
4. *The [WHO Network] laboratories will share experience and provide capacity strengthening support to WHO Member States within their resources where necessary.*
5. *The [WHO Network] laboratories will provide support as specified in their Terms of Reference for the development of potential pandemic vaccine, pandemic vaccine, diagnostic test materials and pharmaceuticals.*
6. *If [WHO Network] laboratories conduct research on influenza viruses received for public health surveillance purposes, they will do so in a manner that includes participation of scientists, to the fullest extent possible, from the submitting National Influenza Centre or other authorized laboratory, especially those from developing countries, including through the publication process.*
7. *The [WHO Network] laboratories will support global public health preparedness and response, especially for urgent situations including international outbreaks and epidemics.*
8. *The [WHO Network] laboratories will share in a rapid, systematic and timely manner biological materials related to pandemic influenza preparedness, using the Influenza Virus Traceability Mechanism as appropriate, including distribution to other qualified laboratories, to facilitate public health risk assessment, risk response activities and scientific research in accordance with the Standard Material Transfer Agreement.*
- [9. *The [WHO Network] laboratories will share [publicly] genetic sequence data consistent with the Standard Material Transfer Agreement.*]
- [10. *The PIP biological materials received by the [WHO Network] laboratories will be provided [due credit] and recognition to the submitting National Influenza Centre or other authorized laboratory.*]

### **Core Terms of Reference**

WHO Collaborating Centres for Influenza are centres of excellence on influenza which are designated by WHO and which agree to the following:

#### **A. General conditions and activities**

1. work under the coordination of the WHO Global Influenza Programme, and provide support to WHO (Guiding Principles 2, 7);

2. fulfil the Core Terms of Reference and Specific Terms of Reference using financial support provided only by governmental and/or other non-commercial sources;
3. use the WHO Influenza Virus Traceability Mechanism to record the receipt and transfer of PIP biological materials (Guiding Principle 8);
4. comply with the [Standard Material Transfer Agreement of the Pandemic Influenza Preparedness Framework for Sharing of Influenza viruses and access to vaccines and other benefits.] (Guiding Principle 1);
5. maintain the capacity to exchange materials and information on a regular and timely basis with other WHO Collaborating Centres (Guiding Principles 3, 8);
6. have full and unrestricted access to biosafety level 3 laboratory facilities that meet recognized international and national standards. The Provider assumes full responsibility for complying with their respective national biosecurity and biosafety regulations on the understanding that such regulations and rules shall, at a minimum, meet the relevant and current WHO standards;
7. serve as a technical resource to WHO for any other urgent issues related to pandemic influenza or influenza outbreaks with pandemic potential (Guiding Principles 2, 5);
8. appropriately acknowledge the originating laboratories providing clinical specimens and/or influenza viruses with pandemic potential (Guiding Principles 8, 10);
9. maintain and strengthen active communication and collaboration with National Influenza Centres<sup>1</sup> and WHO to ensure that up-to-date information and findings of public health significance are rapidly exchanged (Guiding Principles 3, 4, 7, 8);
10. alert WHO and the country from which clinical specimens and/or viruses with pandemic potential were provided, on unusual findings related to pandemic influenza risk assessment (Guiding Principles 3, 7);
11. provide expertise and laboratory support when requested by WHO, to assist Member States, and in particular developing countries, in responding to outbreaks of influenza viruses with pandemic potential and risk assessment (Guiding Principles 2, 3, 4, 7);
12. provide training and laboratory support to National Influenza Centres, especially those in developing countries, on laboratory techniques and skills, including diagnosis, data analyses, risk assessment and other critical capacities (Guiding Principle 4);
13. assist WHO in improving global surveillance for influenza viruses with pandemic potential (Guiding Principles 2, 7) including the development of standards, recommendations and policies as well as improving associated outbreak response and pandemic preparedness (Guiding Principles 2, 3, 4, 7);
14. provide regular and timely surveillance data and results of virus characterization to originating laboratories and to WHO (Guiding Principle 3, 7);

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<sup>1</sup> WHO designated National Influenza Centres <http://www.who.int/csr/disease/influenza/centres/en/index.html>.

15. advise the [WHO Network] on laboratory methods for diagnosis of influenza viruses with pandemic potential, including the adoption of new diagnostic approaches, the improvement of laboratory practices and other operational needs (Guiding Principles 2, 3, 5).

**B. Laboratory analyses and related activities**

1. Conduct accurate laboratory diagnosis, typing and subtyping, and confirmation of influenza A(H5) and other influenza viruses with pandemic potential for specimens received (Guiding Principles 2, 3, 7);

2. conduct isolation of influenza viruses with pandemic potential in embryonated eggs and cell culture;

3. conduct detailed antigenic and genetic analyses of influenza viruses with pandemic potential and make the results available to WHO and the originating laboratories in a timely manner (Guiding Principles 2, 3, 4, 7);

4. share available haemagglutinin, neuraminidase and other gene sequences of A(H5) and other influenza viruses with pandemic potential immediately with the originating laboratory, WHO Collaborating Centres and H5 Reference Laboratories (Guiding Principle 3);

5. upload available haemagglutinin, neuraminidase and other gene sequences of A(H5) and other influenza viruses with pandemic potential to a publicly accessible database in a timely manner but no later than three months after sequencing is completed, unless otherwise instructed by the laboratory or country providing the clinical specimens and/or viruses (Guiding Principle 9);

6. produce and distribute ferret antisera against influenza viruses with pandemic potential to WHO laboratories involved in influenza vaccine virus selection and development (Guiding Principle 5);

7. conduct analyses, provide data and advice to WHO and participate in meetings and teleconferences concerning the selection, development and timely availability of candidate vaccine viruses for H5N1 and other influenza viruses with pandemic potential (Guiding Principles 2, 5, 7);

8. participate in the development of candidate influenza vaccine viruses for pandemic influenza preparedness and response (Guiding Principles 5, 7);

9. conduct antiviral susceptibility testing of H5N1 and other influenza viruses with pandemic potential and provide timely reports to the originating laboratories and WHO (Guiding Principle 3);

10. select, maintain and update a group of reference influenza viruses with pandemic potential, including H5N1, and corresponding antisera if available and update the availability of candidate influenza vaccine viruses and corresponding antisera, if any, to WHO (Guiding Principles 2, 3, 5, 7);

11. develop, update and produce laboratory diagnostic reagents for influenza H5N1 and other viruses with pandemic potential directly or through contracted entities, and distribute them to National Influenza Centres subject to the availability of resources (Guiding Principle 5);

12. share in a timely manner clinical specimens and influenza viruses with pandemic potential in accordance with [the Standard Material Transfer Agreement] with laboratories working in coordination and collaboration with the WHO Global Influenza Programme, including:

- (i) other WHO Collaborating Centres (Guiding Principles 1, 8);
- (ii) essential regulatory laboratories that are involved in the WHO process of candidate influenza vaccine virus selection and development, as well as vaccine potency reagent development (Guiding Principles 1, 8);
- (iii) other laboratories involved in WHO coordinated specialized activities (e.g. the WHO External Quality Assessment Project for the detection of subtype influenza A viruses using polymerase chain reaction; the WHO influenza polymerase chain reaction primer updating), and other activities whose purpose is to strengthen global influenza surveillance and other risk assessment and risk response; as well as capacity building (Guiding Principles 1, 4, 8);

13. select candidate influenza vaccine viruses under the coordination of WHO, for development and production of vaccines against influenza viruses with pandemic potential. Depending on the vaccine production process, the candidate influenza vaccine viruses can include wild type viruses and high-growth reassortant viruses, including those prepared by reverse genetics. Distribute candidate influenza vaccine viruses to appropriate recipients with appropriate biosafety level capacity on request, including influenza vaccine manufacturers, diagnostic companies, research institutes and others interested in receiving influenza vaccine viruses (Guiding Principles 5, 8);

14. select, maintain and update reference A(H5N1) and other influenza viruses with pandemic potential as antigenically and genetically representative of important groups of viruses. Subject to the availability of resources, distribute both reference viruses and corresponding antisera, on request, to National Influenza Centres and other institutes for non-commercial activities including surveillance, and reference and research (Guiding Principle 10);

15. seek approval from the laboratories providing the original clinical specimens and/or viruses for distribution of influenza clinical specimens and/or influenza viruses with pandemic potential for purposes beyond those described above.

### **C. Research and scientific presentations and publications**

1. Actively seek the participation of scientists from originating laboratories/countries in scientific projects associated with research on clinical specimens and/or influenza viruses from their countries and actively engage them in preparation of manuscripts for presentation and publication (Guiding Principle 6);

2. appropriately acknowledge in presentations and publications, the contributions of collaborators, including laboratories/countries providing clinical specimens or influenza viruses with pandemic potential or reagents, using guidelines such as those outlined by the International Committee of Medical Journal Editors<sup>1</sup> (Guiding Principle 6).

### **Specific Terms of Reference**

[These are additional functions attributed to an individual WHO Collaborating Centre in light of its specific expertise in the field of influenza.]

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<sup>1</sup> See: <http://www.icmje.org/>.

## NATIONAL INFLUENZA CENTRES

### TERMS OF REFERENCE RELATED TO WORK WITH PANDEMIC INFLUENZA PREPAREDNESS BIOLOGICAL MATERIALS

#### BACKGROUND

The [WHO Network] serves as a global alert mechanism for the emergence of influenza viruses with important features, including those with pandemic potential. For activities related to pandemic influenza, the [WHO Network] includes four complementary categories of institutions and laboratories: National Influenza Centres, WHO Collaborating Centres, WHO H5 Reference Laboratories and Essential Regulatory Laboratories. The [WHO Network] is coordinated by the WHO Global Influenza Programme. Within each category all institutions and laboratories perform functions defined by core Terms of Reference. Each laboratory or institution that is formally recognized or designated as a part of the Network by WHO has accepted to be bound by the core Terms of Reference applicable to its category. The following are the core Terms of Reference applicable to the National Influenza Centres.

National Influenza Centres play a key role in pandemic influenza risk assessment by alerting WHO immediately to outbreaks of H5N1 or other influenza viruses with pandemic potential. National Influenza Centres collect specimens from suspected cases of H5N1 or other unusual influenza viral infection, perform laboratory diagnosis and analysis, and ship in a timely manner, such specimens or viruses isolated from them, to a WHO Collaborating Centre or H5 Reference Laboratory for advanced virological analysis. Efficient pandemic influenza risk assessment and risk response are based on collective efforts from all [WHO Network] members through rapid exchange of biological materials, reference reagents, epidemiologic data and other information.

It is understood that the Guiding Principles, as agreed by the Intergovernmental Meeting and reproduced below, will guide all activities, specific Terms of Reference or associated functions of the [WHO Network] laboratories when they act in their capacity as a [WHO Network] laboratory. The Terms of Reference for all [WHO Network] laboratories have been developed under the following overarching Guiding Principles:

#### **Guiding Principles for the development of Terms of Reference for current and potential future [WHO Network] laboratories for H5N1 and other human pandemic influenza viruses**

- 1. All activities conducted by [WHO Network] laboratories under their WHO Terms of Reference will be consistent with the [Framework and the] Standard Material Transfer Agreement*
- 2. The [WHO Network] laboratories will be coordinated by, and provide support to, WHO.*
- 3. The [WHO Network] laboratories will provide a timely summary report of laboratory analyses and on request any other available information on tests conducted, test results and associated risk assessment and risk response as is specified in their Terms of Reference.*
- 4. The [WHO Network] laboratories will share experience and provide capacity strengthening support to WHO Member States within their resources where necessary.*

5. *The [WHO Network] laboratories will provide support as specified in their Terms of Reference for the development of potential pandemic vaccine, pandemic vaccine, diagnostic test materials and pharmaceuticals.*

6. *If [WHO Network] laboratories conduct research on influenza viruses received for public health surveillance purposes, they will do so in a manner that includes participation of scientists, to the fullest extent possible, from the submitting National Influenza Centre or other authorized laboratory, especially those from developing countries, including through the publication process.*

7. *The [WHO Network] laboratories will support global public health preparedness and response, especially for urgent situations including international outbreaks and epidemics.*

8. *The [WHO Network] laboratories will share in a rapid, systematic and timely manner PIP biological materials, using the Influenza Virus Traceability Mechanism as appropriate, including distribution to other qualified laboratories, to facilitate public health risk assessment, risk response activities and scientific research in accordance with the Standard Material Transfer Agreement.*

[9. *The [WHO Network] laboratories will share [publicly] genetic sequence data consistent with the Standard Material Transfer Agreement.*]

[10. *The PIP biological materials received by the [WHO Network] laboratories will be provided [due credit] and recognition to the submitting National Influenza Centre or other authorized laboratory.*]

## **Core Terms of Reference**

National Influenza Centres are laboratories that fulfil the Terms of Reference listed below. A National Influenza Centre is formally designated by the health ministry of the country concerned and is recognized by WHO. A National Influenza Centre may have additional obligations under the authority of its Ministry of Health.

