

# **Pandemic influenza preparedness: sharing of influenza viruses and access to vaccines and other benefits**

## **Pandemic Influenza Preparedness Framework 2013 biennial report**

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

1. The attached document EB132/16 was considered and noted by the Executive Board at its 132nd session.<sup>1</sup>

#### **ACTION BY THE HEALTH ASSEMBLY**

2. The Health Assembly is requested to note the report.

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<sup>1</sup> See the summary record of the ninth meeting of the Executive Board at its 132nd session, section 3.





EXECUTIVE BOARD  
132nd session  
Provisional agenda item 8.2

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## **Pandemic influenza preparedness: sharing of influenza viruses and access to vaccines and other benefits**

### **Pandemic Influenza Preparedness Framework 2013 biennial report**

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

1. In resolution WHA64.5 the World Health Assembly adopted the Pandemic Influenza Preparedness Framework ("PIP Framework") on 24 May 2011.
2. Section 7.4.1 of the PIP Framework states that the Director-General shall on a biennial basis inform the World Health Assembly, through the Executive Board, on the status of, and progress on:
  - (i) Laboratory and surveillance capacity (see Framework section 6.6);
  - (ii) Global influenza vaccine production capacity (see Framework sections 6.13.1 and 6.13.2);
  - (iii) Status of agreements entered into with industry, including information on access to vaccines, antivirals and other pandemic material (see Framework sections 6.14.3 and 6.14.4);
  - (iv) Financial report on the use of the partnership contribution (see Framework section 6.14.5);
  - (v) The experience arising from the use of the definition of PIP biological materials (see Framework section 4.1).
3. This report presents summary information on the status and progress of these topics. Annexes 1 and 2 to this report provide detail (respectively *the Pandemic Influenza Preparedness Framework ("PIP Framework") Advisory Group Annual Report to the Director-General Under PIP Framework Section 7.2.5: 2012 Annual Report*; and the *Report of the Meeting of the Pandemic Influenza Preparedness Framework Advisory Group 3–5 October 2012*). The Director-General has accepted the annexed reports and the findings contained therein.

## **LABORATORY AND SURVEILLANCE CAPACITY**

4. A comprehensive review of this topic can be found in Annex 1, Section 2.1, Section 2.2, Section 2.3, and Section 2.4.

## **GLOBAL INFLUENZA VACCINE PRODUCTION CAPACITY**

5. Advancing equitable and universal access to influenza vaccines is a crucial ethical element in both seasonal and pandemic influenza preparedness and response efforts. Since its launch in 2006, the WHO Global Action Plan for Influenza Vaccines (GAP)<sup>1</sup> has proved to be an effective catalyst for a significant expansion in influenza vaccine manufacturing. Seasonal vaccine production has increased from 350 million doses in 2006 to around 900 million doses by 2009.<sup>2</sup> The estimated global annual capacity for seasonal trivalent influenza vaccine production in 2011 was about 1400 million doses.<sup>3</sup>

6. GAP also has facilitated a significant expansion in the manufacturing capacity of influenza vaccines in both developing and developed countries. As at 1 October 2012, 14 developing-country manufacturers had received WHO seed grants and technology-transfer support. These initial grants were leveraged to secure significantly more national and private funding.

7. In July 2011 the Second WHO consultation on the global action plan for influenza vaccines (GAP) was held at WHO headquarters, Geneva. The consultation brought together more than 100 representatives from national governments, donors, regulatory authorities, WHO technology-transfer projects, vaccine manufacturers, nongovernmental organizations, and the research community. Consultation participants reviewed the progress and lessons learnt during the first five years of GAP and proposed a set of key actions to: (1) increase the use of seasonal influenza vaccine; (2) increase influenza vaccine production capacity; and (3) promote influenza vaccine research and development.<sup>4</sup> Included among these priority activities were the need for disease-burden data for national authorities to use in making evidence-based decisions on the introduction of seasonal influenza vaccines, strengthening disease and virological surveillance and response activities, improving communications, and support for regulatory research.

## **STATUS OF AGREEMENTS ENTERED INTO WITH INDUSTRY, INCLUDING INFORMATION ON ACCESS TO VACCINES, ANTIVIRAL MEDICINES AND OTHER PANDEMIC MATERIAL**

8. A comprehensive review of this topic can be found in Annex 1, Section 3; and Annex 2, paragraphs 12 and 13.

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<sup>1</sup> See [http://www.who.int/influenza\\_vaccines\\_pl/.an/en](http://www.who.int/influenza_vaccines_pl/.an/en) (accessed 15 October 2012).

<sup>2</sup> Collin N, de Radiguès X. Vaccine production capacity for seasonal and pandemic (H1N1) 2009 influenza. *Vaccine*, 2009, 27:5184–5186.

<sup>3</sup> WHO, unpublished data.

<sup>4</sup> GAP meeting report available at: [http://whqlibdoc.who.int/publications/2012/9789241564410\\_eng.pdf](http://whqlibdoc.who.int/publications/2012/9789241564410_eng.pdf).

**FINANCIAL REPORT ON THE USE OF THE PARTNERSHIP CONTRIBUTION**

9. A comprehensive review of this topic can be found in Annex 1, Section 3; and Annex 2, paragraphs 16–21.

**EXPERIENCE ARISING FROM THE USE OF THE DEFINITION OF PIP BIOLOGICAL MATERIALS**

10. A comprehensive review of this topic can be found in Annex 2, paragraphs 14 and 15.

**ACTION BY THE EXECUTIVE BOARD**

11. The Executive Board is invited to note this report.



## ANNEX 1

**PANDEMIC INFLUENZA PREPAREDNESS FRAMEWORK (“PIP FRAMEWORK”)  
ADVISORY GROUP ANNUAL REPORT TO THE DIRECTOR-GENERAL  
UNDER PIP FRAMEWORK SECTION 7.2.5**

**2012 Annual Report**

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<sup>1</sup> Web-only supplementary annex. PIP Framework-related tasks/activities.

## EXECUTIVE SUMMARY

This is the first Annual Report of the Pandemic Influenza Preparedness Framework (“PIP Framework”) Advisory Group since adoption of the Framework by the Sixty-fourth World Health Assembly on 24 May 2011. The Report covers the 12 month period beginning in May 2011 up to May 2012. The Report is organized into three substantive sections: virus sharing, benefit sharing and governance.

### Virus sharing

This initial Report provides essential context about the Global Influenza Surveillance and Response System (GISRS) and its key roles and responsibilities in surveillance, preparedness and response. The Advisory Group noted multiple examples of the collaborative work of WHO and Member States to strengthen laboratory and disease surveillance capacity for detection and risk assessment of influenza viruses with human pandemic potential. The continued sharing of viruses enables the development of candidate vaccine viruses with pandemic potential and reference reagents – critically important tools when a pandemic virus emerges. The Influenza Virus Traceability Mechanism (IVTM) has increased the transparency of GISRS activities and the sharing of viruses with human pandemic potential and other PIP biological materials. The Advisory Group noted other areas of work that contribute to pandemic preparedness, including efforts to strengthen regulatory capacity, vaccine deployment capacity, an H5N1 vaccine stockpile, and laboratory and disease surveillance for influenza viruses with human pandemic potential.

Gaps remain, however, as many countries still lack basic capacities for laboratory and disease surveillance, shipping of influenza viruses, and the regulation and deployment of influenza vaccines during a pandemic. Sharing of PIP biological materials is critical for health security and must continue. As provided for in the PIP Framework, any non-GISRS recipient of PIP biological materials must assess what benefits it can contribute based on its nature and capacity and enter into a binding contract, or Standard Material Transfer Agreement 2 (SMTA 2), with WHO. However, work on the SMTA 2s is at an early stage.

### Benefit sharing

The PIP Framework aims to ensure that benefits arising from the sharing of PIP biological materials are made more accessible and available to countries based on public health risk and need. In this regard, WHO has initiated discussions with four large influenza vaccine manufacturers to commence the process to sign the first SMTA 2s; the transition to sharing of PIP biological materials with non-GISRS entities that have concluded a SMTA 2 needs to happen as quickly as possible.

The Framework provides for influenza vaccine, diagnostic and pharmaceutical manufacturers that use the WHO GISRS to make an annual contribution to WHO. Pursuant to Section 6.14.3 of the Framework, these payments, termed the “Partnership Contribution”, are to commence in 2012 in the amount of approximately US\$ 28 million. The Advisory Group recommended to the Director-General that 70% be used for pandemic preparedness and 30% for pandemic response. Of the approximately US\$ 20 million per year for pandemic preparedness activities, the Advisory Group recommended that 70% be used to build and/or strengthen surveillance and laboratory capacity; 10% to conduct disease burden studies; 10% to strengthen regulatory capacity and thereby improve access and effective deployment of pandemic vaccines and antiviral medicines; and 10% to strengthen risk communications. The Advisory Group proposed a general approach, including factors to consider, for selecting countries to receive Partnership Contribution resources in each of these areas and requested that the PIP Secretariat develop a method by which factors will be applied in the selection of countries.

## **Governance**

The Director-General appointed 18 members of the PIP Advisory Group in 2011 upon receipt of nominations from Regional Directors. In accordance with the PIP Framework, there are three members from each of WHO's six regions, representing developed and developing countries, affected countries, and a skill mix of policy-makers, public health experts and influenza experts. The Advisory Group, over the course of its first three meetings, has made recommendations to the Director-General on several key elements of the PIP Framework including: the Partnership Contribution, the urgency to commence SMTA 2 negotiations, and an interim approach for the sharing of PIP biological materials with entities outside GISRS pending the conclusion of SMTA 2s. The Advisory Group anticipates that, as operationalization of the Framework advances, subsequent Annual Reports will focus more on these key elements.

## 1. INTRODUCTION

The PIP Framework became effective on 24 May 2011 when it was adopted by the Sixty-fourth World Health Assembly. It provides a global framework for the sharing of influenza viruses with human pandemic potential and the sharing of benefits arising from such sharing. Implementation of this Framework is integral to increasing global pandemic influenza preparedness and improving response measures for the next pandemic.

As one of the three components of the Framework's oversight mechanism, the Advisory Group monitors the implementation of the Framework and provides evidence-based reporting, assessment and recommendations regarding its functioning.<sup>1</sup> Section 7.2.5 of the PIP Framework requires the Advisory Group to present an Annual Report to the Director-General on its evaluation of the implementation of the Framework.

This is the first Annual Report of the Advisory Group since adoption of the PIP Framework. It covers the 12 month period beginning in May 2011 up to May 2012. The 2013 Annual Report will cover the period May 2012 to October 2013. Thereafter, Annual Reports will cover a 12-month period commencing 1 October and ending 30 September of the following year. To ensure that the data are up-to-date, there may be a need for an Addendum prior to the Director-General's submittal of the Report to the Executive Board in January.

