MEETING OF THE PANDEMIC INFLUENZA PREPAREDNESS (PIP) FRAMEWORK ADVISORY GROUP

21-24 OCTOBER 2014, GENEVA, SWITZERLAND

Report to the Director-General

Organization and process of the meeting


2. Of the 18 members of the Advisory Group, 13 were present. The list of Advisory Group participants is found at Annex 1.

3. The Chair made a number of introductory remarks.

4. The WHO Principal Legal Officer reviewed the process for Declarations of Interest. The summary of Declarations of Interest is found at Annex 2.

5. The Advisory Group adopted the meeting agenda. The agenda is found at Annex 3.

6. The Advisory Group held consultations with industry and other stakeholders as well as representatives of databases\(^1\) for genetic sequence data (GSD) (see Annex 4).

Recent developments: the Ebola outbreak

7. The Assistant Director-General, Health Security, and the Director, Department of Pandemic and Epidemic Diseases (PED) provided an update on the outbreak of Ebola Virus Disease (EVD), including EVD prevention and control activities.

8. WHO has mobilized staff and operations at all levels to respond to the EVD outbreak. This has somewhat slowed the progress made in implementing Partnership Contribution (PC) activities, particularly in the African Region. It was noted, however, that many of the lessons learnt as part of preparedness and response for the A(H1N1) pandemic have applicability for the EVD outbreak. Conversely, capacity strengthening related to EVD may benefit pandemic influenza preparedness and response.

Recent developments: the Nagoya Protocol

9. The PIP Secretariat provided background information on the “Nagoya Protocol on Access to Genetic Resources and the Fair and Equitable Sharing of Benefits Arising from their Utilization”\(^2\) and its possible implications for implementation of the PIP Framework. The Protocol implements the third objective of the Convention on Biological Diversity which is the “fair and equitable sharing of benefits arising from the use of genetic resources” and it entered into force on 12 October 2014.

\(^1\) Throughout this report, the term “database” refers to any institute, collaboration, initiative, organization or other entity that houses genetic sequence data.

\(^2\) See http://www.cbd.int/abs/.
Update on SMTAs 2: issues with diagnostic companies

10. WHO has been negotiating Standard Material Transfer Agreements 2 (SMTAs 2) with “manufacturers of products relevant to pandemic influenza preparedness and response that are not manufacturing vaccines or antivirals”. Under the PIP Framework, this category of manufacturers is required to commit to one of six possible options. In practice, this category comprises manufacturers of influenza diagnostic tools.

11. In approaching discussions with diagnostic manufacturers, the PIP Secretariat reviewed how the matter of diagnostic kits was handled during 2009 pandemic. The review showed that at that time no commercial diagnostic kits were distributed due to several factors. In addition, based on discussions with experts at WHO it was concluded that commercial diagnostic products do not currently appear to be a priority for distribution by WHO during a pandemic.

12. The Advisory Group discussed possible options for securing commitments from manufacturers in SMTA 2 Category B and provided the following advice to the Director-General:

*The Advisory Group concurs with the findings of the Secretariat that, based on the 2009 pandemic influenza precedent, it does not currently appear that commercial diagnostic kits would be priority products for distribution by WHO during a pandemic.*

*In undertaking negotiations with diagnostic manufacturers:*

- WHO should consider the need for flexibility and simplicity when interpreting the six options provided in the PIP Framework, Annex 2, Article 4B.1-4.
- In lieu of diagnostic tests, monetary and non-monetary commitments may be considered. Non-monetary commitments could include, but not be limited to, training in basic surveillance and laboratory capacity, and equipment or supplies needed during a pandemic.
- Although it is not possible to set a firm metric for a diagnostic company’s commitment, the relative value of the commitment should be in the same range as other SMTA 2 commitments.
- The timing of the commitment would be dependent on its nature; e.g. capacity building activities would be part of pandemic preparedness while equipment and supplies would be made available at the declaration of a pandemic.

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3 This group of manufacturers is called “Category B” because they fall under Article 4.1B of the model SMTA2 found in Annex 2 of the PIP Framework.