### **A. General conditions and activities**

1. Work under the coordination of the WHO Global Influenza Programme and provide support to WHO (Guiding Principles 2, 7);

2. use the WHO Influenza Virus Traceability Mechanism to record the receipt and transfer of PIP biological materials (Guiding Principle 8);

3. comply with the [Standard Material Transfer Agreement of the Pandemic Influenza Preparedness Framework for Sharing of Influenza viruses and access to vaccines and other benefits] (Guiding Principle 1);

4. serve as a key point of contact between WHO and the country of the National Influenza Centre on issues related to surveillance, laboratory diagnosis, and sharing of clinical specimens and/or influenza viruses with pandemic potential, as well as sharing of important related clinical or epidemiological information, when available, with WHO (Guiding Principles 2, 3, 4, 7, 8);

5. participate actively in WHO pandemic influenza surveillance activities and maintain active communication and collaboration with other members of the [WHO Network] (Guiding Principles 4, 7, 8).

**B. Laboratory and related activities**

1. Collect or process as appropriate clinical specimens from patients suspected to be infected with H5N1 and other influenza viruses with pandemic potential (Guiding Principle 7);
2. act as a collection point for virus isolates of suspected pandemic influenza from laboratories within the country;
3. conduct testing of clinical specimens for influenza viruses and detect influenza viruses that cannot be readily identified with diagnostic reagents provided through the [WHO Network];
4. ship, within one week, clinical specimens and/or viruses that cannot be readily identified with diagnostic reagents provided through the [WHO Network] to a WHO Collaborating Centre or H5 Reference Laboratory of their choice of] and include the date the specimen was collected and relevant geographical, epidemiological and clinical information (Guiding Principles 2, 3, 5, 7, 8);
5. attend laboratory training courses provided by the WHO Collaborating Centres in an effort to establish and maintain capacity to recognize influenza viruses that cannot be readily identified (Guiding Principle 4);
6. review, maintain and strengthen influenza surveillance in the country (Guiding Principle 2);
7. provide technical advice and support to other influenza laboratories in the country on specimen collection and shipment logistics, laboratory biosafety and other operational procedures related to influenza surveillance (Guiding Principles 2, 7).

**C. Information and communication**

1. Alert WHO immediately when influenza viruses are detected that cannot be readily identified with diagnostic reagents provided through the [WHO Network] or when unusual outbreaks of non-seasonal influenza or influenza-like illness emerge;
2. provide national authorities and the general public with information on H5N1 and other influenza viruses with pandemic potential circulating in the country in a timely manner.

## WHO H5 REFERENCE LABORATORIES

### TERMS OF REFERENCE RELATED TO WORK WITH PANDEMIC INFLUENZA PREPAREDNESS BIOLOGICAL MATERIALS

#### BACKGROUND

The [WHO Network] serves as a global alert mechanism for the emergence of influenza viruses with important features, including those with pandemic potential. For activities related to pandemic influenza, the [WHO Network] includes four complementary categories of institutions and laboratories: National Influenza Centres, WHO Collaborating Centres, WHO H5 Reference Laboratories and Essential Regulatory Laboratories. The [WHO Network] is coordinated by the WHO Global Influenza Programme. Within each category all institutions and laboratories perform functions defined by core Terms of Reference. The core Terms of Reference for WHO Collaborating Centres are the minimum requirements that must be met by each WHO Collaborating Centre and the capacity to fulfil these is a prerequisite to designation as a WHO Collaborating Centre. Each laboratory or institution that is formally recognized or designated as a part of the Network by WHO has accepted to be bound by the core Terms of Reference applicable to its category. The following are the core Terms of Reference applicable to the H5 Reference Laboratories.

WHO H5 Reference Laboratories are laboratories that were designated by WHO on an *ad hoc basis* commencing in 2005, to support the [WHO network] in response to the emergence and spread of highly pathogenic avian influenza H5N1. These laboratories conduct influenza risk assessment and response by providing reliable laboratory diagnosis of influenza infection in humans, especially those suspected of being associated with avian influenza A(H5) viruses or other influenza viruses with pandemic potential. Efficient influenza risk assessment and risk response are based on collective efforts from all [WHO Network] members through rapid exchange of biological materials, reference reagents, epidemiologic data and other information.

It is understood that the Guiding Principles, as agreed by the Intergovernmental Meeting and reproduced below, will guide all activities, specific Terms of Reference or associated functions of the [WHO Network] laboratories when they act in their capacity as a [WHO Network] laboratory. The Terms of Reference for all [WHO Network] laboratories have been developed under the following overarching Guiding Principles:

#### **Guiding Principles for the development of Terms of Reference for current and potential future [WHO Network] laboratories for H5N1 and other human pandemic influenza viruses**

1. *All activities conducted by [WHO Network] laboratories under their WHO Terms of Reference will be consistent with the [Framework and the] Standard Material Transfer Agreement.*
2. *The [WHO Network] laboratories will be coordinated by, and provide support to, WHO.*
3. *The [WHO Network] laboratories will provide a timely summary report of laboratory analyses and on request any other available information on tests conducted, test results and associated risk assessment and risk response as is specified in their Terms of Reference.*
4. *The [WHO Network] laboratories will share experience and provide capacity strengthening support to WHO Member States within their resources where necessary.*

5. *The [WHO Network] laboratories will provide support as specified in their Terms of Reference for the development of potential pandemic vaccine, pandemic vaccine, diagnostic test materials and pharmaceuticals.*
6. *If [WHO Network] laboratories conduct research on influenza viruses received for public health surveillance purposes, they will do so in a manner that includes participation of scientists, to the fullest extent possible, from the submitting National Influenza Centre or other authorized laboratory, especially those from developing countries, including through the publication process.*
7. *The [WHO Network] laboratories will support global public health preparedness and response, especially for urgent situations including international outbreaks and epidemics.*
8. *The [WHO Network] laboratories will share in a rapid, systematic and timely manner PIP biological materials, using the Influenza Virus Traceability Mechanism as appropriate, including distribution to other qualified laboratories, to facilitate public health risk assessment, risk response activities and scientific research in accordance with the Standard Material Transfer Agreement.*
- [9. *The [WHO Network] laboratories will share [publicly] genetic sequence data consistent with the Standard Material Transfer Agreement.*]
- [10. *The PIP biological materials received by the [WHO Network] laboratories will be provided [due credit] and recognition to the submitting National Influenza Centre or other authorized laboratory.*]

### **Core Terms of Reference**

WHO H5 Reference Laboratories are laboratories which are designated through a defined WHO process, on an *ad hoc basis*, and which meet the core Terms of Reference listed below.

#### **A. General conditions and activities**

1. Work under the coordination of the WHO Global Influenza Programme; and provide support to WHO (Guiding Principle 2);
2. meet the WHO criteria for accepting positive results of H5 infection in humans;<sup>1</sup>
3. use the WHO Influenza Virus Traceability Mechanism to record the receipt and transfer of PIP biological materials (Guiding Principle 8);
4. comply with the [Standard Material Transfer Agreement of the PIP Framework for Sharing of Influenza viruses and access to vaccines and other benefits.] (Guiding Principle 1);
5. provide laboratory services to its own country and other countries when needed for diagnosis of influenza A(H5) and other influenza viruses with pandemic potential (Guiding Principles 3, 7);

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<sup>1</sup> [http://www.who.int/csr/disease/avian\\_influenza/H5AcceptanceCriteria\\_16Oct07.pdf](http://www.who.int/csr/disease/avian_influenza/H5AcceptanceCriteria_16Oct07.pdf).

6. alert WHO and the country that provided clinical specimens and/or viruses with pandemic potential about unusual findings related to pandemic influenza risk assessment (Guiding Principles 3, 7);
7. provide feedback to WHO on the use of WHO recommended diagnostic protocols and primers to assist WHO in updating laboratory diagnostic recommendations (Guiding Principles 2, 3, 4, 5).

#### **B. Laboratory and other activities**

1. Provide advice to clinics, hospitals and other specimen collection sites on safe and appropriate clinical specimen collection, storage, packaging and shipping (Guiding Principle 7);
2. conduct accurate laboratory diagnosis, typing and subtyping and confirmation of influenza A(H5) and other influenza viruses with pandemic potential for specimens received and make the results available to WHO Collaborating Centres and the originating laboratories in a timely manner (Guiding Principles 2, 3, 4, 7);
3. provide expertise and laboratory support in response to outbreaks of A(H5) and other influenza viruses with pandemic potential (Guiding Principles 2, 3, 4, 5, 7);
4. routinely share clinical specimens and/or virus isolates from A(H5) and other influenza viruses with pandemic potential with WHO Collaborating Centres for further characterization in accordance with [the Standard Material Transfer Agreement] (Guiding Principles 1, 8, 10);
5. share available haemagglutinin, neuraminidase and other gene sequences of A(H5) and other influenza viruses with pandemic potential immediately with the originating laboratory, WHO Collaborating Centres and H5 Reference Laboratories (Guiding Principle 3);
6. upload available haemagglutinin, neuraminidase and other gene sequences of A(H5) and other influenza viruses with pandemic potential to a publicly accessible database in a timely manner, but no later than three months after sequencing is completed, unless otherwise instructed by the laboratory or country providing the clinical specimens and/or viruses (Guiding Principle 9);
7. appropriately acknowledge the originating laboratories providing clinical specimens and/or influenza viruses with pandemic potential (Guiding Principles 8, 10).

#### **C. Research, scientific presentations and publications**

1. Actively seek the participation of scientists from originating laboratories/countries in scientific projects associated with research on clinical specimens and/or influenza viruses from their countries and actively engage them in preparation of manuscripts for presentation and publication (Guiding Principle 6);
2. appropriately acknowledge in presentations and publications, the contributions of collaborators, including laboratories/countries providing clinical specimens or influenza viruses with pandemic potential or reagents, using guidelines such as those outlined by the International Committee of Medical Journal Editors<sup>1</sup> (Guiding Principle 6).

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<sup>1</sup> See: <http://www.icmje.org/>.

## ESSENTIAL REGULATORY LABORATORIES

### TERMS OF REFERENCE RELATED TO WORK WITH PANDEMIC INFLUENZA PREPAREDNESS BIOLOGICAL MATERIALS

#### BACKGROUND

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Essential Regulatory Laboratories are formally associated with national regulatory agencies, and have a critical role in developing, regulating and standardizing influenza vaccines. They have performed this role for nearly four decades within the WHO Network, and have thereby contributed to the production of safe and effective influenza vaccines through the selection and development of candidate vaccine viruses. While they previously had no formal Terms of Reference with WHO, in practice, they worked closely with both WHO and the influenza vaccine manufacturers. Currently there are four Collaborating Centres: the Center for Biologics Evaluation and Research, United States of America; the National Institute for Biological Standards and Control, United Kingdom of Great Britain and Northern Ireland; the National Institute for Infectious Diseases, Japan, and the Therapeutic Goods Administration, Australia.

The core Terms of Reference are the minimum requirements that must be met by each Essential Regulatory Laboratory, either individually or as a group. Specific Terms of Reference may be discussed with and agreed upon by the Essential Regulatory Laboratory, the WHO Global Influenza Programme and, in some cases, industry before recognition.