In developing the Report, the Advisory Group was mindful that the Framework specifies the Annual Report should cover 7 areas:<sup>2</sup>

- (1) necessary technical capacities of the WHO Global Influenza Surveillance and Response System (GISRS);
- (2) operational functioning of WHO GISRS;
- (3) WHO GISRS influenza pandemic preparedness priorities, guidelines and best practices (e.g. vaccine stockpiles, capacity building);
- (4) increasing and enhancing surveillance for H5N1 and other influenza viruses with human pandemic potential;
- (5) the Influenza Virus Traceability Mechanism (IVTM);
- (6) the sharing of influenza viruses and access to vaccines and other benefits;
- (7) use of financial and non-financial contributions.

Appendix 1 details where information about these areas can be found in the report.

It is important to note that certain key elements of the Framework, e.g. conclusion of Standard Material Transfer Agreement 2s (SMTA 2s) and receipt and use of Partnership Contribution resources, are at an early stage; therefore, few data for these areas are available at this time. The Advisory Group anticipates that, as operationalization of the Framework advances, subsequent Annual Reports will focus more on these key elements.

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<sup>1</sup> See PIP Framework Section 7.2 and Annex 3.

<sup>2</sup> See PIP Framework Section 7.2.5 and Annex 3, Section 2.6.

This initial Annual Report serves as a “baseline” as it provides essential context about GISRS and its key roles and responsibilities. The Report highlights activities during the 12-month period that have improved and strengthened GISRS in accordance with the Framework’s objective and scope. In this regard, it must be remembered that the Framework applies to influenza A(H5N1) and other influenza viruses with human pandemic potential. It does not apply to seasonal influenza viruses or other non-influenza pathogens.<sup>1</sup>

## **Organization and method**

The Report is organized into three substantive sections: virus sharing, benefit sharing and governance with supporting appendices. A supplementary annex will be available on the WHO web site that details PIP Framework-related tasks/activities.

The content of the Report is based on existing data in WHO reports or databases; specific data collections or surveys were not undertaken. Country-specific data and analyses were aggregated for inclusion in the Report.

Information and data for the Report were provided by several clusters at WHO headquarters, WHO regional offices and WHO GISRS laboratories, notably Collaborating Centres. Some information was self-reported by Member States.

## **2. VIRUS SHARING**

### **2.1 Necessary technical capacities of GISRS**

This section of the Annual Report focuses on the structure and function of GISRS and its necessary technical capacities. This descriptive information provides essential context for the subsequent assessment of the operational functioning of GISRS.

The core of WHO GISRS is an international network of influenza laboratories under the coordination of WHO.<sup>2</sup> The WHO GISRS laboratories work collectively to: (a) monitor the evolution of influenza viruses and provide risk assessment and recommendations in areas including laboratory diagnostics, vaccines and antivirals; and (b) serve as a global alert mechanism for the emergence of influenza viruses with pandemic potential.<sup>3</sup>

GISRS is comprised of four complementary categories of laboratories as detailed below. The network regularly expands to include new laboratories, or categories of laboratories, as needed.

- 138 National Influenza Centres (NICs) in 108 countries<sup>4</sup>
- 6 WHO Collaborating Centres (WHO CCs)

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<sup>1</sup> See PIP Framework Section 3.

<sup>2</sup> The laboratory network was formerly known as the Global Influenza Surveillance Network (GISN). The new name of the system came into effect following the adoption of the PIP Framework on 24 May 2011.

<sup>3</sup> See [http://www.who.int/influenza/gisrs\\_laboratory/en/](http://www.who.int/influenza/gisrs_laboratory/en/).

<sup>4</sup> The number of NICs up to 1 May 2012 was 138; from 1 May to 5 October 2012, two additional NICs were recognized: one in Bahrain and one in Mauritius bringing the total to 140 NICs in 110 countries.

- 4 WHO Essential Regulatory Laboratories (WHO ERLs)
- 12 WHO H5 Reference Laboratories (WHO H5 Ref Labs)

Appendix 2 describes the functions and technical capacities for each category of laboratory.

The GISRS is a voluntary network in which member laboratories agree to work under category-specific Terms of Reference (TORs), for their work with influenza viruses with human pandemic potential.<sup>1</sup> The TORs specify that laboratories must comply with the standard conditions under which PIP biological materials<sup>2</sup> may be transferred both within and out of GISRS pursuant to SMTAs;<sup>3</sup> the use of the IVTM, i.e. an electronic, internet-based system to record the movements of PIP biological materials; and other terms and conditions that address, inter alia, laboratory analyses, biosafety and biosecurity, intellectual property rights, research and publications. The TORs for work with seasonal influenza viruses are not a part of the PIP Framework.

## 2.2 Operational functioning of GISRS

This section of the Annual Report assesses how GISRS operates in practice to carry out some of its key roles, responsibilities and functions as specified under the Framework's TORs. Whenever possible, findings are limited to influenza viruses with human pandemic potential. However, since the majority of influenza viruses reported to GISRS are seasonal viruses, it is not possible in all instances to report data restricted to influenza viruses with human pandemic potential.

### Laboratory capacity

Under their PIP Framework's TORs, NICs collect specimens from suspected cases of H5N1 or other unusual influenza viral infections, perform laboratory diagnosis, and ship specimens or virus isolates to a WHO CC or WHO H5 Ref lab for advanced virological analysis.

During May 2011–May 2012, WHO CCs performed detailed analyses to characterize a total of 205 isolates of influenza A(H5N1) from 7 different countries.

The Advisory Group notes that analysis of H5N1 or other influenza viruses with human pandemic potential represents only a small portion of the more than 1.1 million total specimens that GISRS laboratories processed during this period of time. Diagnosing influenza requires special reagents that are updated regularly. During the report period, NICs and other influenza laboratories in 130 different countries, areas or territories had access to, without charge, reagents developed by the Atlanta WHO CC to test for seasonal and other influenza viruses, including those with human pandemic potential.

Efficient and timely transport of specimens or virus isolates may be hampered by logistical challenges in some countries that can delay diagnosis, virus characterization and risk assessment. In addition, countries do not always have financial resources necessary to ship virus samples from NICs or other

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<sup>1</sup> Annex 4 of the PIP Framework establishes Guiding Principles for the development of TORs for WHO GISRS laboratories that are applicable to H5N1 and other human pandemic influenza viruses. Annex 5 details the TORs for each category of laboratory in GISRS.

<sup>2</sup> See PIP Framework Section 4.1 for a definition of PIP biological materials.

<sup>3</sup> The PIP Framework contains two types of SMTAs which are binding contracts. SMTA 1 establishes the conditions which apply to transfer of PIP biological materials among members of GISRS. SMTA 2 establishes the conditions which apply to transfer of PIP biological materials from a GISRS laboratory to an entity outside GISRS.

national laboratories to WHO CCs and other reference laboratories for advanced analysis and characterization. During the reporting period, the WHO Shipping Fund Project was used to ship viruses from 78 laboratories in 69 countries at a cost of US\$ 210,605. Despite the Project's significance in facilitating virus sharing in a timely manner, due to reduced donor funding, the Project can now support only half the number of shipments compared to prior years.

Transport of infectious substances requires qualified local staff that undergo formal training and certification in the proper handling and packaging of infectious substances for international shipment; WHO headquarters and regional offices work collaboratively to support such training. Training is done on an ongoing basis as certificates are valid for only 24 months. From May 2011 to May 2012, 53 laboratory staff from 46 countries were trained and certified (14 from the Eastern Mediterranean Region, 29 from the European Region and 10 from the South-East Asia Region).

### Assessment of laboratory capacity

Few data were available to assess laboratory capacity specifically for H5N1 and other influenza viruses with human pandemic potential. However, data were available to assess two aspects of overall laboratory-related capacity:

- quality of laboratory testing performance
- good laboratory practice.

NICs use the polymerase chain reaction (PCR) as the principal method for diagnosis and surveillance of seasonal influenza viruses and viruses with human pandemic potential. WHO, working with the H5 Reference Laboratory and NIC in China, Hong Kong Special Administration Region, initiated an external quality assessment project (EQAP) in 2007 to monitor the quality and comparability of the performance of PCR testing among participating laboratories. Participation in the project is voluntary. Of 159 NICs and other laboratories that participated in the June–July 2011 EQAP, 124 (78%) returned correct results for all 12 samples which included a mix of seasonal and A(H5N1) viruses. The majority of laboratories correctly identified 9 or more of the 12 samples (Table 1);<sup>1</sup> 89% of laboratories reported correct results for all samples containing influenza A(H5N1).

**Table 1. Performance of participating laboratories in external quality assessment, June–July 2011**

Number of correct results (N=12 samples tested)	Number of laboratories (N=159 participating laboratories)
12 (100%) samples correct	124 (78%)
11 (92%) samples correct	12 (8%)
10 (83%) samples correct	11 (7%)
9 (75%) samples correct	4 (3%)
<9 (<75%) samples correct	8 (5%)

<sup>1</sup> Detection of influenza virus subtype A by polymerase chain reaction: WHO external quality assessment project summary analysis, 2011. *Weekly Epidemiological Record* 2012;87:29–36. Available at: <http://www.who.int/wer/2012/wer8703/en/index.html>.

A good laboratory practice (GLP) survey was undertaken in 2012 among laboratories enrolled in the WHO EQAP. The survey consisted of 38 questions that examined organization and personnel; facility design, specimen handling, equipment and consumables; pre-examination procedures; examination procedures; post-examination procedures and result reporting; quality assurance; and safety. When compared to the GLP survey of 2010, improvements were seen in a number of areas (Table 2).

**Table 2. Results of good laboratory practice surveys, 2010 and 2012**

Survey item	2010 results (% of 142 laboratories)	2012 results (% of 148 laboratories)
Training for new staff	92%	97%
On-job training	63%	70%
Validation of reagents for molecular diagnosis	67%	61%
Evaluation of test and primers/probes for molecular diagnosis	59%	78%
Conduct internal audits	54%	62%
Unidirectional workflow for molecular diagnosis	45%	86%
Regular equipment maintenance	87%	100%
Standard operating procedures (SOPs) for molecular diagnosis	94%	97%
Staff safety guidelines	92%	97%
Staff health programme	78%	85%

### 2.3 WHO GISRS influenza pandemic preparedness priorities, guidelines and best practices (e.g. vaccine stockpiles, capacity building)

This section of the Annual Report provides information about other pandemic preparedness activities that GISRS conducted during the reporting period. Pandemic preparedness activities led by groups other than GISRS are also described.

#### GISRS: laboratory pandemic preparedness

Influenza vaccines are the most effective measure to mitigate the potential impact of an influenza pandemic as most people will be susceptible to infection with the newly emerged virus. The development of candidate vaccine viruses and associated reference reagents is an important part of pandemic preparedness. During May 2011–May 2012, GISRS developed and made available the following candidate vaccine viruses and reference reagents for pandemic preparedness:<sup>1</sup>

- A(H5N1): 4 new candidate vaccine viruses and 3 new reference reagents
- A(H9N2): 1 new candidate vaccine virus

<sup>1</sup> During May 2011–May 2012, there were 8 summaries published on the status of development and the availability of candidate vaccine viruses and potency testing reagents for A(H5N1) (available at: [http://www.who.int/influenza/vaccines/virus/candidates\\_reagents/a\\_h5n1/en/index.html](http://www.who.int/influenza/vaccines/virus/candidates_reagents/a_h5n1/en/index.html)); 2 for A(H9N2) (available at: [http://www.who.int/influenza/vaccines/virus/candidates\\_reagents/a\\_h9n2/en/index.html](http://www.who.int/influenza/vaccines/virus/candidates_reagents/a_h9n2/en/index.html)); and 2 for A(H3N2)v (available at: [http://www.who.int/influenza/vaccines/virus/candidates\\_reagents/variant\\_a\\_h3n2/en/index.html](http://www.who.int/influenza/vaccines/virus/candidates_reagents/variant_a_h3n2/en/index.html)).

- A(H3N2)v: 3 new candidate vaccine viruses.

Summary reviews of the antigenic and genetic characteristics of A(H5N1) and A(H9N2) and the current status of the development of new candidate vaccine viruses for potential use for human vaccine development are available following the vaccine composition meetings for northern and southern hemispheres in February and September of each year.<sup>1</sup>

GISRS regularly works to develop or update existing laboratory guidelines and best practices. These activities are often applicable to both seasonal influenza viruses and viruses with human pandemic potential. A brief synopsis of relevant activities during May 2011–May 2012 follows.

- **Improving influenza vaccine virus selection:** To explore ways to improve the influenza vaccine virus selection process for both seasonal influenza viruses and viruses with human pandemic potential, WHO held an informal consultation in December 2011. Participants included WHO CCs and ERLs, NICs, national regulatory authorities, research, academic and veterinary laboratories, institutions and organizations, and human influenza vaccine manufacturers. The major areas of focus were the extent, timeliness and quality of virological and epidemiological surveillance data; the development and application of new assays and new modeling approaches; the relationship between virus characteristics and vaccine efficacy; and regulatory considerations.
- **Standardization of terminology for the variant A(H3N2) virus recently infecting humans:** Since July 2011, increasing numbers of human cases of infection with a variant influenza A(H3N2) virus have been detected in the United States of America (USA). No reports have been received from other Member States. This virus has different virological characteristics from current circulating seasonal influenza viruses in humans. In order to improve communications and avoid confusion, the Food and Agriculture Organization of the United Nations (FAO), the World Organisation for Animal Health (OIE) and WHO established a working group of experts to standardize the terminology for variant influenza viruses. The joint recommendation was A(H3N2)v, where “v” stands for “variant”.
- **Updated unified nomenclature system for the highly pathogenic H5N1 avian influenza viruses:** In October 2011 the WHO/OIE/FAO H5N1 Evolution Working Group published an updated unified nomenclature system for highly pathogenic avian influenza A(H5N1) viruses. A unified system facilitates the interpretation of sequence/surveillance data from different laboratories. Since the previous update in 2009, H5N1 viruses have continued to evolve and diversify as they spread and infect animals and humans. The 2011 recommendations were based on detailed analyses and comparisons for nearly 3000 H5N1 virus gene sequences.<sup>2</sup>
- **Recommendations on laboratory methods for antiviral susceptibility surveillance:** Over the last ten years antiviral drugs have become an important intervention for the treatment and prophylaxis of influenza virus infection. In countries where antiviral drugs are licensed, national guidance on their use in clinical management is developed and updated. Use and stockpiling of antiviral drugs is a key component of the pandemic preparedness plans of many countries. For these reasons, monitoring of antiviral susceptibility of influenza viruses through laboratory surveillance is an increasingly important need. An Expert Working Group

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<sup>1</sup> See [http://www.who.int/influenza/vaccines/virus/characteristics\\_virus\\_vaccines/en/index.html](http://www.who.int/influenza/vaccines/virus/characteristics_virus_vaccines/en/index.html).

<sup>2</sup> See [http://www.who.int/influenza/gisrs\\_laboratory/h5n1\\_nomenclature/en/index.html](http://www.who.int/influenza/gisrs_laboratory/h5n1_nomenclature/en/index.html).

on Antiviral Susceptibility for WHO GISRS, therefore, was established to develop practical guidance for NICs setting up surveillance of antiviral susceptibility; to provide recommendations on the appropriate antiviral surveillance strategy; and to develop guidance on interpretation of laboratory antiviral susceptibility surveillance data. At their first meeting in November 2011, the expert Working Group reviewed and developed practical guidance for NICs on current laboratory methodologies for testing the antiviral susceptibility of influenza viruses to current antivirals.

- **Protocols for A(H5N1) testing:** The continuous evolution of A(H5N1) genetic clades makes it critical to regularly review, update and validate H5 primers and protocols. The WHO PCR working group meets annually to make recommendations for the GISRS network on the use of PCR in the surveillance and diagnosis of influenza.<sup>1</sup> Currently, the most commonly used protocol in the network is the H5 assays provided by the WHO CC in Atlanta, USA; 18 countries use protocols provided by other WHO CCs and reference laboratories.
- **Updated seasonal influenza TORs for NICs:** The NIC TORs are in the process of being updated for seasonal influenza viruses.

### Regulatory capacity

During the reporting period WHO organized 20 country-level training programmes and workshops for national regulatory authorities and held a global training on lot release procedures for national control laboratory staff new to influenza vaccine manufacturing.

Representatives from 34 countries attended the WHO cosponsored *Workshop on International Regulatory Capacity Enhancement for Influenza Vaccines, 8–10 June 2011, São Paulo, Brazil* and proposed a number of priorities and next steps for enhancing regulatory capacity for influenza vaccines including support to:<sup>2</sup>

- designate a percentage of grants provided to countries for developing vaccine manufacturing capacity be set aside for national regulatory authority (NRA) capacity building;
- strengthen regional regulatory partnerships, approaches and networks, particularly models that address the regulatory needs of developing countries;
- enhance post-marketing surveillance and monitoring of adverse events following immunization in countries with and without influenza vaccine manufacturing capacity;
- strengthen the evaluation of clinical trial data for regulatory registration;
- support WHO regulatory capacity building initiatives and recommendations including the NRA Strengthening Programme, the Vaccine Prequalification Programme, the NRA Strategic Forum of Regulatory Agencies for Vaccines, the Global Learning Opportunities for Vaccine Quality, and the Global Action Plan for Influenza Vaccines.

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<sup>1</sup> The report of the 4th meeting of the WHO working group on polymerase chain reaction protocols for detecting subtype influenza A viruses is available at: [http://www.who.int/influenza/gisrs\\_laboratory/pcr\\_4thworking\\_group\\_meeting\\_report/en/index.html](http://www.who.int/influenza/gisrs_laboratory/pcr_4thworking_group_meeting_report/en/index.html).

<sup>2</sup> Workshop report available at: [http://www.who.int/immunization\\_standards/national\\_regulatory\\_authorities/wirceiv\\_report\\_18jan2012.pdf](http://www.who.int/immunization_standards/national_regulatory_authorities/wirceiv_report_18jan2012.pdf).

These and other proposals from the *Workshop* helped to inform the *Second WHO Consultation on the Global Action Plan for Influenza Vaccines (GAP), 12–14 July 2011 Geneva*. The consultation report noted that “strengthening of national and other regulatory agencies to promote the timely and efficient assessment and approval of locally manufactured or imported influenza vaccines will require a long-term strategy and strong political commitment”.<sup>1</sup>

### **Vaccine deployment capacity**

WHO finalized in 2012 its *Guidance on Development and Implementation of a National Deployment and Vaccination Plan for Pandemic Influenza Vaccines*.<sup>2</sup> It is designed for public and private sector officials at all levels with responsibility for planning and managing deployment and vaccination operations. The initial draft was completed and field-tested shortly before the start of the 2009 (H1N1) pandemic. Countries used the Guidance to develop their pandemic national deployment and vaccination plans (NDVPs). It was revised in 2010–2011, incorporating experience and lessons learned from the pandemic at global, regional and country levels, as well as key recommendations from global and regional workshops on NDVP implementation.

The guidance and accompanying planning tools can assist countries to develop, assess and update their NDVPs. The guidance covers all the processes and structures that need to be functional for vaccine deployment, and operations before and during a pandemic. A sample template for drafting an NDVP is included. In addition, a checklist to assist in the assessment of NDVPs has been developed and included in a supplementary document.

### **H5N1 vaccine stockpile**

An international stockpile of 150 million doses of H5N1 vaccine was established in 2008 through pledges from two manufacturers. In response to the 2009 H1N1 pandemic, these two manufacturers agreed to convert their H5N1 pledges into H1N1 pandemic vaccine. They also increased their pledges to a total of 160 million doses. Of the 78 million doses of pandemic H1N1 vaccine that WHO deployed to low- and middle-income countries, 40 million doses came from the H5N1 vaccine stockpile. This reduced the remaining number of pledged pandemic vaccine doses to 120 million. Manufacturers subsequently agreed to reconvert the 120 million doses of pledged pandemic vaccine back to H5N1 vaccine, or other pandemic influenza vaccine, if needed.

The Strategic Advisory Group of Experts (SAGE) Working Group on Influenza Vaccines and Immunizations was tasked in February 2011 to reconsider options for the nature, deployment and storage of the 120 million doses of pledged pandemic H5N1 vaccine. The Working Group proposed three options and considered that a virtual stockpile with a small physical stockpile of filled doses of H5N1 vaccine for outbreak control may provide flexibility, minimum costs and simplify the logistics of storage. Discussions are ongoing to explore other options and technical aspects of implementing the various options for the final recommendations to SAGE.

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<sup>1</sup> GAP consultation report available at: [http://whqlibdoc.who.int/publications/2012/9789241564410\\_eng.pdf](http://whqlibdoc.who.int/publications/2012/9789241564410_eng.pdf).

<sup>2</sup> Guidance available at: [http://www.who.int/influenza\\_vaccines\\_plan/resources/deployment/en/](http://www.who.int/influenza_vaccines_plan/resources/deployment/en/).

## **Revision of pandemic preparedness guidelines**

The revision of the pandemic preparedness and response guidance has commenced, with various background documents being produced. WHO is developing a multisectoral, all-hazards, generic approach to preparedness, which is expected to form the basis for the influenza guidance document. A discussion paper on revision of the pandemic phases has been circulated for engagement with internal and external stakeholders.

In addition, the WHO European Regional Office (EURO) has gathered experiences of the pandemic to contribute to the drafting of a EURO-ECDC (European Centre for Disease Control and Prevention) planning guide. These and lessons from other WHO regions and Member States worldwide will be incorporated into the revised global guidance. It is intended that the new guidance will be largely completed over a one-year period.