It is understood that the Guiding Principles, as agreed by the Intergovernmental Meeting and reproduced below, will guide all activities, specific Terms of Reference or associated functions of the [WHO Network] laboratories when they act in their capacity as a [WHO Network] laboratory. The Terms of Reference for all [WHO Network] laboratories have been developed under the following overarching Guiding Principles:

#### **Guiding Principles for the development of Terms of Reference for current and potential future [WHO Network] laboratories for H5N1 and other human pandemic influenza viruses**

- 1. All activities conducted by [WHO Network] laboratories under their WHO Terms of Reference will be consistent with the [Framework and the] Standard Material Transfer Agreement.*
- 2. The [WHO Network] laboratories will be coordinated by, and provide support to, WHO.*

3. *The [WHO Network] laboratories will provide a timely summary report of laboratory analyses and on request any other available information on tests conducted, test results and associated risk assessment and risk response as is specified in their Terms of Reference.*
4. *The [WHO Network] laboratories will share experience and provide capacity strengthening support to WHO Member States within their resources where necessary.*
5. *The [WHO Network] laboratories will provide support as specified in their Terms of Reference for the development of potential pandemic vaccine, pandemic vaccine, diagnostic test materials and pharmaceuticals.*
6. *If [WHO Network] laboratories conduct research on influenza viruses received for public health surveillance purposes, they will do so in a manner that includes participation of scientists, to the fullest extent possible, from the submitting National Influenza Centre or other authorized laboratory, especially those from developing countries, including through the publication process.*
7. *The [WHO Network] laboratories will support global public health preparedness and response, especially for urgent situations including international outbreaks and epidemics.*
8. *The [WHO Network] laboratories will share in a rapid, systematic and timely manner PIP biological materials, using the Influenza Virus Traceability Mechanism as appropriate, including distribution to other qualified laboratories, to facilitate public health risk assessment, risk response activities and scientific research in accordance with the Standard Material Transfer Agreement.*
9. *The [WHO Network] laboratories will share [publicly] genetic sequence data consistent with the Standard Material Transfer Agreement.]*
10. *The PIP biological materials received by the [WHO Network] laboratories will be provided [due credit] and recognition to the submitting National Influenza Centre or other authorized laboratory.]*

### **Core Terms of Reference**

Essential Regulatory Laboratories meet the following core Terms of Reference listed below, either individually or as a group:

#### **A. General conditions and activities**

1. Advise WHO on the selection of H5N1 and other influenza viruses with pandemic potential for use in influenza vaccines (Guiding Principles 2, 3, 5);
2. assist WHO and Member States in developing vaccine-related aspects of preparedness and response plans for pandemic influenza (Guiding Principles 2, 4, 3, 7);
3. advise WHO on relevant regulatory and development aspects of vaccines for H5N1 and other influenza viruses with pandemic potential (Guiding Principles 2, 3, 5);
4. when requested, inform and advise WHO on work programmes and new technologies aimed at improving development and standardization of vaccines for H5N1 and other influenza viruses with pandemic potential (Guiding Principles 2, 3, 4, 5);
5. use the WHO Influenza Virus Traceability Mechanism to record the receipt and transfer of PIP biological materials (Guiding Principles 8);

6. comply with the [Standard Material Transfer Agreement of the Pandemic Influenza Preparedness Framework for sharing of influenza viruses and access to vaccines and other benefits] (Guiding Principle 1).

#### **B. Laboratory and related activities**

1. Store, and, if required, amplify representative H5N1 and other influenza viruses with pandemic potential obtained from the [WHO Network] for the purpose of developing influenza vaccine viruses (Guiding Principles 1, 2);

2. on request by WHO, develop candidate H5N1 and other influenza vaccine viruses with pandemic potential and characterize them using agreed standards (Guiding Principles 1, 2, 3, 5, 6);

3. store, and, if required, amplify candidate H5N1 and other influenza vaccine viruses with pandemic potential obtained from the [WHO Network] (Guiding Principles 1, 2, 3, 5);

4. prepare and calibrate reference reagents for standardization of candidate influenza vaccine viruses for H5N1 and other influenza viruses with pandemic potential in conjunction with other Essential Regulatory Laboratories (Guiding Principles 1, 2, 5);

5. distribute, subject to the Standard Material Transfer Agreement, candidate influenza vaccine viruses for H5N1 and other influenza viruses with pandemic potential to interested laboratories, including laboratories within the [WHO Network] and influenza vaccine manufacturers (Guiding Principles 1, 2, 5);

6. directly or through contractors, supply reference reagents for standardization of H5N1 and other potential pandemic influenza vaccines to laboratories, such as laboratories within the [WHO Network], national regulatory laboratories and influenza vaccine manufacturers (Guiding Principles 1, 2, 5);

7. analyse, provide data and advice to WHO and participate in meetings and teleconferences concerning the selection, development and timely availability of candidate vaccine viruses for H5N1 and other influenza viruses with pandemic potential (Guiding Principles 2, 5, 7).

#### **C. Research and scientific presentations and publications**

1. Actively seek the participation of scientists from originating laboratories/countries in scientific projects associated with research on clinical specimens and/or influenza viruses from their countries and actively engage them in preparation of manuscripts for presentation and publication (Guiding Principle 6);

2. appropriately acknowledge in presentations and publications, the contributions of collaborators, including laboratories/countries providing clinical specimens or influenza viruses with pandemic potential or reagents, using guidelines such as those outlined by the International Committee of Medical Journal Editors<sup>1</sup> (Guiding Principle 6).

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<sup>1</sup> See: <http://www.icmje.org/>.

## ANNEX 3

**PANDEMIC INFLUENZA PREPAREDNESS FRAMEWORK FOR THE SHARING OF INFLUENZA VIRUSES AND ACCESS TO VACCINES AND OTHER BENEFITS****DRAFT TECHNICAL PROVISIONS OF THE STANDARD MATERIAL TRANSFER AGREEMENT****BACKGROUND****General considerations**

The threat of pandemic influenza persists. Timely sharing of surveillance information and highly pathogenic avian influenza viruses, as well as ensuring equitable access to effective vaccinations, medicines and related technology are important aspects of global readiness to respond to the pandemic. The Pandemic Influenza Preparedness Framework for the Sharing of Influenza Viruses and Access to Vaccines and Other Benefits (the “Framework”) is an international mechanism to implement a fairer, more transparent, equitable and efficient system. In developing countries, support to implement national integrated human and animal influenza action plans and build national minimum core capacity for detection, risk assessment, laboratory confirmation and rapid containment are critical success factors. (*IGM Text Principles – Introductory paragraph*)<sup>1</sup>

**Drafting considerations**

The following draft standard material transfer agreement has been prepared in response to the request by the Intergovernmental Meeting to the Director-General to prepare “a revised version of the technical part of the Standard Material Transfer Agreement, following the agreed principles of the Intergovernmental Meeting text”.<sup>2</sup>

The specific part of the request to revise “the technical part” of the Agreement raised a question of interpretation. Many, if not all, of the provisions of the Agreement are technical in some sense, that is to say they are either scientifically or legally technical. Accordingly, and in the interest of completeness, the Secretariat has provided as comprehensive a draft Agreement as possible. The text follows as closely as possible the agreed principles of the Intergovernmental Meeting’s text. Where agreed principles were absent or unclear, placeholder language has been inserted indicating that relevant provisions of the Framework would be added as they become agreed in the course of the intergovernmental process, or an option for consideration has been provided, in all cases clearly indicated as such. Such options are not intended to suggest agreed outcomes but rather to facilitate discussion on the relevant topic.

In preparing this draft, the Secretariat examined several models of format and technical provisions, including, in particular, the standard material transfer agreement connected with the International

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<sup>1</sup> Document EB124/4 Add.1, Annex 2.

<sup>2</sup> Document EB124/4 Add.1, Annex 1.

Treaty on Plant Genetic Resources for Food and Agriculture adopted by the Food and Agriculture Organization of the United Nations in 2001 (“the FAO treaty”). Eight other material transfer agreements regularly used or proposed for transfer of biological materials were also reviewed as useful examples of format and technical provisions generally familiar to the community of providers and recipients of biological materials.

Regarding compliance with the standard material transfer agreement, Articles 7 and 8 address applicable law and dispute settlement. They are modelled on the relevant provisions of the agreement in the FAO treaty. As in the case of the latter’s standard material transfer agreement a range of dispute settlement options are provided, including negotiation, mediation and, ultimately, binding arbitration. By its terms, the applicable law, under Article 7, would be the general principles of international commercial law, as opposed to particular domestic law. Enforcement of any arbitral decisions would be in accordance with the aforementioned principles.

## Draft Standard Material Transfer Agreement

### Preamble

**Whereas** WHO coordinates a network of influenza laboratories (hereinafter, the “WHO network”) that conduct pandemic influenza risk assessment and risk response activities under agreed terms of reference;

**Whereas** enabling the global public health community to prevent, protect against, control and provide a public health response to the threat of pandemic influenza through the Framework is a global public good for health;

**Whereas** the Framework recognizes that Member States have a commitment to share on an equal footing H5N1 and other influenza viruses of human pandemic potential and the benefits, considering these as equally important parts of the collective action for global public health; (*IGM Text preambular paragraph 3, consensus*)

**Whereas** the Parties to the Framework recognize that the commitment to share on an equal footing H5N1 and other influenza viruses of human pandemic potential and the benefits enables WHO Member States and the Director-General to assess the global risk of an influenza pandemic and allows WHO Member States and the Director-General to take actions to reduce the risk of the emergence of a pandemic and to facilitate the development and production of vaccines, diagnostic materials and other pharmaceuticals that can assist in rapidly responding to and containing an emerging pandemic; (*IGM Text preambular paragraph 15, consensus*)

**Whereas** the Framework is to be implemented in a manner consistent with relevant national and international laws, regulations, ethical norms, and obligations;

**Whereas** the objective of the Framework is to improve pandemic influenza preparedness and strengthen the protection against the spread of pandemic influenza by implementing a fair[er, and more] transparent, equitable, efficient and effective system for:

- (i) the sharing of H5N1 and other influenza viruses with human pandemic potential; and
- (ii) the sharing of the benefits arising from the use of H5N1 and other influenza viruses with human pandemic potential including the generation of information, diagnostics, medicines, vaccines and other technologies.];(*IGM Text preambular paragraph 2.1*)

**Whereas** Parties to the Framework have adopted this Standard Material Transfer Agreement, referred to in Section 5.3 of the Framework, for use by all entities that use, transfer or receive influenza viruses through or from the [WHO Network];

## **ARTICLE 1 – PARTIES TO THE AGREEMENT**

1.2 This Agreement is:

BETWEEN: *(name and address of the provider or providing institution,<sup>1</sup> name of authorized official, contact information for authorized official)* (hereinafter referred to as “the Provider”),

AND: *(name and address of the recipient or recipient institution, name of authorized official, contact information for authorized official)* (hereinafter referred to as “the Recipient”<sup>2</sup>).

1.3 The parties to this Agreement hereby agree as follows:

## **ARTICLE 2 – DEFINITIONS**

In this Agreement, the definitions and use of terms referred to in Section 4 of the Framework are incorporated herein by reference.

## **ARTICLE 3 – SUBJECT MATTER OF THE STANDARD MATERIAL TRANSFER AGREEMENT**

Pandemic Influenza Preparedness (PIP) Biological Materials are hereby transferred from the Provider to the Recipient subject to the terms and conditions set out in this Agreement.

## **ARTICLE 4 – GENERAL PROVISIONS**

4.1 This Agreement is entered into under the Framework and shall be implemented and interpreted in accordance with the objectives and provisions of said Framework.

## **[ARTICLE 5 – RIGHTS AND OBLIGATIONS OF THE PROVIDER]**

The Provider undertakes that the PIP Biological Materials specified in Appendix 1 are transferred in accordance with the following provisions:

5.1 The Provider will make the transfer of such PIP Biological Materials in accordance with its applicable WHO Terms of Reference and record the transfer in the WHO Influenza Virus Traceability Mechanism.

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<sup>1</sup> This identifies the entity that sends the PIP Biological Materials – it could be, for example, a National Influenza Centre, or a WHO Collaborating Centre or any other institution that transfers PIP Biological Materials to another entity.

<sup>2</sup> This is the recipient of the PIP Biological Materials in this transaction.

5.2 The Provider will ensure that such PIP Biological Materials contain materials treated as optimally as possible to retain the viability of the materials.

**[Insert other provisions as agreed ...]**

## **ARTICLE 6 – RIGHTS AND OBLIGATIONS OF THE RECIPIENT**

The Recipient undertakes that the PIP Biological Materials specified in Appendix 1 shall be used or conserved in accordance with the following provisions:

6.1 The Recipient shall record receipt of such Material in the WHO Influenza Virus Traceability Mechanism. In the event that the Recipient further transfers the PIP Biological Materials, such transfer will be subject to this SMTA and such transfer shall be recorded in the WHO Influenza Virus Traceability Mechanism.

6.2 Any Recipient that receives PIP Biological Materials in its capacity as a [WHO Network] entity shall handle PIP Biological Materials in accordance with its WHO Terms of Reference.

6.3 *The Recipient shall not seek to obtain any intellectual property rights in connection with such PIP Biological Materials, unless the Recipient agrees to grant to WHO a royalty-free, non-exclusive, transferable licence with respect to such rights. WHO may then transfer this licence to developing countries, with appropriate terms and conditions, as determined by the Director-General in accordance with sound public health principles, with transparent rules and procedures, informed by expert guidance and evidence. (Option for consideration)*

6.4 *For a recipient who produces or is capable of producing influenza vaccines: In the event of an influenza pandemic, such a recipient agrees to reserve at least [10]% of doses of pandemic influenza vaccine it produces, after the start of pandemic vaccine production, for purchase, at cost, by organizations in the United Nations system for use first in developing countries. (Option for consideration)*

**[Insert other provisions as agreed, such as those concerning publication information and acknowledgement ...]**

## **ARTICLE 7 – APPLICABLE LAW**

The applicable law shall be the Principles of International Commercial Contracts 2004 of the International Institute for the Unification of Private Law (UNIDROIT), as well as the objectives, principles and other relevant provisions of the Framework.

## **ARTICLE 8 – DISPUTE SETTLEMENT**

- 8.1 Dispute settlement may be initiated by the Provider or the Recipient.
- 8.4 Any dispute arising from this Agreement shall be resolved in the following manner:
- (a) amicable dispute settlement: the Parties shall attempt in good faith to resolve the dispute by negotiation;
  - (b) mediation: If the dispute is not resolved by negotiation, the parties may choose mediation through a neutral third party mediator, to be mutually agreed;
  - (c) arbitration: If the dispute has not been settled by negotiation or mediation, any Party may submit the dispute for arbitration under the Arbitration Rules of an international body as agreed by the parties to the dispute. Failing such agreement, the dispute shall be finally settled under the Rules of Arbitration of the International Chamber of Commerce, by one or more arbitrators appointed in accordance with the said Rules. Either party to the dispute may, if it so chooses, appoint its arbitrator from such list of experts as the [Advisory Group] may establish for this purpose; both parties, or the arbitrators appointed by them, may agree to appoint a sole arbitrator, or presiding arbitrator as the case may be, from such list of experts. The result of such arbitration shall be binding.
- 8.5 Any costs associated with dispute settlement shall be shared equally between the Parties.

## **ARTICLE 9 – ADDITIONAL ITEMS**

### Warranty

9.1 Notwithstanding provision 5.2, the Provider makes no warranties as to the safety of the PIP Biological Materials, nor as to the accuracy or correctness of any data provided with them. Neither does it make any warranties as to the quality, viability, or purity (genetic or mechanical) of the PIP Biological Materials being furnished. The Provider and the Recipient assume full responsibility for complying with their respective national biosecurity and biosafety regulations and rules as to import, export or release of biological materials, on the understanding that such regulations and rules shall, at a minimum, meet the relevant WHO standards that are current at the time of acceptance of this Agreement.

### Duration of Agreement

9.2 This Agreement shall remain in force so long as the Framework remains in effect.

## ARTICLE 10 – SIGNATURE/ACCEPTANCE

The Provider and the Recipient may choose one of the three following methods of acceptance, it being understood that all three methods are equally valid, binding and enforceable to confirm acceptance of this Agreement and that only one method is required to establish acceptance.<sup>1</sup>

### **Method 1 – Acceptance by signature of printed document**

I, (*Full Name of Authorized Official*), represent and warrant that I have the authority to execute this Agreement on behalf of the **Provider** and acknowledge my institution's responsibility and obligation to abide by the provisions of this Agreement, both by letter and in principle, in order to promote the sustainable sharing of PIP Biological Materials and benefits under the Framework.

Signature..... Date .....

Name of the Provider.....

I, (*Full Name of Authorized Official*), represent and warrant that I have the authority to execute this Agreement on behalf of the **Recipient** and acknowledge my institution's responsibility and obligation to abide by the provisions of this Agreement, both by letter and in principle, in order to promote sustainable sharing of PIP biological materials and benefits under the Framework.

Signature..... Date .....

Name of the Recipient .....

### **Method 2 – Acceptance of Agreement by acceptance of PIP Biological Materials (Shrink-wrap Standard Material Transfer Agreements)<sup>2</sup>**

The PIP Biological Materials are provided conditional on acceptance of the terms of this Agreement. The provision of the PIP Biological Materials by the Provider and the Recipient's acceptance of the PIP Biological Materials (i.e., the retention of the materials expressed by the signature of the courier's delivery documentation) constitutes acceptance of the terms of this Agreement.

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<sup>1</sup> Where the Provider chooses signature of printed document, only the wording for Method 1 will appear in the Standard Material Transfer Agreement. Similarly where the Provider chooses either Method 2 or 3 (shrink-wrap or click-wrap), only the wording for that Method will appear in the Standard Material Transfer Agreement. Where the "click-wrap" form is chosen, the PIP Biological Materials should also be accompanied by a printed copy of the Standard Material Transfer Agreement.

<sup>2</sup> A "shrink-wrap" Standard Material Transfer Agreement is where a copy of the Standard Material Transfer Agreement is included in the packaging of the PIP Biological Materials, and the Recipient's acceptance of the PIP Biological Materials constitutes acceptance of the terms and conditions of the Standard Material Transfer Agreement.

**Method 3 – Acceptance of Agreement electronically (Click-wrap Standard Material Transfer Agreement)<sup>1</sup>**

The PIP Biological Materials are provided upon acceptance of this Agreement concluded through electronic means, such as the Internet. For example, “digital signature” may be used instead of physical signatures to establish acceptance of the terms of this Agreement.

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<sup>1</sup> A “click-wrap” Standard Material Transfer Agreement is where the agreement is concluded on the Internet and the Recipient accepts the terms and conditions of the Standard Material Transfer Agreement by clicking on the appropriate icon on the web site or in the electronic version of the Standard Material Transfer Agreement, as appropriate.

APPENDIX 1

**LIST OF MATERIALS PROVIDED**

This *Appendix* contains a list of the PIP Biological Materials provided under this Agreement:  
[List to be completed by Provider]

## ANNEX 4

**IDENTIFICATION OF NEEDS AND PRIORITIES FOR EACH OF THE BENEFITS LISTED IN SECTION 6 OF THE INTERGOVERNMENTAL MEETING TEXT<sup>1</sup>**

Pandemic influenza is one of the few natural disease events with the potential to cause serious disease in persons of all age groups in all regions of the world and in numbers great enough to disrupt the social and economic well-being of countries. Pandemics of influenza also are complex events that have occurred episodically for centuries.

The current state of science cannot eliminate the emergence of the next pandemic nor can it predict when the next pandemic will occur or how severe it will be. However, the adverse impact of pandemics can be mitigated by implementing key activities, including virus sharing and surveillance, basic scientific and public health research, timely communication and disease prevention and control measures. In addition, improvements in essential capacities such as functional laboratories and access to vaccines and antiviral medicines are critical. These approaches can strengthen preparedness for the next pandemic while building capacity in readiness to face a range of emergencies.

For nearly six decades, WHO has worked to strengthen preparedness for pandemic influenza through activities such as providing critical information and technical guidance and by coordinating, maintaining and strengthening an influenza surveillance network supported by Member States. With regards to pandemic influenza, two principal purposes of the existing network are:

- to monitor the risk of pandemic influenza by collecting samples of circulating influenza viruses and conducting detailed virological and risk assessment analyses;
- to strengthen the world's ability to respond to a pandemic by selecting and developing candidate vaccine viruses and making them widely available to vaccine manufacturers for potential use in vaccines.

It is important to note that while the WHO network is directly responsible for virus surveillance, risk assessment, selection of candidate vaccine viruses and development and provision of vaccine candidate viruses, vaccine manufacturers in either the private or the public sector develop seed viruses from candidate vaccine viruses and produce the vaccines.

**The Intergovernmental Meeting process and access to vaccines and other benefits**

With the emergence of H5N1 as a potential pandemic influenza virus, the world became acutely aware of the risks of pandemic influenza, its likely impact in all sectors of society and the need for access at the earliest time possible to life-saving vaccine. Member States focused greater attention on the WHO network and its operations and called for improvements to its transparency as well as to the fairness and equity of access to the benefits derived from it. In 2007, the Health Assembly adopted resolution WHA60.28, in which it requested the Director-General to undertake several actions to improve the functions and operations of the WHO network and, in so doing, increase the overall global preparedness for pandemic influenza. The relationship between the WHO network and the many

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<sup>1</sup> Document EB124/4 Add.1, Annex 2.

related benefits is complex because some benefits, such as global risk assessment, are directly related to the work of the WHO network while other benefits, such as the production of potential pandemic vaccines, are done by entities outside of this network.

The complex and cross-sectoral development of a framework for the sharing of influenza viruses and access to benefits is under the aegis of the Intergovernmental Meeting, which was first convened by the Director-General in November 2007. Discussions have focused on both the technical and operational aspects of virus and benefit sharing, and have included a review of the virus sharing system and how it functions, as well as identifying benefits that are derived from the system and may be shared. In its resumed session in December 2008, the Intergovernmental Meeting requested the Director-General to prepare a report identifying the needs and priorities for each of the benefits listed in Section 6 of the Pandemic Influenza Framework for the Sharing of Influenza Viruses and Access to Vaccines and other Benefits.<sup>1</sup> These benefits consist of:

1. Pandemic risk assessment and risk response (Section 6.2)
2. Provision of PIP candidate vaccine viruses (Section 6.3)
3. Provision of diagnostic reagents and test kits (Section 6.4)
4. Provision of reference reagents for potency determination of vaccines (Section 6.5)
5. Laboratory and influenza surveillance capacity building (Section 6.6)
6. Regulatory capacity building (Section 6.7)
7. [WHO and [other] multilateral] antivirals stockpiles (Section 6.8)
8. [WHO] pandemic influenza preparedness vaccine stockpile (Section 6.9)
9. Access to vaccines for developing and least developed country use (Section 6.10)
10. [Production of ] Pandemic influenza vaccines (Section 6.11)
11. [Tiered][Affordable] Pricing OR [concessional and/or preferential rates] OR [differential pricing policies] (Section 6.12)
12. Technology transfer (Section 6.13)
13. Sustainable financing mechanism (Section 6.14)
14. Innovative financing mechanisms for national vaccine requirements (Section 6.15)

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<sup>1</sup> Document EB124/4 Add.1, Annex 2.

This response to the request to the Director-General is structured as follows:

- Benefits 1–7, on which consensus was almost reached, are presented individually, and include continuing and new or planned activities for each.
- Benefit 8, on which also consensus was nearly reached, is presented as a short summary of the detailed report on the Options for the Design and Financing of an H5N1 Vaccine Stockpile (further detail is given in Appendix 1).
- Benefits 9, 10 and 12, on which consensus was not gained, have been consolidated. (A short narrative text in the report is expanded in Appendix 2.)
- Benefit 11, on which also consensus was not reached, is presented as considerations for discussion.
- Benefits 13 and 14, on which consensus was not reached, have been consolidated. (The short narrative text is expanded in Appendix 3.)

### **Funding considerations**

All continuing activities implemented by WHO are covered by the Programme budget 2008–2009. As a general rule, “planned or new activities” requested by the Intergovernmental Meeting or otherwise identified in this document are subject to the availability of funds. The direct financial costs associated with activities implemented by WHO Collaborating Centres, National Influenza Centres, Essential Regulatory Laboratories or H5 Reference Laboratories are borne by the national governments concerned and represent a contribution to, and benefit from, the WHO network.

### **Specific benefits identified in the Intergovernmental Meeting text**

#### **1. *Pandemic risk assessment and risk response (Section 6.2)***

*6.2.1 [WHO Network] laboratories will make available to the WHO Secretariat and the originating Member State [...], – a summary report of laboratory analyses – on request any other available information required regarding Pandemic Influenza Preparedness (PIP) biological materials to enable the affected countries and in particular, developing countries, an effective and meaningful risk response. Consensus*

#### **Ongoing activities**

- Through the International Health Regulations (2005), WHO has mechanisms in place to receive information about potential pandemic related events.
- WHO Collaborating Centres and H5 Reference Laboratories immediately report results of virus identification and/or characterization to originating laboratories and WHO.
- WHO reports results of H5N1 virological analyses through WHO’s *Weekly Epidemiological Record* and the Internet after each seasonal influenza vaccine virus selection meeting.