## **2.4 Increasing and enhancing surveillance for H5N1 and other influenza viruses with human pandemic potential**

Maintaining and improving the GISRS network for surveillance of seasonal influenza is critical for response capacity during a pandemic. This section of the Annual Report provides information about activities undertaken during May 2011–May 2012 to enhance both laboratory and disease surveillance for H5N1 and other influenza viruses with human pandemic potential.

### **Laboratory surveillance**

Strengthening GISRS, through efforts to build capacity at country level, is integral to robust pandemic preparedness and response. Efforts are ongoing to increase the number of NICs. During May 2011–May 2012, 2 new NICs were recognized: one in Doha, Qatar in March 2012 and one in Amman, Jordan in April 2012. However, gaps in the network remain as many countries, particularly in the African Region, do not have a NIC. Oftentimes, lack of a NIC correlates with lack of overall capacity for surveillance and response to influenza. The network regularly expands to include new laboratories or categories of laboratories, as needed. For instance, a new category of Collaborating Centres working at the human-animal interface is under development.

The Guiding Principles that underpin the TORs for GISRS laboratories call for sharing of experience and provision of capacity strengthening to Member States; WHO CCs in particular provide training and laboratory support to NICs, especially in developing countries, on laboratory techniques and skills. During May 2011–May 2012, more than 50 training courses and onsite capacity building activities were organized and/or supported by WHO regions, WHO CCs and ERLs for countries in all six WHO regions. Training included laboratory management; strengthening capacity for detection, diagnosis, and monitoring; serology; data management and basic epidemiological analysis; bioinformatics on molecular evolution; sequencing; antiviral susceptibility testing; and licensing for transport of infectious substances.

### **Disease surveillance**

During the reporting period a total of 51 confirmed human cases of H5N1 were reported to WHO from six countries.<sup>1</sup>

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<sup>1</sup> See [http://www.who.int/influenza/human\\_animal\\_interface/H5N1\\_cumulative\\_table\\_archives/en/](http://www.who.int/influenza/human_animal_interface/H5N1_cumulative_table_archives/en/) for the number of confirmed human cases for avian influenza A(H5N1) reported to WHO.

Surveillance for human infections with influenza A(H5N1) and emerging viruses with human pandemic potential requires systematic, good quality routine surveillance for influenza-related disease. The 2009 pandemic revealed multiple gaps in global influenza surveillance capacity. To address these gaps, WHO embarked on a multistep process to revise global influenza surveillance guidelines; this process formally commenced with the *Global Consultation on Influenza Surveillance Standards* held in Geneva in March 2011. An interim document, *WHO Interim Global Epidemiological Surveillance Standards for Influenza (July 2012)*, has been posted for review.<sup>1</sup>

## 2.5 Sharing of influenza viruses with pandemic potential

### Influenza Virus Traceability Mechanism (IVTM)

In November 2007, the Intergovernmental Meeting on Pandemic Influenza Preparedness: Sharing of influenza viruses and access to vaccines and other benefits requested that WHO develop a system to track all influenza viruses with human pandemic potential contributed by Member States to the WHO GISRS. In response to this request, an Interim Virus Tracking System (IVTS) was implemented in January 2008. The IVTS was replaced by the IVTM which was initially launched in December 2010; its use became obligatory upon adoption of the PIP Framework on 24 May 2011.<sup>2</sup>

The IVTM is an electronic, internet-based system for tracking the transfer and movement of PIP biological materials into, within and out of the WHO GISRS. It documents the sharing of influenza viruses with pandemic potential in a transparent manner; users can trace the geographic transfer of such influenza viruses and view the Derivation Tree for the same.

Review of IVTM records indicates that during May 2011 to May 2012 a total of 120 shipments of PIP biological materials were sent and recorded in the IVTM; 72 (60%) of these 120 shipments were sent to 38 non-GISRS laboratories.<sup>3</sup> During this same period, a total of 82 human or animal viruses with pandemic potential (i.e. A(H5N1), A(H3N2)v, and A(H9N2) viruses) were recorded in the IVTM by eight different countries.

The IVTM, while an important tool for recording virus sharing, is a relatively new tool for both GISRS users and public users, alike. WHO has developed and pilot-tested training modules to familiarize users with the IVTM: one is for public users to assist them in “how to” search the IVTM database; a second training module assists registered GISRS laboratory users in “how to” use the IVTM system to record receipt and transfers of PIP biological materials. Future plans include increasing awareness among registered users and WHO Regional and IHR National Focal Points about reporting to IVTM; and providing hands-on support to complement the “how to” tutorial series to enhance the timely sharing of PIP biological materials via the IVTM. Improvements in the information technology (IT) platform are also planned; they will take into account feedback and lessons learned from registered and public users.

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<sup>1</sup> WHO Interim Global Epidemiological Surveillance Standards for Influenza (July 2012) is available at: <http://www.who.int/influenza/resources/documents/INFSURVMANUAL.pdf>.

<sup>2</sup> Information in the IVTM is available at: <http://www.who.int/influenza/pip/ivtm/en/>.

<sup>3</sup> Some shipments included more than one PIP biological material.

## Public-access databases

During the reporting period, genetic sequence data for 46 influenza A(H5N1) isolates from five different countries and five A(H3N2)v isolates from a single country were shared through public-access databases. No genetic sequence data for H7 or H9 influenza viruses were deposited in a public-access database during this period.

## Interim process for sharing PIP biological materials

Since adoption of the PIP Framework in May 2011, GISRS laboratories have received requests for PIP biological materials from entities outside GISRS. Direct application of Article 4.3 of SMTA 1 would have resulted in complete cessation of sharing PIP biological materials until WHO and recipients concluded SMTA 2 agreements. In view of this, WHO shared with the Advisory Group during its February 2012 meeting an interim approach for transferring PIP biological materials that had been developed and implemented. The Advisory Group, noted that sharing of PIP biological materials is critical for health security and must continue. However, for the sake of benefit sharing, the incentive to conclude SMTA 2s cannot be lost. The Advisory Group recommended:

- the Secretariat should elaborate a practical, balanced and uniform approach for the transitional period to obtain recognition from recipients of PIP biological materials outside GISRS that they will enter into discussions with WHO on a SMTA 2;
- if a SMTA 2 is not concluded with the recipient within six months after the beginning of negotiations, no further PIP biological materials will be transferred to that recipient.<sup>1</sup>

The Director-General acknowledged the advice provided by the Advisory Group in the matter of the “Interim Approach” and communicated to the Advisory Group in May 2012 her proposed way forward to address their concerns as follows:

- The Director-General recognizes the urgency to efficiently conclude SMTA 2s with non-GISRS recipients of PIP biological materials (PIBPM).
- As such, the recommendation to define a time limit to complete individual negotiations on SMTA 2s is reasonable.
- The Interim Approach, however, needs to take into consideration the reality that there are still significantly different levels of understanding of the PIP Framework among recipients of PIBPM that are outside GISRS.
- The Director-General therefore believes that an interim, stepwise approach, consistent with the Advisory Group’s advice, will best enable WHO to conclude SMTA 2s and thereby achieve the public health objectives of the PIP Framework.
- To this end, the Director-General proposes the following Interim Approach:
  - Step 1 – Discussions: An informal period of time to allow WHO and individual non-GISRS recipients of PIBPM to exchange information with each other and gain knowledge about the PIP Framework, as appropriate;

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<sup>1</sup> See: [http://apps.who.int/gb/ebwha/pdf\\_files/WHA65/A65\\_19-en.pdf](http://apps.who.int/gb/ebwha/pdf_files/WHA65/A65_19-en.pdf).

- Step 2 – Negotiations: The formal period of negotiations that will start with the exchange of negotiating documents. The Secretariat will send the party a “Notice of Commencement of SMTA 2 Negotiations” to record the date of commencement and the anticipated date of conclusion which should be no longer than 6 months. The Secretariat will regularly update the Advisory Group on the progress in negotiations.
- If an SMTA 2 is not concluded within six months after the beginning of negotiations the recipient should expect no further transfers of PIPBM. The Director-General will bring the matter to the attention of the PIP Advisory Group and request advice on when and under what conditions transfers of PIPBM might resume for that recipient.
- This Interim Approach may be reviewed as necessary to take into account the experience arising from its application, notably the need for time-bound discussions under Step 1.

An Information Note with this Interim Approach was dispatched to all GISRS laboratories for their information and action on 23 May 2012.

## **2.6 Virus sharing: summary and recommendations**

The work of WHO GISRS laboratories underpins global influenza surveillance, prevention, preparedness and response. The Advisory Group has noted multiple examples of the collaborative work of WHO and Member States to strengthen laboratory and disease surveillance capacity for detection and risk assessment of influenza viruses with human pandemic potential. The continued sharing of viruses enables the development of candidate vaccine viruses with pandemic potential and reference reagents – critically important tools when a pandemic virus emerges. The IVTM has increased the transparency of GISRS activities and increased the transparency of the sharing of viruses with human pandemic potential. The Advisory Group has additionally noted other areas of work that contribute to pandemic preparedness, including efforts to strengthen regulatory capacity, vaccine deployment capacity, an H5N1 vaccine stockpile, and laboratory and disease surveillance for influenza viruses with human pandemic potential.

Many gaps remain, however. The Advisory Group is aware that many countries still lack basic capacities for laboratory and disease surveillance, shipping of influenza viruses, and the regulation and deployment of influenza vaccines during a pandemic. Sharing of PIP biological materials is critical for health security and must continue. However, the transition to sharing these materials with outside entities that have concluded a SMTA 2 needs to happen as quickly as possible.

### **Recommendations**

- (1) Information supplied for this Report continues to support the Advisory Group’s prior recommendation that Partnership Contribution resources focus initially on pandemic preparedness.<sup>1</sup>

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<sup>1</sup> See Annex 3 of this report for a synopsis of recommendations from the Advisory Group to the Director-General on potential uses of PIP Partnership Contribution resources for pandemic preparedness and response.

(2) The Advisory Group has recommended previously that a self-assessment of GISRS with respect to its role, function and capacities in connection with the Framework be undertaken. The Advisory Group notes that this will be undertaken in 2013 subject to the availability of funds.<sup>1</sup>

(3) The Advisory Group recommends that WHO seek support from Member States and other stakeholders to supplement resources for the WHO Shipping Fund Project and the conduct of training programmes to certify staff in the shipping of infectious substances. The 2009 pandemic demonstrated the key role that shipping of virus samples played in the global response.

### 3. BENEFIT SHARING

The PIP Framework aims to ensure that benefits arising from the sharing of PIP biological materials are made more accessible and available to countries based on public health risk and need. Benefits include vaccines and other pandemic supplies, as well as technical assistance, and transfer of technology, skills and knowledge needed by developing countries to build pandemic influenza preparedness and response capacity.<sup>2</sup> The Framework further provides for influenza vaccine, diagnostic and pharmaceutical manufacturers who use the WHO GISRS to make an annual contribution to WHO. This annual payment, termed the Partnership Contribution, was created to help safeguard the financial sustainability of the PIP benefit sharing system.