- WHO has in place a functioning web-accessible interim Influenza Virus Traceability Mechanism that provides information on the location and movement of H5N1 viruses shared with WHO since November 2007.
- In coordination with many partners, WHO Collaborating Centres occasionally publish detailed reports of influenza viruses and their evolution.

#### **Planned or new activities**

- WHO is developing a longer term Influenza Virus Traceability Mechanism after seeking consultation from a broad range of stakeholders. This system will allow countries to trace the location and movement of H5N1 and other influenza viruses with potential pandemic that have been shared with WHO for analysis and risk assessment. It will also provide easy access to analysis results, reports and other information generated from the PIP biological materials.
- WHO is considering more regular publications on the detailed characterization and evolution of H5N1 viruses.

6.2.2 WHO will provide information on risk response including, but not limited to information on development of vaccines, candidate virus and effective antivirals to all affected countries and in particular, to developing countries, to enable an effective and meaningful risk response. **Consensus**

#### **Ongoing activities**

- WHO provides information on the Internet about the availability of new H5N1 candidate vaccine viruses and how to obtain the viruses and associated reagents.
- WHO provides semi-annual guidance for national authorities and vaccine companies on the selection of candidate viruses for use in vaccine development.<sup>1</sup>
- WHO provides information on the antiviral susceptibility of influenza viruses on its web site, in the *Weekly Epidemiological Record* and in other publications.
- WHO maintains two international stockpiles of antiviral medicines against influenza (see also Section 6.8 below).
- WHO has published clinical guidelines on the use of antiviral medicines against influenza on its web site.
- WHO has published guidance on rapid containment of a pandemic virus on its web site.

#### **Planned or new activities**

- WHO is developing a longer term Influenza Virus Traceability Mechanism (see section 6.2.1).

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<sup>1</sup> See “Antigenic and genetic characteristics of H5N1 viruses and candidate H5N1 vaccine viruses developed for potential use as human vaccines” on the WHO web site ([http://www.who.int/csr/disease/avian\\_influenza/guidelines/h5n1virus/en/](http://www.who.int/csr/disease/avian_influenza/guidelines/h5n1virus/en/)).

- WHO is developing updated and expanded guidance on rapid containment including logistical and operational considerations for a containment operation and distribution of antiviral medicines.
- WHO will support countries as needed in rapid containment interventions through: (i) deployment of international experts; (ii) provision of antiviral medicines and vaccine (if available) (see Section 7 for antiviral stockpile); and (iii) training in conducting rapid containment operations.

6.2.3 *[The WHO Secretariat] will make available to all Member States [...] pandemic risk assessments [and risk response] with all necessary supporting information.*

#### **Ongoing activities**

- WHO provides regularly updated information on human cases of H5N1 infection on its web site and in other publications, including a table of H5N1 cases by date and country; brief synopses of new human cases and relevant epidemiological information as available through Member States; and periodic descriptive epidemiological analyses of H5N1 cases.
- WHO is publishing pandemic preparedness guidelines including a six-phase structure to aid pandemic preparedness and response planning.
- Under the International Health Regulations (2005), the Secretariat will make information on pandemic influenza available to Member States on a timely basis.

#### **Planned or new activities**

- WHO will provide updated pandemic preparedness and response planning guidance in 2009. This updated guidance includes a revision of the six-phase structure to more accurately reflect the pandemic risk and epidemiological situation.
- WHO will provide regional training to implement the 2009 pandemic preparedness guidance.
- WHO will provide tools and materials to facilitate testing of national pandemic plans.
- The Secretariat is working with many partners and Member States to develop approaches for conducting surveillance to assess key epidemiological and clinical features of pandemic virus infections, quickly characterize the severity of pandemic cases and monitor the evolution of the pandemic so Member States can be updated on a timely basis. As part of this effort the Secretariat has developed a minimum set of data for countries to collect and share with the Secretariat.
- The Secretariat will support countries to strengthen their pandemic information and surveillance systems.

6.2.4 *WHO Collaborating Centres on Influenza and WHO H5 Reference Laboratories and the Director-General will actively continue to provide technical assistance to Member States to enhance research and surveillance capacity, including staff training, with the objective of improving national pandemic risk assessment and pandemic risk response. **Consensus***

**Ongoing activities**

- WHO provides laboratory training and support through technical assistance projects. Laboratory training includes in-country or intraregional training courses for many Member States as well as in-depth, long-term training for selected staff from Member States at a WHO Collaborating Centre or H5 Reference Laboratory.
- The Secretariat develops and updates guidelines on technical activities related to pandemic preparedness, including clinical management, laboratory safety, specimen collection and laboratory procedures, use of antiviral medicines, and effective communication.

**Planned or new activities**

- WHO will publish regular updates of existing guidelines and documents on disease control measures during a pandemic and provide the most up-to-date knowledge on existing tools for response.
- WHO is developing revised guidance on the role of National Influenza Centres during the pandemic phases as well as a contingency plan for National Influenza Centres during a pandemic and guidance for laboratory-based virological surveillance during a pandemic.
- WHO will continue to promote research on innovative public health approaches and facilitate access to modern technologies for developing countries (e.g. use of mathematical modelling for pandemic preparedness planning). (See also Section 6.6.1 on development of a global research agenda.)

**2. *Provision of pandemic influenza candidate vaccine viruses (Section 6.3)***

*6.3.1 Any entity receiving PIP candidate vaccine viruses will meet appropriate biosafety guidelines (WHO Laboratory Biosafety Manual, 3rd edition) [and employ laboratory protection best practices.] The Director-General will ensure that WHO Collaborating Centres/H5 Reference Laboratories and Essential Regulatory Laboratories, provide [at no cost] PIP candidate vaccine viruses upon request:*

- (i) to influenza vaccine manufacturers on a no preference basis **Consensus***
- (ii) at the same time to the laboratories of originating and other Member States **Consensus***
- [(iii) to any other laboratory, as agreed in the Terms of Reference.]*

**Ongoing activities**

- WHO provides regular technical assistance to laboratories to assist them to meet appropriate biosafety standards.
- WHO continuously reviews information on candidate H5N1 vaccine viruses (and other viruses with pandemic potential) developed for potential use as human vaccines; WHO publishes every six months a summary of this information on its web site (see also section 6.2.2).
- WHO Collaborating Centres and Essential Regulatory Laboratories provide pandemic influenza candidate vaccine viruses without charge to all other interested influenza

manufacturers and institutes, including the originating laboratory and other Member States, following vaccine virus selection.

### 3. *Provision of diagnostic reagents and test kits (Section 6.4)*

*6.4.1 WHO Collaborating Centres on Influenza, WHO H5 Reference Laboratories and Essential Regulatory Laboratories, working with the WHO Secretariat, will continue to make available to National Influenza Centres and Other authorized laboratories, without charge, supplies of noncommercial diagnostic reagents and test kits for the identification and characterization of clinical specimens of influenza. Consensus*

#### **Ongoing activities**

- WHO provides specimen collection, packing and shipping materials to laboratories in resource-poor countries in the African and Eastern Mediterranean Regions.
- WHO Collaborating Centres provide on a regular basis, without charge to National Influenza Centres and other national influenza laboratories in countries without a National Influenza Centre, supplies of noncommercial, updated diagnostic reagents and test kits for the identification and characterization of influenza.
- WHO provides updated laboratory diagnostic protocols for the detection of emerging new variant viruses.

#### **Planned or new activities**

- Subject to the availability of funds, WHO will expand provision of specimen collection, packing and shipping materials to laboratories in other resource-poor countries in other WHO regions.

*6.4.2 Influenza diagnostic manufacturers receiving PIP biological materials are urged to make available to [WHO Network] laboratories, without charge or at concessional and/or preferential rates, supplies of diagnostic reagents and test kits for the identification and characterization of clinical specimens of influenza, if circumstances warrant. Consensus*

#### **Planned or new activity**

- WHO will work with its partners to encourage diagnostic manufacturers receiving PIP biological materials to contribute in-kind goods for use by developing country WHO network laboratories.

### 4. *Provision of reference reagents for potency determination of vaccines (Section 6.5)*

*6.5.1 Essential Regulatory Laboratories will continue to provide, upon request, reference reagents for potency determination of vaccines against H5N1 and other viruses of human pandemic potential to national regulatory laboratories and influenza vaccine manufacturers of all Member States. Consensus*

### **Ongoing activities**

- Essential Regulatory Laboratories provide reference reagents to laboratories of all Member States for potency determination of vaccines against H5N1 and other viruses of human pandemic potential.
- Essential Regulatory Laboratories continue to develop and standardize vaccine potency testing assays and standards.
- Essential Regulatory Laboratories conduct international multicentre collaborative studies to evaluate the standards developed as above.

*6.5.2 Essential Regulatory Laboratories will continue to provide upon request, training in quality control of vaccines against H5N1 and other viruses of human pandemic potential to national regulatory laboratories of all Member States. **Consensus***

- Essential Regulatory Laboratories do not provide training at this time. Subject to the availability of funds, Essential Regulatory Laboratories could work to provide training in quality control.

### **5. Laboratory and influenza surveillance capacity building (Section 6.6)**

*6.6.1 Upon request, Member States with advanced laboratory and influenza surveillance capacity are urged to continue to work with the Secretariat and other Member States, particularly developing countries to develop national laboratory and influenza surveillance capacity, including: **Consensus***

- (i) to conduct early detection, isolation and characterization of viruses; **Consensus***
- (ii) to participate in pandemic risk assessment and response; **Consensus***
- (iii) to develop research capacity related to influenza; **Consensus***
- (iv) to achieve technical qualifications for consideration of laboratories as National Influenza Centres, WHO H5 Reference Laboratories and WHO Collaborating Centres on Influenza. **Consensus***

### **Ongoing activities**

- WHO provides training, for example in rapid detection of influenza viruses by polymerase chain reaction methods, virus isolation, and biosafety procedures, in order to strengthen national laboratory capacity.
- WHO conducts an external quality assessment project that evaluates polymerase chain reaction testing proficiency for detecting emerging influenza viruses with pandemic potential in order to strengthen national laboratory capacity.
- WHO supplies some essential equipment to laboratories (e.g. biosafety cabinets, incubators, and dry ice-machines) in resource-poor countries in Africa.

- WHO provides training in packing and shipping of infectious substances within the framework of applicable dangerous goods international transport regulations.
- WHO runs a shipment fund project to assist countries, especially resource-poor countries, in sending shipments to WHO Collaborating Centres and H5 Reference Laboratories without charge.

(See also section 6.2.3 for capacity building activities related to early severity assessment and development of national pandemic surveillance approaches; section 6.2.4 for laboratory and other technical support activities; and section 6.2.2 for activities related to risk assessment and response capacity including rapid containment.)

### **Planned or new activities**

- WHO is developing activities to strengthen national surveillance capacity in some 104 resource-poor countries with limited or no influenza surveillance (e.g. development of influenza sentinel sites).
- WHO is developing a global research agenda for influenza to identify research gaps according to priority public health needs in risk assessment and response. Based on the priorities defined in the global research agenda, WHO will facilitate and channel international funding to developing countries in order to enhance their capacity for applied research related to influenza prevention and control.
- WHO is working with partners to develop burden of disease studies with related economic impact analysis.
- WHO and members of the WHO network will work actively to seek participation of scientists from originating laboratories/countries in scientific projects associated with research on clinical specimens and/or influenza viruses from their countries and work with them on the preparation of manuscripts for presentations and publication.

## **6. Regulatory capacity building (Section 6.7)**

*6.7.1 Upon request, Member States with advanced regulatory capacity should improve and strengthen the work that has been undertaken by Member States with WHO, particularly developing countries to strengthen the capacity of regulatory authorities to carry out the necessary measures for the rapid approval of safe and effective human influenza vaccines, diagnostics and pharmaceutical products, including products developed from the use of PIP biological materials, especially those derived from new sub-types of influenza viruses. **Consensus***

*[6.7.2 [[Member States should make available through the WHO Secretariat in a timely manner] /WHO Secretariat should examine the feasibility of creating a database] publicly available information related to health regulatory approval of H5N1 and other influenza viruses with human pandemic potential vaccines, diagnostics and pharmaceutical products including those developed from the use of PIP biological materials.] WHO Secretariat should examine the feasibility of creating a database of such information.]*

### **Ongoing activities**

- The Secretariat is conducting assessments of existing regulatory preparedness in Member States for veterinary and human vaccine licensing.
- WHO regularly provides training to improve regulatory capacity to evaluate and license vaccines where necessary.
- WHO provides technical assistance to ensure regulatory capacity to assess clinical trial results for regulatory approval.
- WHO provides assistance to create new, or strengthen existing, post-marketing surveillance/vaccine safety monitoring, including reporting of adverse events.
- The Secretariat provides support to Member States in the enforcement of Good Manufacturing Practices and conducting biosafety inspections.
- WHO provides training and capacity building to ensure appropriate lot release.

### **Planned or new activities**

- WHO will carry out regulatory capacity assessments, in countries new to human influenza vaccine manufacturing and regulation.
- WHO will develop and implement institutional development plans to build regulatory capacity for human influenza vaccines.
- WHO will provide training and technical support in all areas of regulatory oversight specific to human influenza vaccines.

## **7. [WHO and [other] multilateral] antivirals stockpiles (Section 6.8)**

6.8.1 *The Director-General will continue to work with other multilateral agencies, donors, international philanthropic organizations/entities, private foundations, and other potential partners, including institutions, organizations and entities and in particular influenza vaccine, diagnostic and pharmaceutical manufacturers, to seek commitments for contributions, maintain and further develop a stockpile of antiviral medicines and associated equipment for use in containment of outbreaks of H5N1 and other influenza viruses with human pandemic potential. **Consensus***

6.8.2 *The Director-General will continue to coordinate with Member States, institutions, organizations and other entities and encourage them to maintain and further develop stockpiles of antiviral medicines and associated equipment for use in containment of outbreaks of H5N1 and other influenza viruses with human pandemic potential. **Consensus***

6.8.3 *The Director-General will continue to seek the guidance of expert advice in determining the size, composition, replenishment, operational use and deployment procedures for use of the WHO antivirals stockpile. **Consensus***

### **On-going activities**

- WHO continues to maintain two separate stockpiles of oseltamavir and is working with the donor manufacturer on extending the shelf-life of the oseltamavir stockpiles which will expire in 2010 and 2011.

### **8. [WHO] pandemic influenza preparedness vaccine stockpile (Section 6.9)**

6.9.1 *The Director-General will establish and maintain a stockpile of vaccines for H5N1 and other influenza viruses with human pandemic potential and associated equipment, including syringes, needles and applicators, consistent with expert guidance. The WHO stockpile will initially include 150 million doses of H5N1 vaccine for use in accordance with expert guidance including that of the Strategic Advisory Group of Experts on immunization. Indicatively: **Consensus***

- *50 million doses will be for use in Affected countries, according to public health risk and need, to assist in containing the first outbreak or outbreaks of an emerging pandemic; Consensus, and*
- *100 million doses will be for distribution, once a pandemic begins, to developing countries that have no or inadequate access to H5N1 influenza vaccines, on a per capita basis, with use to be determined by those countries. Consensus*

6.9.2 *The Director-General will [continue to] seek the guidance of experts in determining the size, composition, replenishment and operational use of the vaccines in the [WHO] PIP vaccine stockpile.*

6.9.3 *Member States should urge influenza vaccine manufacturers to [provide] / [donate] sufficient doses of H5N1 vaccine for the [WHO] PIP vaccine stockpile. If insufficient doses are [provided] / [donated], the Director-General will work with Member States to explore use of [sustainable financing mechanisms] (in Section 6.12 below) to meet the requirements of the [WHO] PIP vaccine stockpile.*

*[6.9.4A Member States should urge influenza vaccine manufacturers to prioritize and immediately respond to the needs of the WHO PIP vaccine stockpile.]*

**AND/OR/ OR DELETE BOTH**

*[6.9.4B Member States should urge influenza vaccine manufacturers to set aside x% of [production][future production unallocated as of November 2008] for provision to the WHO PIP a vaccine stockpile.]*

6.9.5 *The Director-General will, with the guidance of experts, keep under review the potential for the pre-pandemic use of the [WHO] PIP vaccine stockpile in Affected countries, including by supporting trials as appropriate.*

6.9.6 *The Director-General will work with relevant experts and Member States to develop and exercise operational plans for the deployment of the vaccines in the [WHO] PIP vaccine stockpile.*

## **Considerations**

With a view to establishing an international stockpile of H5N1 vaccines as requested by the Health Assembly through resolution WHA60.28, WHO has collaborated with the Bill & Melinda Gates Foundation to develop options for the stockpile logistical design, as well as associated costs and potential sustainable financing mechanisms. A report on these options was released in February 2009<sup>1</sup> and a summary of the major findings and recommendations is attached as Appendix 1.

On 4 March 2009, WHO held a technical meeting to consult with experts and Member State representatives and review the technical options presented in the report. Based on expert guidance, including that received during the technical meeting, as well as the evidence and findings contained in the report, and sound public health principles, the Director-General considers that the optimal configuration for the international stockpile of H5N1 vaccines is as follows:

- short-term (three-to-five years) physical stockpile of donated vaccines that does not require replenishment
- vaccine to be held in filled doses with ancillary supplies
- stockpile to be located in up to three cities, selected according to cost implications and other criteria which include, but are not limited to:
  - international air and cargo hubs (reliability of airport facilities and services in times of crisis)
  - geographical/regional balance
  - commitment of host country to ensure access and facilitate international deployment
  - demonstrated logistics infrastructure capacity (e.g. storage, handling and maintenance).

The estimated present value cost of this option is US\$ 70 million. The Director-General will consult with potential donors to secure in-kind and other donations to meet this estimated cost.

## **Assumptions and considerations on costs and financing**

It is assumed that the initial 150 million doses of H5N1 vaccine will be donated in-kind to the stockpile by influenza vaccine manufacturers. At present, only 110 million doses have been pledged by industry. As such, additional pledges from industry will be needed to cover the remaining 40 million doses. In-kind contributions (e.g. warehousing, ancillary supplies, transportation, deployment funds and infrastructure) will also be sought to reduce cash outlays for the establishment of the stockpile. Detailed cost estimates for all stockpile elements (storage, shipment, maintenance, replenishment, and deployment) are provided in the report.

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<sup>1</sup> [http://www.who.int csr/disease/influenza/H5N1\\_Stockpile\\_Design\\_Feb2009.pdf](http://www.who.int csr/disease/influenza/H5N1_Stockpile_Design_Feb2009.pdf).

**9. Access to vaccines for developing and least developed country use (Section 6.10)**

[6.10.1 Separately from the [WHO] PIP vaccine stockpile, Member States should continue to work with each other, with the Director-General and with influenza vaccine manufacturers with the aim of ensuring that adequate quantities of vaccines for H5N1 and other influenza viruses with human pandemic potential, and pandemic influenza vaccines, are made available [to developing and least developed countries at the same time as to developed countries,] on the basis of public health risk and needs and at affordable prices.]

OR

[6.10.1B Separately from the [WHO] PIP vaccine stockpile, Member States should urge vaccine manufacturers to set aside [x%] of each production cycle of vaccines for H5N1 and other influenza viruses of human pandemic potential for provision to developing and least developed countries.] (or DELETE 6.10.1B).

**[Production of] Pandemic influenza vaccines (Section 6.11)**

6.11.1 Noting that pandemic influenza vaccines can only be produced after a pandemic begins.  
**Consensus**

[6.11.2A Member States should urge vaccine manufacturers to set aside [x%] of each production cycle of pandemic influenza vaccine for use by developing and least developed countries.] (or DELETE 6.11.2A)

AND/OR

[6.11.2B The Director-General, consulting Member States and the Advisory Group, will convene an expert group to develop [or continue to develop] international mechanisms [including existing ones] on the production and distribution of influenza vaccines during a pandemic for consideration by the Sixty-third World Health Assembly in 2010.]

**Technology transfer (Section 6.13)**

6.13.1 The Director-General will continue to work closely with Member States and influenza vaccine manufacturers to implement the WHO Global Pandemic Influenza Action Plan to Increase Vaccine Supply, notably Strategy 4.2 to increase [human] influenza vaccine production capacity by building new production facilities in, and transferring technology [, skills] and know-how as appropriate to, developing and/or industrialized countries.

[6.13.2 Member States should urge [institutions,] organizations [and entities] with access to vaccine manufacturing and other technologies for the control of influenza to make specific efforts to transfer these technologies [as appropriate] to other Member States, particularly developing countries.] (or DELETE 6.13.2)

6.13.3 Technology transfer should be conducted in a manner consistent with national laws and international laws and obligations, facilitated progressively over time, on mutually agreed terms, and be [appropriate] / [suitable] to the capacity of recipient Member States, to empower developing countries to study and manufacture influenza vaccines, diagnostics and pharmaceuticals.

*[6.13.4A Member States should urge influenza vaccine manufacturers that receive PIP biological materials to grant, on request, a non-exclusive, royalty-free licence to any influenza vaccine manufacturer from the Member State where the relevant clinical specimen was collected from which the relevant PIP biological materials were derived, to use its intellectual property and other protected substances, products, technology, [skills,] know-how, information and knowledge used in the process of influenza vaccine development and production in particular for pre-pandemic and pandemic vaccines.] (or DELETE 6.13.4A)*

OR

*[6.13.4B Influenza vaccine manufacturers who receive PIP biological materials may grant [as appropriate and subject to any existing licensing restrictions] [on a voluntary basis], [and mutually agreed terms] a [non-exclusive, royalty-free] licence to any influenza vaccine manufacturer from a developing country, to use its intellectual property and other protected substances, products, technology, know-how, information and knowledge used in the process of influenza vaccine development and production, in particular for pre-pandemic and pandemic vaccines [for use in that developing country.]*

### **Considerations**

An influenza pandemic that causes high mortality may entail vaccination of the entire global population in the shortest possible time. Today, this would mean the need for up to 13 400 million doses of pandemic vaccine if two immunizations were required to assure immunity in a naïve population.

Currently, most developing countries do not have domestic influenza vaccine production capacity, leaving them totally dependent on the availability and accessibility of vaccine produced by multinational manufacturers. Given current global production capacity, demand is expected to outstrip supply in the event of a pandemic. Fortunately, with political commitment and advances in technology, prospects are improving: significantly more seasonal, H5N1 and other potential pandemic vaccine doses are expected to be available over the next five years, either through expansion of existing facilities or the creation of new ones. Additionally, antigen-per-dose requirements are now lower due to the development of new adjuvants and production yields have improved. Most multinational manufacturers have expanded their production of seasonal influenza doses. Production capacity should increase even further as new cell-based facilities become operational in the next decade.

Despite this progress, however, the number of available doses to immunize the world population within the first six-to-nine months of a pandemic will still fall short by several billion doses. Modelling of increased production capacity until 2015 (data from the International Federation of Pharmaceutical Manufacturers Associations, due to be released in March 2009) indicates that the situation is unlikely to change in the next 10 years at least.

Appendix 2 details ongoing activities undertaken as part of the Global Pandemic Influenza Action Plan to Increase Vaccine Supply. These include work on knowledge management, technology transfer, including grants to six developing country manufacturers, and the creation of a technology hub to promote access to influenza vaccine manufacturing technology by developing countries.

### **Considerations on costs and financing**

At least US\$ 20 million per year over five years is required to complete WHO's technology transfer hub project under the Global Pandemic Influenza Action Plan, and US\$ 500 million over the same period for the establishment of influenza vaccine production plants in 10 developing countries.

#### **10. *[Tiered][Affordable] Pricing OR [concessional and/or preferential rates] OR [differential pricing policies] (Section 6.12)***

*6.12.1 Member States should urge influenza vaccine manufacturers to implement [tiered pricing][affordable pricing] OR [concessional and/or preferential rates] OR [differential pricing policies] for vaccines for H5N1 and other influenza viruses with human pandemic potential and for pandemic influenza vaccines.*

*[6.12.2 "Tiered pricing" involves different countries paying different prices for the same product, usually according to their income level.] (or DELETE 6.12.2)*

*[6.12.3 "Affordable pricing" could be defined to mean:*

- (i) for developing countries, a price no higher than marginal cost per unit plus 5%;*
- (ii) for least developed countries, at "no profit no loss" to the manufacturer.] (or DELETE 6.12.3)*

### **Considerations**

Affordability of H5N1 and potential pandemic influenza vaccines is a vital element in ensuring equitable access. Models of pooled procurement of vaccines for developing countries at concessionary prices exist in the form of the GAVI Alliance, the PAHO Revolving Fund, and the mechanisms to purchase vaccines for emergency response for meningitis and yellow fever. These pooled mechanisms have been successful in part because they offer two-way security to both manufacturers and vaccine recipients in the form of advance knowledge of product demand for the former and affordable pricing for the latter. In the case H5N1 and potential pandemic vaccines, however, there are unique challenges due to the lack of firm knowledge about the cost of production and availability of supply.