This section of the Annual Report reviews how sharing of various benefits has progressed in the first 12 months of the Framework's implementation.

#### 3.1 Access to vaccines and other benefits

As provided for in Annex 2 of the PIP Framework, any non-GISRS recipient of PIP biological materials must assess what benefits it can contribute based on its nature and capacity and enter into a binding contract, or SMTA 2, with WHO. During May 2011–May 2012, the Director-General initiated discussions with four large influenza vaccine manufacturers to commence the process to sign SMTA 2s. The PIP Secretariat has also provided information on the SMTA 2 and the process to conclude it to over 30 prospective recipients of PIP biological materials.

#### 3.2 Use of financial contributions: the Partnership Contribution

Pursuant to Section 6.14.3 of the Framework, Partnership Contribution payments to WHO are to commence in 2012 in the amount of approximately US\$ 28 million.<sup>3</sup> In anticipation of this, and as provided by the Framework,<sup>4</sup> the Advisory Group first presented a series of recommendations to the Director-General on how the Partnership Contribution should be allocated between pandemic preparedness and pandemic response. In developing these recommendations, the Advisory Group, in accordance with Framework Section 6.14.6, interacted with industry and other stakeholders on 23 February 2012 at which time important information and considerations were provided to the Advisory Group and the Director-General relevant to the Partnership Contribution.

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<sup>1</sup> See: [http://apps.who.int/gb/ebwha/pdf\\_files/WHA65/A65\\_19-en.pdf](http://apps.who.int/gb/ebwha/pdf_files/WHA65/A65_19-en.pdf).

<sup>2</sup> See PIP Framework Section 6 for more information about benefit sharing.

<sup>3</sup> The annual amount of the Partnership Contribution was established by the Member States at 50% of the annual cost to run GISRS. For more information see Framework Section 6.14.3, footnote 1.

<sup>4</sup> See Framework Sections 6.14.5 and 6.14.6 and Section 2.4 of the Advisory Group's Terms of Reference in Annex 3.

These initial recommendations were contained in the Advisory Group's February 2012 meeting report which the Director-General subsequently transmitted to the Sixty-fifth World Health Assembly for its consideration.<sup>1</sup> In May 2012 the Advisory Group transmitted to the Director-General its fully developed recommendations on the potential uses of the Partnership Contribution.<sup>2</sup>

### 3.3 Benefit sharing: summary and recommendations

The Framework places virus sharing on an equal footing with benefit sharing; sharing of viruses and benefits is to be fair, transparent, equitable and efficient. In the year since the PIP Framework was adopted, essential groundwork has been laid to facilitate benefit sharing as envisioned in the Framework. WHO has initiated discussions with influenza vaccine manufacturers to commence the process to sign the first SMTA 2s. The Executive Board at its 131st session on 28–29 May 2012 considered and accepted the Director-General's proposals, based on the Advisory Group's recommendations, on the proportional distribution of the Partnership Contribution between pandemic preparedness and response.<sup>3</sup> The Advisory Group also provided the Director-General with recommendations about potential uses of the Partnership Contribution.

Substantial work remains, nonetheless, to advance this initial work into concrete benefits.

#### Recommendations

- (1) WHO should conclude one or more SMTA 2s as soon as possible.
- (2) With respect to the Partnership Contribution, the Director-General and the Advisory Group should continue to collaborate with industry in further defining the specific amounts to be contributed by each company as well as the mechanism for implementation<sup>4</sup> and interact with industry and other stakeholders on the use of the resources.<sup>5</sup>
- (3) WHO should develop and share with the Advisory Group a method by which factors will be applied in the selection of countries to receive Partnership Contribution funds.

## 4. GOVERNANCE

### 4.1 Appointment and composition of the first PIP Advisory Group

The Director-General appointed 18 members of the PIP Advisory Group in 2011 upon receipt of nominations from Regional Directors. In accordance with Sections 7.2.2 and 7.2.3 and Annex 4 of the PIP Framework, there are three members from each of WHO's six regions, representing developed and developing countries, affected countries, and a skill mix of policy-makers, public health experts and influenza experts. A list of members may be found in Appendix 4 of this Report. At its first meeting, the Advisory Group elected Professor Didier Houssin (France) as Chair and Professor Tjandra Y. Aditama (Indonesia) as Vice-Chair.

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<sup>1</sup> Meeting report available at: [http://apps.who.int/gb/ebwha/pdf\\_files/WHA65/A65\\_19-en.pdf](http://apps.who.int/gb/ebwha/pdf_files/WHA65/A65_19-en.pdf).

<sup>2</sup> See Appendix 3 of this Report for a synopsis of these recommendations.

<sup>3</sup> See Document EB131/DIV/2 available at: [http://apps.who.int/gb/e/e\\_eb131.html](http://apps.who.int/gb/e/e_eb131.html).

<sup>4</sup> See PIP Framework Section 6.14.3.

<sup>5</sup> See PIP Framework Section 6.14.6.

In accordance with the provisions of the PIP Framework, all members will serve for three years. A three-year appointment period was deemed particularly important for the Advisory Group in the early stages of its work as this would allow for continuity of discussions and facilitate implementation of critical and time-sensitive tasks under the PIP Framework.<sup>1</sup> Subsequently, renewal of one third of the members will be initiated every year per the PIP Framework.<sup>2</sup> The Director-General will regularly accept nominations of representatives for the Advisory Group.<sup>3</sup>

## **4.2 Meetings and recommendations of the Advisory Group**

The Advisory Group held two meetings in Geneva (21–22 November 2011<sup>4</sup> and 22–24 February 2012<sup>5</sup>) and one meeting by teleconference (3–4 May 2012). Special attention was paid at the beginning of each meeting to update the declaration of interests of each member of the Advisory Group; all declarations of interest were detailed in the report of each meeting. Following its first two meetings, the Chair of the Advisory Group led Information Sessions in Geneva for the Permanent Missions on 1 December 2011 and 5 March 2012.

The Advisory Group has made recommendations to the Director-General in several key areas as follows.

### **The Partnership Contribution**

The Advisory Group had extensive discussions during its February and May 2012 meetings on the Partnership Contribution. The Advisory Group presented recommendations with supporting documentation to the Director-General on the proportional distribution of the Partnership Contribution between pandemic preparedness and pandemic response and actual uses of the Partnership Contribution. A synopsis of these recommendations can be found in Appendix 3 of this Report.

### **Urgency to commence SMTA 2 negotiations**

The Advisory Group advised that discussions on the SMTA 2 commence no later than the Sixty-fifth World Health Assembly. To aid in the process, they agreed that the Director-General should encourage Member States to provide legal support.

### **Interim approach for the sharing of PIP biological materials with entities outside GISRS pending the conclusion of SMTA 2s**

While understanding the reasons for an interim approach, the Group recommended that if an SMTA 2 is not concluded with the recipient within six months after the beginning of negotiations, no further PIP biological materials will be transferred to the recipient. The Director-General acknowledged the advice provided by the Advisory Group in the matter of the “Interim Approach” and communicated to them in May 2012 her proposed way forward to address this. This Interim Approach is detailed in Section 2.5 of this Report.

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<sup>1</sup> See [http://apps.who.int/gb/ebwha/pdf\\_files/EB130/B130\\_18-en.pdf](http://apps.who.int/gb/ebwha/pdf_files/EB130/B130_18-en.pdf).

<sup>2</sup> PIP Framework Annex 3, section 3.2.

<sup>3</sup> PIP Framework, Annex 3, Section 3.3.

<sup>4</sup> Meeting report available at: [http://apps.who.int/gb/ebwha/pdf\\_files/EB130/B130\\_18-en.pdf](http://apps.who.int/gb/ebwha/pdf_files/EB130/B130_18-en.pdf).

<sup>5</sup> Meeting report available at: [http://apps.who.int/gb/ebwha/pdf\\_files/WHA65/A65\\_19-en.pdf](http://apps.who.int/gb/ebwha/pdf_files/WHA65/A65_19-en.pdf).

### **4.3 Governance: summary and recommendations**

The Advisory Group has a broad range of expertise and experience which has been an asset in addressing its TORs under the PIP Framework. The Advisory Group is aware of the keen interest in the Framework and its operationalization. The Advisory Group has endeavored to keep Member States updated through Information Sessions and reports to the World Health Assembly and Executive Board and to interact with industry and other stakeholders.

#### **Recommendations**

- (1) The Advisory Group expressed a view that any decision on the future mandate of the Advisory Group (per PIP Framework Section 7.2.6) should be deferred until the Group had completed a reasonable amount of work.<sup>1</sup>
- (2) The Advisory Group recommends maintaining the Information Sessions, led by the Chair, for Permanent Missions that follow Advisory Group meetings.

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<sup>1</sup> Meeting report available at: [http://apps.who.int/gb/ebwha/pdf\\_files/EB130/B130\\_18-en.pdf](http://apps.who.int/gb/ebwha/pdf_files/EB130/B130_18-en.pdf).

## APPENDIX 1

## INDEX OF TOPICS COVERED IN THE ANNUAL REPORT

Topic area (PIP Framework Section 7.2.5)	Location in the Annual Report
1. Necessary technical capacities of the WHO Global Influenza Surveillance and Response System (GISRS)	Section 2.1 Appendix 2
2. Operational functioning of WHO GISRS	Section 2.2
3. WHO GISRS influenza pandemic preparedness priorities, guidelines and best practices (e.g. vaccine stockpiles, capacity building)	Section 2.3
4. Increasing and enhancing surveillance for H5N1 and other influenza viruses with human pandemic potential	Section 2.4
5. Influenza Virus Traceability Mechanism (IVTM)	Section 2.5
6. Sharing of influenza viruses and access to vaccines and other benefits	Section 2.3 (H5N1 vaccine stockpile) Section 2.5 Section 3.1
7. Use of financial and non-financial contributions	Section 3.2

## APPENDIX 2

**FUNCTIONS AND TECHNICAL CAPACITIES OF GISRS LABORATORIES****National Influenza Centres**

National Influenza Centres (NICs) typically are the principal resource for influenza-related virological and epidemiological expertise in their country. They serve as the key point of contact between WHO and their country for influenza-related technical issues. NICs analyze specimens obtained from patients and make an initial identification of the influenza virus type and subtype, principally using the polymerase chain reaction (PCR) test. Representative viruses, as well as influenza viruses with potential public health significance, and any available clinical and epidemiological information, are sent to a WHO Collaborating Centre for further virus characterization.

**WHO Collaborating Centres**

WHO Collaborating Centres for Influenza (WHO CCs) are internationally-recognized centres of excellence for influenza that perform critical and highly technical services. WHO CCs employ sophisticated testing methods such as haemagglutination inhibition, microneutralization and also perform viral gene sequencing. These analyses form the basis for WHO recommendations on influenza vaccines (both seasonal vaccines and vaccines for influenza viruses with pandemic potential) and the development and characterization of candidate vaccine viruses. In collaboration with scientists from Cambridge University, antigenic cartography has been used in recent years as an adjunct to standard methods to improve influenza vaccine virus selection.<sup>1</sup> WHO CCs also monitor antiviral susceptibility using genotypic and phenotypic methods; update and produce the standardized reagents which are distributed to NICs and used to identify circulating influenza viruses; provide advice and training on the most up-to-date laboratory methods; and assess the risk of, and respond to, outbreaks of influenza, especially if there is concern about a new virus with pandemic potential.

**WHO Essential Regulatory Laboratories**

WHO Essential Regulatory Laboratories (WHO ERLs) are formally associated with national regulatory agencies. The WHO ERLs, together with WHO CCs, conduct human serology studies to assess if the previous season's vaccine will offer suitable protection against more recent circulating influenza viruses. The WHO ERLs and CCs, in collaboration with vaccine manufacturers, evaluate the growth of candidate vaccine viruses to help manufacturers select the optimal virus for vaccine development and production. The WHO ERLs, with support from vaccine manufacturers, develop, update and calibrate reference agents that are used to test the "potency" of influenza vaccines, including seasonal vaccines and those for pandemic preparedness, before vaccines can be released for marketing or clinical trials.

**WHO H5 Reference Laboratories**

The WHO H5 Reference Laboratory group (WHO H5 Ref Labs) perform diagnostic testing and analyses of A(H5N1) and novel influenza subtypes from humans and animals worldwide. The WHO H5 Ref Labs also contribute to the updating of the candidate vaccine viruses for H5 and H9 influenza viruses and assess the pandemic potential of new influenza viruses, i.e. virological risk assessment.

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<sup>1</sup> Antigenic cartography is a novel computational methodology that is used to analyze and visualize large volumes of laboratory data generated by GISRS laboratories. See <http://www.antigenic-cartography.org/cam/ac.html> for more information.

## APPENDIX 3

**SYNOPSIS OF RECOMMENDATIONS FROM THE ADVISORY GROUP TO THE  
DIRECTOR-GENERAL ON POTENTIAL USES OF PIP PARTNERSHIP  
CONTRIBUTION RESOURCES FOR PANDEMIC PREPAREDNESS  
AND RESPONSE****Guiding principles**

- The Advisory Group recommends that the allocations should:
  - take into account Framework principles including fairness, equity, public health risk and need of all Member States, and the particular vulnerability of countries affected by influenza viruses with pandemic potential, especially H5N1;
  - be evidence-based and consider indicators adapted to the Framework such as the International Health Regulations' (IHR) core capacities, income, health and epidemiology;
  - consider the critical foundation of epidemiological and laboratory surveillance;
  - take into account the modest amount of Partnership Contribution resources.

**Proportional distribution of the Partnership Contribution (see Box)**

- The Advisory Group recommends, in a first phase, to direct a greater proportion of the Partnership Contribution resources to pandemic preparedness activities and a lesser proportion to the reserve for pandemic response.
- The Advisory Group recommends that 70% (or approximately US\$ 20 million per year) of the Partnership Contribution be directed toward pandemic preparedness activities and 30% (or approximately US\$ 8 million per year) be directed toward pandemic response activities. For reasons of flexibility and practicality, 70% and 30% should be considered as approximate targets, e.g. in the range of 65% to 75% and 25% to 35%, respectively. The Director-General should be able to temporarily modify the allocation of Partnership Contribution resources as required to respond to pandemic influenza emergencies. The Director-General would report on any such modification to Member States.
- The Advisory Group recommends that this proportional split be fixed for an initial period of 5 years, i.e. from 2012 through 2016.

**Use of the Partnership Contribution: pandemic preparedness activities (see Box)**

- The Advisory Group recommends starting with activities in support of the three technical areas identified in Section 6.14.4 of the Framework, i.e. strengthening laboratory and surveillance capacity, conducting disease burden studies, and improving access and effective deployment of pandemic vaccines and antiviral medicines, as well as in one additional area that will strengthen effective pandemic response: risk communications.

- The Advisory Group recommends that of the approximately US\$ 20 million per year for pandemic preparedness activities, (1) 70% be used to build and/or strengthen surveillance and laboratory capacity; (2) 10% to conduct disease burden studies; (3) 10% to strengthen regulatory capacity and thereby improve access and effective deployment of pandemic vaccines and antiviral medicines; and (4) 10% to strengthen risk communications.<sup>1</sup> For reasons of feasibility, flexibility and practicality, each of these proportions should be viewed as an approximate target, i.e. +/- 5% for each.

### **Use of the Partnership Contribution: pandemic response**

- The Advisory Group recommends that the approximately US\$ 8 million per year available through the Partnership Contribution for pandemic response be reserved to purchase vaccine and antiviral medicines at the time of a pandemic for countries without access.

### **Implementation of activities**

- The Advisory Group recommends that WHO headquarters work with and through its regional and country offices to seek their assistance in the implementation of activities supported by Partnership Contribution resources.
- The Advisory Group recommends that WHO (headquarters, regional offices, and country offices) also provide technical guidance, as needed, to develop protocols/methodology and implementation plans for each activity, and that the reporting of measurable results be carried out within defined periods of time.
- The Advisory Group recommends that WHO establish and maintain ways to track the distribution and use of Partnership Contribution resources over time.

### **Box. Recommendations of the PIP Framework Advisory Group on the distribution and uses of the Partnership Contribution**

#### **70% directed to pandemic preparedness activities**

- 70% disease and laboratory surveillance capacity
- 10% disease burden studies
- 10% regulatory capacity
- 10% risk communications

#### **30% directed to pandemic response activities**

- reserved for purchase of vaccine and antiviral medicines at the time of a pandemic for countries without access

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<sup>1</sup> The Advisory Group proposed a general approach, including factors to consider, for selecting countries to receive Partnership Contribution resources in each of these areas. The Advisory Group requested that WHO develop a method by which factors will be applied in the selection of countries and share this with the Advisory Group at its meeting in October 2012.

## APPENDIX 4

## ADVISORY GROUP MEMBERS

**Professor Tjandra Y. Aditama**, Director General of Disease Control and Environmental Health, Ministry of Health, Indonesia

**Dr William Kwabena Ampofo**, Senior Research Fellow & Head – Virology, Noguchi Memorial Institute for Medical Research, University of Ghana, Ghana

**Dr Jarbas Barbosa da Silva Jr**, Secretary (Vice Minister) of Health Surveillance, Ministry of Health, Brazil

**Dr Silvia Bino**, Associate Professor of Infectious Diseases, Head, Control of Infectious Diseases Department, Institute of Public Health, Albania

**Professor Rajae El Aouad**, Director, National Institute of Hygiene, Morocco

**Dr Rainer Engelhardt**, Assistant Deputy Minister, Infectious Disease Prevention and Control Branch, Public Health Agency of Canada, Canada

**Mr David E. Hohman**, Former Deputy Director, Office of Global Affairs, Department of Health and Human Services, United States of America

**Professor Didier Houssin**, President, French Evaluation Agency for Research and Higher Education (AERES), France

**Dr Mark Jacobs**, Director of Public Health, Ministry of Health, New Zealand

**Professor Ziad Memish**, Assistant Deputy Minister of Health for Preventive Medicine, Ministry of Health, Saudi Arabia

**Dr Hama Issa Moussa**, National Technical Assistant, Institutional Support Unit, Ministry of Public Health, Niger

**Dr Amr Mohamed Kandeel**, Chief of Preventative Affairs and Endemic Diseases Sector, First Undersecretary, Ministry of Health and Population, Egypt

**Professor Oleg Ivanovich Kiselev**, Director, Research Institute of Influenza, Russian Academy of Medical Sciences, National Influenza Centre, Russian Federation

**Dr Nobuhiko Okabe**, Director General, Kawasaki City Institute for Public Health, Japan

**Dr Adrian J. Puren**, Deputy Director, National Institute for Communicable Diseases, South Africa

**Professor Prasert Thongcharoen**, Professor Emeritus, Department of Microbiology, Faculty of Medicine, Siriraj Hospital, Mahidol University, Thailand

**Dr P.V. Venugopal**, Former Director of International Operations, Medicines for Malaria Venture, Public Health Specialist, India

**Professor Yu Wang**, Director-General, Chinese Center for Disease Control and Prevention, China

## ANNEX 2

**MEETING OF THE PANDEMIC INFLUENZA PREPAREDNESS  
FRAMEWORK ADVISORY GROUP  
3–5 OCTOBER 2012, GENEVA, SWITZERLAND****Report to the Director-General****ORGANIZATION AND PROCESS OF THE MEETING**

1. The fourth meeting of the Advisory Group took place at WHO headquarters in Geneva, 3–5 October 2012, with the following revised provisional agenda:

1. Registration
2. Welcome remarks from the Chair
3. Declarations of Interest
4. Adoption of agenda
5. Review experience of audio teleconference method for AG meetings
6. Feedback to the AG from the last WHA and EB
7. Review and discuss draft Annual Report to DG
8. Update on SMTA 2 negotiations
9. Discussion of PIP BM definition
  - Perspectives from GISRS
10. Partnership Contribution
  - Identification of pool of manufacturers using GISRS
  - Distribution among manufacturers using GISRS
  - Factors to consider in selecting countries
11. Preparations for meetings with industry and stakeholders
12. Collaborate with representatives of industry associations (IFPMA, DCVMN, BIO, ADVAMedDx, etc): *Distribution of Partnership Contribution among manufacturers using GISRS*
13. Interact with industry: *Use of the Partnership Contribution*

14. Interact with other stakeholders: *Use of the Partnership Contribution*
  15. Interact with industry and other stakeholders: *Use of the Partnership Contribution*
  16. GISRS presentations
    - Methodology for GISRS assessment
    - Terms of Reference for GISRS laboratories
  17. Vaccine and antiviral stockpiles presentation
  18. Review and discuss Meeting Report
  19. Approve reports
    - Advisory Group Annual Report
    - Meeting Report
  20. Next steps
    - Next meeting of the Advisory Group
    - Any other business
  21. Close of meeting
2. Of the 18 members of the Advisory Group, 13 were present. The list of meeting participants is found in Appendix 1.
  3. The Chair made a number of introductory remarks.
  4. The WHO Principal Legal Officer reviewed the process for Declarations of Interests. The summary of Declarations of Interest is found in Appendix 2.
  5. The Advisory Group adopted the agenda.

### **Review experience of audio teleconference method for AG meetings**

6. The audio teleconference method for the May 2012 meeting of the Pandemic Influenza Preparedness (PIP) Advisory Group was viewed favourably by the members of the Advisory Group. There were few technical difficulties. Engagement in the discussion was challenging for members who require an interpreter. It was agreed that audio teleconference was best suited for follow-up of topics that had been discussed at a prior face-to-face meeting of the Advisory Group.
7. The Assistant Director-General, Health Security and Environment (HSE) provided a brief update on infections associated with a novel coronavirus. The World Health Organization (WHO) continues to monitor the situation and inform its Member States through the designated National Focal Points under the International Health Regulations (IHR) (2005).