Agreement needs to be reached by vaccine manufacturers and Member States on what pricing bands should be made available to whom, based on concrete criteria that can be objectively evaluated, without creating unnecessary governance mechanisms.

### **Considerations on costs and financing**

Costs to reach and implement an agreement as described above would depend on the form that such a negotiation would take. If a pooled procurement mechanism was used and needed to be sustained, this would entail additional costs for management and governance.

#### **11. *Sustainable financing mechanism (Section 6.14)***

*[6.14.1 Member States should work with the Director-General to [establish a sustainable financing mechanism] / [seek sustainable financing] to support the PIP benefit sharing system.]*

[6.14.2 *The sustainable financing mechanism should have a particular priority on meeting the needs of affected developing and least developed countries for access to vaccines for H5N1 and other influenza viruses with human pandemic potential, including through the [WHO] PIP vaccine stockpile[, but may also be used to support the provision of other benefits including technology transfer and capacity building.]*

[6.14.3 *The Director-General, with the support of Member States and the Advisory Group, will explore the use of existing fund-holding institutions and organizations to hold and administer funds for the sustainable financing mechanism, before any new arrangement within the WHO or elsewhere is considered.]*

[6.14.4 *The Director-General will report to the World Health Assembly [in 2009] on whether a suitable existing fund-holding institution or organization is willing to hold and administer funds for the sustainable financing mechanism. If such an arrangement cannot be agreed, the Director-General, in consultation with the Advisory Group and Member States, will propose a new arrangement to the World Health Assembly [in 2009].]*

[6.14.5 *The sustainable financing mechanism will receive funding from:]*

[A. *voluntary contributions from influenza vaccine, diagnostic and pharmaceutical manufacturers, Member States, nongovernmental organizations and any other individuals or entities;]*

AND/OR

[B. *mandatory contributions from influenza vaccine, diagnostic and pharmaceutical manufacturers based on [x%] of the sales of products developed using PIP biological materials;]* (or DELETE 6.14.5B)

AND/OR

[C. *annual assessed contributions from Member States [according to the UN scale of assessment], ranging from US\$ 0.006 per capita from Member States in the lowest decile of per capita gross domestic product to US\$ 0.015 per capita for Member States in the highest decile of per capita gross domestic product;]* (or DELETE 6.14.5C)

AND/OR

[D. *annual assessed contributions from influenza vaccine manufacturers, at US\$ 0.20 per influenza vaccine dose manufactured by them in that year].* (or DELETE 6.14.5D)

#### ***Innovative financing mechanisms for national vaccine requirements (IGM Text 6.15)***

[6.15.1 *Interested Member States may work together, with the Director-General and with nongovernmental and international organizations as appropriate, to establish urgently a fund for the procurement of national stocks of vaccines for H5N1 and other influenza viruses of human pandemic potential, using a revolving fund for immunization, potentially modelled after the Pan American Health Organization (PAHO) Revolving Fund for Immunization, or other similar types of funds, as a reference point.]* (or DELETE 6.15.1)

[6.15.2 The fund may be used for, but not limited to:

- (i) procure supplies of vaccine for H5N1 and other viruses with human pandemic potential, and associated equipment, that meet WHO standards, on behalf of participating countries;
- (ii) seek to provide such vaccines and associated equipment for developing countries at concessional or preferential rates;
- (iii) provide affordable financing arrangements to developing [and least-developed] countries to support procurement of vaccines and associated equipment.] (or DELETE 6.15.2)

[6.15.3 The mechanism for capitalization and governance arrangements for the fund should be agreed by participating Member States and organizations, but may include voluntary contributions from Member States and nongovernmental organizations.] (or DELETE 6.15.3)

[6.15.4 Neither the existence of, nor participation in, the sustainable financing mechanism or the innovative financing mechanism will prevent Member States from making other unilateral or multilateral arrangements to procure vaccines [for H5N1 and other viruses with human pandemic potential].] (or DELETE 6.15.4)

### **Considerations**

There are various mechanisms for innovative and sustainable financing for public health activities. The three key elements common to any mechanism are:

- defining the actual elements to be financed and sustained, their duration and their costs;
- determining how the financial resources will be obtained (e.g., through voluntary contributions or through assessments); and
- deciding who will administer the financial resources and how, including disbursement.

A selected overview of some of these mechanisms is attached at Appendix 3.

### **Considerations on costs and financing**

Until consensus is reached regarding what kind of specific activities are to be financed and sustained, as well as the financial mechanisms themselves, it is not possible to estimate costs.

## APPENDIX 1

**H5N1 VACCINE STOCKPILE DESIGN AND FINANCING OPTIONS**

A detailed study of logistical design options for the H5N1 vaccine stockpile and associated costs and possible financing mechanisms was undertaken with support from the Bill & Melinda Gates Foundation. The results of the study have been issued and may be found on the WHO web site.<sup>1</sup> A summary of the principal findings are set forth below.

## Logistical design findings

- Holding vaccine in bulk form, as opposed to filled doses, has a minimal impact on the overall stockpile cost because it is possible to hold novel adjuvants (which are expected to have a longer shelf-life and represent a significant portion of vaccine costs) separate from the antigen.
- Holding vaccine in bulk form would have a number of consequences unrelated to cost but which favour holding filled doses. Those consequences include:
  - increased deployment time because of the time required to fill and finish vaccine doses;
  - increased management and liability complexity, as fill and finish operations carry inherent risks of contamination or other errors that could compromise the vaccine;
  - the need to fill and finish limits the placement of bulk vaccine to countries with fill and finish capacity and is politically unattractive to some recipient countries.
- Holding a physical stockpile in a few (between one and three) logistically optimal, regionally strategic locations best balances the need for efficient management and rapid deployment of the stockpile.
- Stockpile locations should have superior logistical infrastructure, top-tier cargo airports, and be in countries with small populations (to minimize the effect of possible nationalization of the stockpile at the time of need).
- There should be regional balance in selecting locations. Dubai, Panama City and Singapore were considered good examples of the type of locations that could be selected.
- Ancillary supplies (e.g. syringes and personal protective equipment) that the WHO Strategic Advisory Group of Experts on immunization (recommended be held with the stockpiled vaccine represent a small portion of the stockpile costs; such costs do not vary substantially based on the placement decision. Given that the vaccine cannot be administered without these materials, the lowest-risk solution is for ancillary supplies to be held and deployed with the vaccine.

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<sup>1</sup> [http://www.who.int/csr/disease/influenza/H5N1\\_Stockpile\\_Design\\_Feb2009.pdf](http://www.who.int/csr/disease/influenza/H5N1_Stockpile_Design_Feb2009.pdf).

- According to currently pledged manufacturer donation schedules, delivery of vaccine donations is likely to be staggered over several years. This would pose challenges to constituting a concurrently available, physical stockpile of 150 million doses.
- The replenishment of vaccine (replacing product that has expired or has been used) would make up the majority of the stockpile cost over the long term (~70% over 10 years). Thus, controlling this cost is crucial.

### **Stockpile options**

Based on these findings, the following three options for the design of the 150 million dose H5N1 vaccine stockpile were defined and considered:

- A.** Short-term physical stockpile – estimated present value cost US\$ 70 million: The vaccine donated by manufacturers would be held in filled doses in up to three logistically optimized locations with no guarantee or funding secured for the replenishment of the vaccine upon use or expiry. Upon use or expiry of the donated vaccine, either the vaccine would be replenished (through purchase or new donations) or the size of the stockpile would decrease.
- B.** Longer-term physical stockpile – estimated nominal cost between US\$ 360 million (one replenishment cycle) and US\$ 610 million (two replenishment cycles): Vaccine would be held in filled doses in up to three locations. Guarantees would be provided by the manufacturer or financing mechanisms would be employed to ensure the maintenance and replenishment (one or two cycles) of the stockpile for up to a 10-year period.
- C.** Virtual stockpile – estimated nominal cost US\$ 70 million: If, at some time in the future, H5N1 vaccine is put into regular use, a stockpile could be part of manufacturers' regular, revolving stock of vaccine. This would substantially reduce the cost of the stockpile by eliminating the need to store and replenish vaccine. However, given the current market, this option is not economically feasible. Moreover, this option has significant non-cost tradeoffs, and is not necessarily aligned with the intent of the manufacturers' donations.

### **Financing strategies for the stockpile**

The findings of the study indicate that financing an H5N1 vaccine stockpile is different from other immunization programmes in two important ways:

- the annual funding need could be highly variable and difficult to predict, driven by the uncertain nature of the H5N1 vaccine shelf-life and the possibility that it may change due changes in the reference virus, manufacturer, and/or other factors;
- the timing of deployment of vaccine from the stockpile is unknown, creating an open-ended funding need.

These differences add to the complexity of financing the stockpile and suggest consideration of insurance-style mechanisms to address these uncertainties. Two such mechanisms are:

- **Product warranty:** In exchange for an upfront or annual payment, manufacturers would guarantee the shelf-life and potency of their vaccine for a period of time. This would transfer

the uncertainties around the shelf-life of the vaccine from the stockpile holder(s) to the manufacturers that are best equipped to manage it.

- **Annuity:** In exchange for an upfront fee, an insurer would provide annual payments to the stockpile to cover management and replenishment costs until the stockpile is fully deployed. This mechanism would provide funding certainty to the stockpile as well as an attractive financial hedge to insurers against other pandemic risks they are carrying. The financial hedge value could result in discounted pricing and/or favourable terms.

Funds to deploy the stockpile will need to be available on an urgent basis and should be planned for in advance. The estimated costs are considerable: if deployment(s) occur(s) within 10 years, the cost is expected to exceed US\$ 300 million (US\$ 170 million in present value). A number of mechanisms could be considered for ensuring the availability of such funds:

- **Casualty insurance:** purchase of an insurance policy that pays for the deployment and delivery costs at the time of release from the stockpile;
- **Guaranteed line of credit:** a pre-negotiated line of credit that countries or organizations can draw upon to cover deployment and vaccine delivery costs from the stockpile; and
- **Donor advanced pledges** to pay for the cost of deployment and delivery in those countries that are in greatest need of aid.

The study was completed before the global financial crisis which will necessarily have an impact on the assumptions used (e.g., inflation and discount rates) and the attractiveness of some of the financing options discussed. The full report provides significantly more details on these and other issues related to the establishment of the H5N1 vaccine stockpile.

#### **Other Policy issues** – Strategic Advisory Group of Experts on immunization **H5N1 Working Group**

In addition to the options for stockpiling and financing identified in the external report, the Strategic Advisory Group of Experts on immunization has been actively considering whether it is appropriate to use the newly licensed H5N1 vaccines to immunize certain groups of people against avian H5N1 virus infection in countries where the virus is entrenched in poultry, or as a precautionary measure against a potential H5N1 pandemic. Policy recommendations regarding interpandemic vaccination will be made through Strategic Advisory Group of Experts which has been asked specifically by the Director-General to evaluate the following questions:

1. What is the evidence and is it sufficient to recommend use of licensed H5N1 vaccine in the interpandemic period to protect against avian H5N1 influenza in high-risk and low-risk populations?
2. What is the evidence and is it sufficient to recommend use of licensed H5N1 vaccine in the interpandemic period to prime or fully immunize against infection with a potential pandemic H5N1 in essential personnel and the general public?
3. What should the Strategic Advisory Group of Experts on immunization recommend be done with expiring H5N1 vaccine stockpiles during the interpandemic period?
4. Should the Strategic Advisory Group of Experts on immunization recommend a change in the size of the H5N1 vaccine stockpile?

The Strategic Advisory Group of Experts on immunization Working Group on H5N1 Vaccine aims to help the Advisory Group answer these questions by:

- assessing the safety and immunogenicity of current and late developmental H5N1 vaccines;
- analysing risk- and cost-benefits of using H5N1 vaccines in the interpandemic period;
- reviewing interpandemic H5N1 vaccine policies especially with regard to vaccinating specific “at risk” populations and what to do with stockpiles of expiring vaccine;
- reviewing new evidence that might influence the size of the H5N1 stockpile;
- identifying and prioritizing knowledge gaps that might affect decisions regarding options for interpandemic vaccine use.

## APPENDIX 2

**INCREASING VACCINE PRODUCTION CAPACITY  
AND TECHNOLOGY TRANSFER**

The following text describes the activities carried out by WHO.