### **Feedback to the AG from the last World Health Assembly and Executive Board**

8. The Executive Board at its 131st session on 28–29 May 2012 considered and accepted the Director-General's proposals, based on the Advisory Group's recommendations, on the proportional distribution of the Partnership Contribution between pandemic preparedness and pandemic response. The Chair reported that Member States expressed support for the Advisory Group's work to date at the Sixty-fifth World Health Assembly in May 2012.

9. The Advisory Group discussed if documents related to their work, i.e. meeting reports and their recommendations to the Director-General on the proportional distribution and use of the Partnership Contribution, could be made available in the public domain. All members of the Advisory Group supported making such documents available to promote transparency. Possible options proposed for disseminating documents included publication on the WHO web site, internal dissemination within WHO including regional offices, the IHR event web site, and Information Sessions for Member States.

### **Draft Annual Report to the Director-General**

10. Members of the Advisory Group reviewed the draft Annual Report and accompanying table with PIP Framework-related tasks/activities. Revisions were proposed to the Report and the table of PIP Framework-related tasks/activities. The Advisory Group proposed to include the table of PIP Framework-related tasks/activities as a supplementary annex. The annex would be referenced in the Report and made available on the WHO web site due to its length and use of colours. It was noted that the Annual Report and the supplementary table should cover the same time period. The Chair clarified that the table of PIP Framework-related tasks/activities is intended as a tool to monitor, but not evaluate, the implementation of the Framework. The Advisory Group requested that the table be updated in advance of each Advisory Group meeting; publication of the table would, however, occur on an annual basis as part of the Advisory Group's Annual Report.

11. The Advisory Group discussed the time period to be covered in subsequent Annual Reports. It was agreed that the 2013 Annual Report will cover the period May 2012 to October 2013. Thereafter, Annual Reports will cover a 12-month period commencing 1 October and ending 30 September of the following year. To ensure that the data are up-to-date, there may be a need for an Addendum prior to the Director-General's submission of the Report to the Executive Board in January.

### **Update on SMTA 2 negotiations**

12. The Assistant Director-General, HSE updated the Advisory Group on the status of Standard Material Transfer Agreement 2 (SMTA 2) negotiations. The Director-General has initiated discussions with four large influenza vaccine manufacturers to commence the process to sign SMTA 2s and expects to contact two other manufacturers in the next few weeks. In addition, the Secretariat has provided information on the SMTA 2 process to 30 other prospective recipients of PIP biological materials. WHO has been unable to obtain any legal support from Member States to assist in negotiations.

13. Advice to the Director-General on SMTA 2

The Advisory Group welcomes the progress to date in the negotiations of SMTA 2s and urges the Director-General to accelerate interaction with the entities concerned and finalize these agreements. In recognition of both the importance of this process, and the need to obtain results rapidly in coming months, the Advisory Group recommends that adequate resources are made available to support WHO's negotiation and establishment of these agreements.

## Discussion of PIP BM definition

14. Section 7.4.1 of the PIP Framework requires that the Director-General shall, on a biennial basis, inform the World Health Assembly, through the Executive Board, on the status of, and progress on, (v) the experience arising from the use of the definition of PIP biological materials in Section 4.1.

15. Advice to the Director-General on the PIP BM definition

Since the adoption of WHA64.5 in May 2011, the Global Influenza Surveillance and Response System (GISRS) has accumulated experience related to the use of the definition of “PIP biological materials”.<sup>1</sup> The experience is primarily based in ongoing influenza surveillance and response activities, and collaborations and direct discussions with representatives of the animal sector related to application of the PIP biological materials definition. Based on these discussions, the Directors of WHO Collaborating Centres (CCs) and Essential Regulatory Laboratories (ERLs) of GISRS informed the Advisory Group during the session of their concerns related to the application of the definition.

The definition covers wild type H5N1 and/or other influenza viruses with human pandemic potential obtained from infected humans as well as any candidate vaccine viruses that had been prepared for the purposes of developing a pandemic or potential pandemic vaccine.

A less strict application of the definition could cover all wild type viruses obtained from infected animals as well as infected humans, and subsequently modified viruses.

It was considered that the less strict application of the definition could reduce the willingness or ability of collaborating laboratories in the animal sector, including the World Organisation for Animal Health (OIE), the Food and Agriculture Organization of the United Nations (FAO), the OIE–FAO Network of Expertise on Animal Influenza (OFFLU), and academic and other laboratories to share such viruses obtained from infected animals. This would be highly undesirable if it dampened current and long-term collaboration between the animal sector and GISRS since increased collaboration is considered critical for strengthening pandemic influenza preparedness. Moreover, the less strict application could also markedly increase the burden of work within GISRS laboratories owing to the need to implement PIP Framework activities, e.g. use of the Influenza Virus Traceability Mechanism (IVTM).

In view of the foregoing, and based on discussion, the PIP Advisory Group expressed its view that a strict application of the definition met the intent of Member States during the PIP Framework negotiations and would have the least potential for dampening important collaborations between

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<sup>1</sup> Section 4.1 of the PIP Framework defines “PIP biological materials” as follows: “‘PIP biological materials’,<sup>1</sup> for the purposes of this Framework (and its annexed Standard Material Transfer Agreements (SMTAs) and terms of reference (TORs)) and the Influenza Virus Tracking Mechanism (IVTM), includes human clinical specimens, virus isolates of wild type human H5N1 and other influenza viruses with human pandemic potential; and modified viruses prepared from H5N1 and/or other influenza viruses with human pandemic potential developed by WHO GISRS laboratories, these being candidate vaccine viruses generated by reverse genetics and/or high growth re-assortment.

Also included in “PIP biological materials” are RNA extracted from wild-type H5N1 and other human influenza viruses with human pandemic potential and cDNA that encompass the entire coding region of one or more viral genes.<sup>a</sup>

<sup>a</sup> OPERATIONAL EXEMPTION: materials shared within the WHO GISRS or with other laboratories specifically for non-commercial public health uses including surveillance activities, diagnostic applications, and quality assurance, are not handled as PIP Biological Materials. Their onward transfer for purposes other than those specified in the terms of reference of National Influenza Centres, WHO Collaborating Centres, Essential Regulatory Laboratories and H5 Reference Laboratories is not allowed under this operational exemption.”

human and animal sector laboratories. However, GISRS was asked to monitor the implementation of this application to determine if critical viruses could fall outside of this approach. The Secretariat was asked to report back to the PIP Advisory Group at its next meeting.

## **Partnership Contribution**

### **Identification of pool of manufacturers using GISRS**

16. Section 6.14.3 of the PIP Framework states that “influenza vaccine, diagnostic and pharmaceutical manufacturers using the WHO GISRS will make an annual partnership contribution to WHO for improving global pandemic influenza preparedness.” Section 4.3 of the Framework defines these manufacturers as “... public or private entities including academic institutions, government owned or government subsidized entities, nonprofit organizations or commercial entities that develop and/or produce human influenza vaccines or other products derived from or using H5N1 or other influenza viruses of human pandemic potential.” Identification of the pool of manufacturers using GISRS is tied to a clear understanding of terms used in the Framework such as “develop”, “produce” and “using GISRS”; the Advisory Group considered proposed definitions developed by the Secretariat. The Advisory Group also considered an approach, proposed by the Secretariat, to identify “manufacturers using GISRS”, i.e. transmittal by the Secretariat of a brief questionnaire through industry associations and directly to known “users” that are not affiliated with associations.

### **Distribution among manufacturers using GISRS**

17. Section 6.14.3 of the PIP Framework states that “The distribution between companies is to be based on transparency and equity, based on their nature and capacities.” The Secretariat reviewed the principles upon which defining a formula to distribute the Partnership Contribution among manufacturers should be based:

- All manufacturers using GISRS should contribute.
- How much each manufacturer contributes should be based on their nature and capacity.
- The formula should be easy to apply and based on verifiable information; applicable across companies; and transparent.
- The formula should be reassessed periodically.

18. The Secretariat summarized its discussions/collaborations with industry associations to date on this matter, including a proposal from the International Federation of Pharmaceutical Manufacturers and Associations (IFPMA).

### **Factors to consider in selecting countries**

19. In response to the Advisory Group’s request at its May 2012 meeting, the Secretariat presented a proposed method by which factors will be applied in the selection of countries to receive Partnership Contribution funds. The proposed method was tailored to the selection of countries to build and/or strengthen laboratory and surveillance capacity; US\$ 14 million of Partnership Contribution funds are to be used for this purpose each year. In brief, the proposed method focused (per the PIP Framework) on developing Member States; IHR core capacity; needs for influenza surveillance; and H5N1 vulnerability. Factors were selected and weighted for each of these four criteria to score and rank Member States according to the level of their needs.

20. In its discussion the Advisory Group noted the importance of developing plans for implementation, monitoring and oversight; the identification of measurable outcomes; the important role of WHO regional and country offices in providing assistance to countries; and a country's ability to sustain the work on a long-term basis without the support of Partnership Contribution funds. The Advisory Group also noted the desirability, while retaining a primary focus on Member States with the highest need, of ensuring the involvement of at least one Member State from each WHO region.

21. Advice to the Director-General on the Partnership Contribution

The Advisory Group considers that the use of GISRS has contributed to the development and registration of vaccines, antivirals and diagnostics. Therefore, it is logical that all such manufacturers contribute to the Partnership Contribution.

(1) Identifying contributors

Recognizing that certain contributors have been identified through representative associations, the Director-General should make reasonable efforts to identify all other potential contributors to the Partnership Contribution through the use of a questionnaire and other available means.

(2) Defining a Partnership Contribution "formula"

In accordance with Section 6.14.3 of the Framework, the Director-General should consider the IFPMA proposal as reference for joint negotiation with industry with a view to presenting (through electronic means) an agreed formula to the Advisory Group for its consideration by 12 November 2012 and its finalization by the Director-General by 16 November 2012.

The formula should explicitly include Partnership Contributions from antiviral manufacturers. This is because the Advisory Group considers that the sales of influenza antivirals by manufacturers benefit directly or indirectly from the use of GISRS, considering its role in monitoring the susceptibility of the circulating virus to antivirals.

Further work should be conducted to explore the possibility of contributions from entities that fall into the Research and Development category.

(3) Receiving Partnership Contributions

The Advisory Group strongly recommends that every effort is made to begin receiving Partnership Contributions in 2012. The process should not be delayed until the complete list of potential contributors is available.

(4) Use of the Partnership Contribution

The Advisory Group recommends that the Director-General develop a plan that is ready for use as soon as the contributions are available. Drafts should be shared with the Advisory Group.

### **Meetings with industry and other stakeholders**

22. The Advisory Group met with representatives of industry associations, manufacturers, and stakeholders on the Partnership Contribution (see Appendix 3 for a list of participants). The following views were expressed, inter alia:

- In view of the Framework's foundational principle of placing virus sharing and benefit sharing on an equal footing, it is critical for Partnership Contributions to commence in 2012.
- Industry expressed its support for the Framework's goals and objectives and its commitment to provide fair and equitable annual Partnership Contributions.
- Industry is prepared to engage in collaborative dialogue with WHO on the Partnership Contribution.
- There is a need to define key terms that are not defined in the Framework and that are relevant to the Partnership Contribution.
- The principles for identifying all contributors should be based on transparency and equity as specified in Section 6.14.3 of the Framework.
- It is important to identify all contributors to the Partnership Contribution using criteria that are clear and well-delineated, transparent in methodology, and inclusive of all companies on a global basis. There are many challenges, however, to developing a comprehensive list.
- Various approaches for defining the formula to distribute the Partnership Contribution among contributors can be considered.
- Transparency in how countries are selected to receive Partnership Contribution resources is important. Following selection, it will be critical to monitor and evaluate how countries use Partnership Contribution resources.
- There was general agreement that such interactions are useful and should continue.

23. The Director-General made several interventions. She stressed the importance of having WHO, its Member States, industry and other stakeholders exchange and understand each other's views and perspectives. All parties must work to honour their commitment and commence Partnership Contributions in 2012 as specified in the Framework. Global health security relies on the efforts of countries. The judicious use of Partnership Contribution funds to build and strengthen capacity, therefore, benefits not only the individual country, but all countries. The Director-General remains committed to operationalization of the Framework and its principles of transparency and equity.

### **GISRS assessment and Terms of Reference**

24. The Secretariat updated the Advisory Group on the scope, goals and proposed methodology for an assessment of GISRS. The assessment will use indicators of GISRS functions and capacity. Data will be derived from existing databases and reports, as well as new surveys of GISRS members and external GISRS partners. It was noted that the scope of the assessment is subject to available funding.

25. In its discussion the Advisory Group noted that although some countries do not have a NIC, they have other national laboratories that have capacities similar to a NIC or have access to laboratories in other countries. Using such information, the Advisory Group asked the Secretariat to provide a more comprehensive picture of global laboratory surveillance.

26. TORs for GISRS laboratories under the PIP Framework have not changed. The development of a new category of WHO CCs on the human-animal interface is underway. Proposed draft TORs for this new category of CCs are being prepared by GISRS, WHO regional and country offices and other experts. The Advisory Group welcomes further information about the process of assessment of the GISRS and about the recruitment of new Collaborating Centres in order to provide guidance on the

general process and on the animal-human interface. The Secretariat noted that review of these TORs is to follow the processes specified in PIP Framework Section 7.3.2.

### **Vaccine and antiviral stockpiles**

27. The Secretariat updated the Advisory Group on the WHO pandemic vaccine (H5N1) stockpile and WHO antiviral stockpiles, including their initial development, use during the 2009 pandemic, and their current status.

28. The Secretariat indicated that the Strategic Advisory Group of Experts (SAGE) Working Group on Influenza Vaccines and Immunizations considered three main options for the use of the remaining 120 million doses of H5N1 vaccine. The SAGE Working Group favoured one of three proposed options (“option c”), namely that a virtual stockpile with a small physical stockpile of filled doses of H5N1 vaccine (~1 million doses) would provide reassurance to countries in the event of an H5N1 outbreak. The PIP Advisory Group generally viewed this same option as the most viable with a possible consideration of having the physical stockpile stored in bulk. The Advisory Group noted the potential linkage of the WHO vaccine stockpiles with the 30% of Partnership Contributions reserved for pandemic response and may wish to review this issue at a future meeting.

### **Approval of reports**

29. The Annual Report and the Meeting Report were adopted unanimously by the Advisory Group.

### **Next steps**

#### **Next meeting**

30. The next meeting of the Advisory Group will take place 20–22 March 2013 in Geneva. Agenda items for the next meeting were discussed, to include:

- GISRS assessment
- Guidance on GISRS TORs
- Follow-up on the Partnership Contribution
- Follow-up on SMTA 2s
- Follow-up on implementation plans for the Partnership Contribution
- Vaccine stockpile (to be coordinated with other groups)
- Updated table of PIP Framework-related tasks/activities
- Overview of surveillance for influenza disease, e.g. syndromic surveillance

### **Any other business**

31. An Information Session for Permanent Missions is scheduled for 18 October 2012; the Advisory Group requested that the Secretariat develop a slide presentation for the Information Session which could be distributed to WHO regional offices. A briefing for other stakeholders is to be scheduled.

32. The Advisory Group may reconvene by teleconference on 10 December 2012 at 12:00 GMT +1 hour if necessary to discuss the status of the Partnership Contribution.

## APPENDIX 1

**PANDEMIC INFLUENZA PREPAREDNESS FRAMEWORK  
ADVISORY GROUP MEETING****3–5 OCTOBER 2012****List of Advisory Group participants**

**Professor Tjandra Y. Aditama**, Director General of Disease Control and Environmental Health, Ministry of Health, Indonesia

**Dr William Kwabena Ampofo**, Senior Research Fellow & Head – Virology, Noguchi Memorial Institute for Medical Research, University of Ghana, Ghana

**Dr Jarbas Barbosa da Silva Jr**, Secretary (Vice Minister) of Health Surveillance, Ministry of Health, Brazil

**Dr Silvia Bino**, Associate Professor of Infectious Diseases, Head, Control of Infectious Diseases Department, Institute of Public Health, Albania

**Dr Rainer Engelhardt**, Assistant Deputy Minister, Infectious Disease Prevention and Control Branch, Public Health Agency of Canada, Canada

**Mr David E. Hohman**, Former Deputy Director, Office of Global Affairs, Department of Health and Human Services, United States of America

**Professor Didier Houssin**, President, French Evaluation Agency for Research and Higher Education (AERES), France

**Dr Mark Jacobs**, Director of Public Health, Ministry of Health, New Zealand

**Dr Hama Issa Moussa**, National Technical Assistant, Institutional Support Unit, Ministry of Public Health, Niger

**Dr Nobuhiko Okabe**, Director General, Kawasaki City Institute for Public Health, Japan

**Dr Adrian J. Puren**, Deputy Director, National Institute for Communicable Diseases, South Africa

**Professor Prasert Thongcharoen**, Professor Emeritus, Department of Microbiology, Faculty of Medicine, Siriraj Hospital, Mahidol University, Thailand

**Dr P.V. Venugopal**, Former Director of International Operations, Medicines for Malaria Venture, Public Health Specialist, India

## APPENDIX 2

**PANDEMIC INFLUENZA PREPAREDNESS FRAMEWORK  
ADVISORY GROUP MEETING****3–5 OCTOBER 2012****Summary of Declarations of Interest by members**

In accordance with WHO policy, all PIP Framework Advisory Group members completed the “WHO Declaration of Interests for WHO Experts”. In advance of the meeting, all members were asked to confirm the interests they had previously declared, disclose any relevant changes that had intervened subsequently, and provide any additional information that could be relevant to the subject matter of the meeting. Pursuant to WHO guidelines, their declarations were reviewed and assessed for real, potential or apparent conflicts of interest. The experts participating in the Advisory Group meeting were, by WHO region:

## Africa:

- Dr William Kwabena Ampofo (Ghana)
- Dr Hama Issa Moussa (Niger)
- Dr Adrian J. Puren (South Africa)

## Americas:

- Dr Jarbas Barbosa da Silva Jr (Brazil)
- Dr Rainer Englehardt (Canada)
- Mr David E. Hohman (United States of America)

Eastern Mediterranean:<sup>1</sup>Europe:<sup>1</sup>

- Dr Silvia Bino (Albania)
- Professor Didier Houssin (France)

## South-East Asia:

- Dr P.V. Venugopal (India)
- Professor Tjandra Y. Aditama (Indonesia)

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<sup>1</sup> Dr Rajae El Aouad (Morocco), Dr Amr Mohamed Kandeel (Egypt), Dr Ziad A. Memish (Saudi Arabia), Professor Oleg Ivanovich Kiselev (Russian Federation), and Professor Yu Wang (China) were unable to attend.

- Professor Prasert Thongcharoen (Thailand)

Western Pacific:<sup>1</sup>

- Dr Nobuhiko Okabe (Japan)
- Dr Mark Jacobs (New Zealand)

In the interest of transparency, the following interests and/or affiliations were deemed relevant to the subject of work and are hereby disclosed:

<b>Name</b>	<b>Interest declared</b>
Dr William Kwabena Ampofo	Affiliated with a GISRS laboratory
Dr Hama Issa Moussa	Civil Servant
Dr Adrian J. Puren	Civil Servant
Dr Jarbas Barbosa da Silva, Jr	Civil Servant
Dr Rainer Englehardt	Civil Servant
Dr Silvia Bino	Affiliated with a GISRS laboratory
Professor Tjandra Y. Aditama	Civil Servant
Dr Mark Jacobs	Civil Servant
Dr Nobuhiko Okabe	Civil Servant
Professor Prasert Thongcharoen	Affiliated institution received funding from a vaccine manufacturer to conduct research*

\* The interest declared by Professor Prasert Thongcharoen was reviewed by WHO and determined not to present a conflict of interest with the objectives of the meeting.

No other interests declared by members of the Advisory Group were deemed relevant to the work of the group.

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<sup>1</sup> Dr Rajae El Aouad (Morocco), Dr Amr Mohamed Kandeel (Egypt), Dr Ziad A. Memish (Saudi Arabia), Professor Oleg Ivanovich Kiselev (Russian Federation), and Professor Yu Wang (China) were unable to attend.

## APPENDIX 3

**PANDEMIC INFLUENZA PREPAREDNESS FRAMEWORK  
ADVISORY GROUP MEETING****3–5 OCTOBER 2012****Civil society organizations and other stakeholders:  
Participants<sup>1</sup>**

- Berne Declaration
- International Property Watch
- Knowledge Ecology International
- Medicines Patent Pool
- Third World Network

**Manufacturers and industry associations:  
Participants<sup>2</sup>**

- AdvaMedDx
- Baxter
- Becton Dickinson
- BIKEN
- Biotechnology Industry Organization (Bio)
- CSL Biotherapies
- Developing Countries Vaccine Manufacturers Network (DCVMN)
- Denka Seiken Co., Ltd.
- GSK Vaccines
- International Federation of Pharmaceutical Manufacturers & Associations (IFPMA)

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<sup>1</sup> The China Preventive Medicine Association and the National Institute of Infectious Diseases (Japan) followed the meeting via audio-conferencing.

<sup>2</sup> Adimmune, the Japanese Association of Vaccine Industries, the China National Biotec Group, and MedImmune followed the meeting via audio-conferencing.

- Kaketsuken
- Kitasato Daiichi Sankyo Co., Ltd.
- Novavax
- Novartis Vaccines and Diagnostics
- Sanofi Pasteur
- Takeda Pharmaceuticals International

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