**Technology transfer and production of pandemic influenza virus vaccine**

Increasing vaccine production capacity is part of the remit of the Global Pandemic Influenza Action Plan to Increase Vaccine Supply. The goal is to increase influenza vaccine manufacturing capacity so as to be able to immunize the world's 6700 million people in no more than six to nine months after the onset of a pandemic. Currently, 90% of influenza vaccine production is located in nine countries, most in Europe and North America. Much of this capacity is already pledged in the form of purchasing contracts. More widespread influenza vaccine production would redress this situation to some extent, by ensuring greater equity in the deployment of what may be a scarce resource in the early months of a pandemic. Technology transfer is arguably the most effective route for developing countries to secure access to quality influenza vaccination technology.

In October 2006, WHO invited proposals from developing country vaccine manufacturers willing to initiate domestic production of influenza vaccine. The technologies eligible for funding were killed subunit, split or whole virus, live attenuated influenza vaccines, and cell-culture or egg-based production. Expectations were large-scale production of seasonal influenza vaccine that would be rapidly operational, cost-effective and sustainable. Grant conditions included the requirement that grantees make available up to 10% of their production to United Nations purchasers in the event of a pandemic.

Six developing country manufacturers received grants of US\$ 2.0–2.7 million each to establish pilot facilities for the production of influenza vaccines (Table 1). All projects were initiated in 2007.

**Table 1. WHO technology transfer grants**

Country/Institute	Technology	Main achievements at end 2008
Brazil Instituto Butantan	Egg-based inactivated split and/or whole-virion H5N1 with adjuvant.	New pandemic vaccine pilot plant established, with 10 experimental lots having been produced: seven H3N2 and three recombinant H5N1 vaccines.
India Serum Institute of India	Cell-based inactivated split virus and egg-based live attenuated influenza vaccine, depending on access to live attenuated strain.	H1N1 and H3N2 strains successfully grown in laboratory conditions. Quality control system in place.
Indonesia BioFarma	Fill and finish operations for egg-based split seasonal vaccine.	Facility established, three clinical-grade lots produced and a clinical trial completed.

Mexico Birmex	Blending, filling, packaging of egg-based inactivated split seasonal vaccine.	Product-specific equipment for quality control laboratory purchased. Construction and engineering plans for blending facility under validation.
Thailand Government Pharmaceutical Organization	Egg-based split inactivated vaccine and live attenuated influenza vaccine, depending on access to live attenuated strain.	Successful laboratory-scale production of trivalent seasonal vaccine with quality control confirmation. Technology ready to test in pilot-plant conditions.
Viet Nam IVAC	Egg-derived whole-virion, alum adjuvanted vaccine.	Facility under construction. Three recombinant H5N1 experimental lots sent to NIBSC <sup>1</sup> for confirmatory testing for antigen content.

New applications from vaccine manufacturers in developing countries are currently being considered for funding by WHO under a second round of grants. However considerable challenges remain: finding technology providers; providing financial support; and providing staff training, as there are few experienced personnel at the new sites. A possible solution is a “technology hub” that could serve as a provider of generic transferable technology to interested developing country manufacturers. This is being established by the Netherlands Vaccine Institute, in collaboration and with technical and financial assistance from WHO.

#### **Access to technology**

WHO signed a licensing agreement with Nobilon (Schering-Plough Corporation) to provide access to live attenuated influenza vaccine manufacturing technology to developing countries. Under the agreement, Nobilon granted WHO a non-exclusive licence to develop, register, manufacture, use and sell seasonal and pandemic live attenuated influenza vaccines, produced in embryonated chicken eggs. WHO will be permitted to grant a sub-licence to vaccine manufacturers in developing countries working within the framework of WHO’s Global Pandemic Influenza Action Plan to Increase Vaccine Supply. Vaccine manufacturers to which a sub-licence is granted will be able to provide vaccines to the public sector of developing countries royalty-free.

Egg-based live attenuated influenza vaccine technology is considered attractive for this purpose because the manufacturing technology process is easier to transfer, capital investment is lower and yields are higher, by comparison with inactivated influenza vaccines.

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<sup>1</sup> National Institute for Biological Standards and Controls, United Kingdom of Great Britain and Northern Ireland.

**Knowledge management**

Activities in this area include the organization of regular meetings to evaluate broad-spectrum and long-lasting immune responses to influenza vaccines and the status of pandemic prototype vaccines in clinical trials; dissemination of clinical trial data<sup>1</sup> and maintenance of an inventory of completed and ongoing studies of H5 and other prototype pandemic vaccines; and support to the Strategic Advisory Group of Experts on immunization for advice on WHO vaccine policies.

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<sup>1</sup> [http://www.who.int/vaccine\\_research/diseases/influenza/flu\\_trials\\_tables/en/index.html](http://www.who.int/vaccine_research/diseases/influenza/flu_trials_tables/en/index.html).

## APPENDIX 3

**EXAMPLES OF SUSTAINABLE AND INNOVATIVE FINANCING MECHANISMS  
(SECTIONS 6.14 AND 6.15)**

A wide range of mechanisms designed to provide sustainable and innovative financing for health programmes in developing countries has been developed, notably since the adoption of the Millennium Development Goals. Innovative and sustainable financing has been the focus of many international symposia and workshops and the subject of many publications.<sup>1</sup> Several innovative financing tools or models could potentially be applied to influenza, and some are briefly reviewed below.

**1. PAHO Strategic Fund for Public Health Supplies (or PAHO Revolving Fund)**

*What is being financed?* The PAHO Strategic Fund is a mechanism created to promote access to high-quality essential public health supplies in the Americas. The Strategic Fund links the acquisition of medicines and essential public health supplies with technical processes in planning and programming. Through the Strategic Fund, the procurement of essential medicines and basic public health products is accompanied by technical support from PAHO in supply systems management and acquisition of low cost products that meet international quality standards.

The Strategic Fund assists PAHO's Member States:

- to forecast their demand for pharmaceutical products to ensure continuous availability;
- to acquire products that meet international quality standards;
- to negotiate competitive prices by consolidating demand and achieving economies of scale, notably for expensive products and supplies of limited availability;
- by providing price referencing information to PAHO Member States;
- by serving as a link with suppliers of pharmaceutical products available through other global initiatives.

The principal recipients of projects financed by the Global Fund to Fight AIDS, Tuberculosis and Malaria may also use the Strategic Fund for procurement of Strategic Fund products by signing a Memorandum of Understanding with PAHO.

*How are resources obtained?* The Strategic Fund is capitalized through the allocation of a portion of a 3% procurement service charge to the Fund's capital account. As countries purchase through the Strategic Fund, the purchasing power of the Fund increases, resulting in lower product prices for participating countries.

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<sup>1</sup> See, e.g. "Innovative Financing for Global Health: Tools for Analyzing the Options" in Brookings Global Economy and Development Working Paper series, August 2008.  
[http://www.brookings.edu/~media/Files/rc/papers/2008/08\\_global\\_health\\_de\\_ferranti/08\\_global\\_health\\_de\\_ferranti.pdf](http://www.brookings.edu/~media/Files/rc/papers/2008/08_global_health_de_ferranti/08_global_health_de_ferranti.pdf).

*How are the resources administered?* The Strategic Fund is administered by PAHO and financial management of the Fund is governed by PAHO's Financial Rules and Financial Regulations. Member States and/or the principal recipients participating in the Strategic Fund deposit funds with PAHO in order to purchase products through the Fund. PAHO deposits the funds in a separate Member State account from which supplier invoices are paid. Any balances are retained in this account for future procurement by the Member State, or refunded as required.

In some instances, the Strategic Fund allows participating members to utilize a common fund for payment of authorized purchases of essential public health commodities. Members make reimbursement to the fund for the cost of each purchase within a specified period of time.

## **2. International Finance Facility for Immunization**

*What is being financed?* The Facility was designed to provide support to 72 of the world's poorest countries for front-loaded immunization activities that will contribute to achieving Millennium Development Goals 4 and 5 (reduce child mortality and improve maternal health). The fund is intended to provide US\$ 4000 million over 10 years (2006–2015) to prevent five million child deaths and five million future adult deaths.

*How are the resources obtained?* Donor countries have made long-term pledges (up to 20 years) against which bonds have been issued in capital markets to make the funds available in a shorter time frame than if provided directly by 20-year commitments on an annual basis.

*How they are administered?* The funds are administered within the framework of the GAVI Alliance, through a separate governance structure, having its own board and separate financial considerations.

## **3. Advance market commitments**

*What is being financed?* The purchase of new types of pneumococcal conjugate vaccines by GAVI Alliance-eligible countries is the first tangible project being funded by an advance market commitment. These commitments constitute a "pull" mechanism meant to provide incentives for manufacturers to invest in development and accelerated or increased production of pharmaceuticals and vaccines for developing countries. The advance market commitment finances the guaranteed purchase of set quantities of products at a specific price for a specified duration of time, and based on other pre-defined criteria, and has as a condition that the product price post-advance market commitment be set a pre-defined affordable level.

*How are the resources obtained?* There are two components to the financial resources in an advance market commitment. One component is a co-payment commitment from recipient countries, which is paid only when the receiving country receives the actual product. The second (and larger) component is donor financing which is paid in accordance with an agreed payment schedule subject to products being available and selected for purchase by recipient countries.

*How they are administered?* Through the GAVI Alliance's framework, an independent assessment committee determines whether a given manufacturer's product meets the approved target specifications (e.g., efficacy, physical characteristics, and long-term open market price for developing countries). Once the committee has approved a candidate product, GAVI Alliance-eligible countries apply through the Alliance to obtain the subsidy for a given time period and specific quantity of product.

#### **4. Subsidized pricing (e.g. malaria and the global artemisinin-based combination therapy subsidy)**

*What is being financed?* Artemisinin is a relatively new, powerful and effective treatment for malaria, but is more expensive than the older therapies and hence not readily accessible to patients in need, most of whom live in resource-poor settings. The combination therapy is sold to governments at a manufacturer's price of US\$ 1 per treatment, while manufacturers' prices to the private sector range from US\$ 4 to US\$ 5 per treatment. The programme provides a subsidy for public sector purchase of artemisinin-based combination therapies, thus increasing the use of the more effective treatments, delaying onset of resistance, and crowding out less effective therapies.

*How the resources are obtained?* The Global Fund to Fight AIDS, Tuberculosis and Malaria and other donors provide resources to support the subsidy.

*How are they administered?* The Global Fund to Fight AIDS, Tuberculosis and Malaria administers the subsidy, providing direct support for both the public and private sector purchases of artemisinin-based combination therapy. By providing the subsidy to both the public- and private-sector distribution chains and thus equalizing prices in both sectors, the subsidy works to drive older, ineffective treatments from the market, improving patient outcomes and slowing the spread of resistance.

#### **5. Airline solidarity contribution (UNITAID)**

*What is being financed?* The airline solidarity contribution, essentially a tax on airline passengers, is used to generate resources to support UNITAID, an international drug purchase facility, which aims to generate sustainable, predictable resources for global health. Specifically UNITAID raises funds for the purchase of high-quality medicines and diagnostics for developing countries with a high burden of AIDS, tuberculosis, and malaria.

*How are the resources obtained?* Launched in 2006, UNITAID adds the airline solidarity contribution to existing airline taxes. This is a unit (per passenger) tax added on to airline tickets by participating countries. The proceeds are earmarked for UNITAID.

*How are they administered?* The Executive Board of UNITAID reviews project proposals from partners such as UNICEF, WHO, the Clinton Foundation, and the Global Fund to Fight AIDS, Tuberculosis and Malaria. UNITAID provides funds directly to these partners who use the resources to purchase medicines and diagnostics in accordance with their own procurement policies.

#### **6. Debt relief (e.g. Polio Eradication Initiative IDA buy-downs)**

*What is being financed?* Debt relief involves developed countries and potentially other donors making lump sum payments to reduce the debt, or securing the loans, of developing and least-developed countries, allowing the countries to use the savings to invest in public health.

*How are the resources obtained?* Donors to the poliomyelitis eradication programme took over the debt-service payments of International Development Association credits (low interest loans that eligible countries had received from the World Bank through its soft-loan arm), so that the funds from the credits became akin to grants to the countries.

*How are they are administered?* A trust fund was established by donors to repay the International Development Association loans on the condition that each country uses its loan credits for the agreed public health purposes. Thus, when used for their intended purpose, the credits under this scheme become grants, given that they are repaid by the trust fund – not the country.

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