4 See PIP Framework, Annex 2, Articles 4(A.5), 4(A.6) and 4(B.1-4).

5 The factors were as follows: 1) low-sensitivity tests, such as rapid or bedside diagnostics, which constitute a substantial portion of commercially produced products, do not reliably provide accurate determinations of virus subtype; 2) diagnostic kits have a limited shelf life, and the logistic and financial implications regarding disposal of expired devices are not clear; WHO runs the risk of appearing to endorse specific commercial diagnostic products or kits that it would distribute; and 3) commercial diagnostic kits use proprietary equipment, reagents and/or technology. Building capacity in Member States to use such tests could result in governments having to purchase proprietary materials not donated, and could be perceived as WHO opening markets for a company or product.
Update on SMTAs 2: assurances from vaccine producing countries

13. In April 2014, the AG recommended that the Director-General seek periodic assurances from Member States that they would enable companies to fulfil their SMTA 2 commitments to supply pandemic vaccine to WHO on a real-time basis. The Secretariat updated the Advisory Group on work to date. The Advisory Group reaffirmed the importance of making further progress on this matter.

Partnership Contribution: update on Partnership Contribution collection

14. The Secretariat updated the Advisory Group on the status of the collection of the 2014 PC. The Advisory Group noted the efforts of the Secretariat to improve the process to collect the 2014 PC. As a result, as compared with 2013, there was an increase in the number of entities contacted, the number of Questionnaire responses received, and the number of Contributors identified. This is very positive, particularly as the PC is still a recent mechanism for many contributors.

15. For 2014, 56 companies were identified as Contributors. The Secretariat requested a 2014 Band Selection Form (BSF) from each company; to date, 31 have not responded despite repeated efforts by the Secretariat.

16. The BSF is an essential piece of information that must be received from all Contributors to allow WHO to apply a formula and determine how much each Contributor will pay into the PC. The BSF requires an entity to calculate its average annual influenza product sales over four years and to use that figure to place itself into one of 23 sales bands. For 2014, those years are 2009, 2011, 2012 and 2013. Some companies that had high product sales in 2010 due to the sale of pandemic-related products will move to a lower band in 2014, as 2010 sales are not included in the 2014 band calculation.

17. The Secretariat requested guidance from the Advisory Group on the band placement for the 31 entities identified as Contributors and for which there is no 2014 BSF.

18. In discussions with industry and other stakeholders, it was noted that any approach to address Contributors identified as such by the Secretariat and that have not submitted a BSF should aim to minimize the impact on the total amount of contributions that will be received in 2014. It was also noted that the effect on the 2014 collection of funds of non-paying Contributors that end up in default of the payment requested would potentially reduce the total amount of PC funds collected by WHO and would not increase individual Contributor’s payment allocation to WHO in 2014.

19. Advice to the Director-General on the collection of 2014 PC funds:

The Advisory Group recommended that the Director-General individually thank companies that have paid their 2013 contribution and consider publicly acknowledging them. Such public acknowledgement may serve as a reminder or impetus to other companies that have not yet met their obligations.

The PIP Secretariat should continue its efforts to obtain PC payments. Member States should be invited to encourage, as appropriate, companies located in their country to fulfill their obligations under the PC.
For companies that have not provided a 2014 BSF, the Advisory Group recommended that the Director-General:

- Place the 20 companies that were identified as 2013 Contributors into the same band as in 2013.
- Place all 11 new companies that were not Contributors in 2013 and, for which there is no band information, into the modal band (Band 23).

**Partnership Contribution: implementation, communications and Critical Path Analysis**

20. The Secretariat updated the Advisory Group, industry and other stakeholders on the implementation of PIP pandemic preparedness activities for the five areas of work. The PIP PC Implementation Portal was demonstrated; the portal provides transparency in the use of PC funds and over time will be refined and expanded. Industry and other stakeholders appreciated the developments and encouraged continued progress.

21. The Director, PED presented the Critical Path Analysis (CPA) which will serve as a roadmap for pandemic preparedness. Engagement with industry and other stakeholders will continue with the aim of finalising the CPA by the end of 2014.

22. The impact of EVD was discussed and the Advisory Group noted that the Secretariat is taking the EVD outbreak into account in its planning for activities in 2015, particularly in the African Region.

23. Advice to the Director-General on the continuing threat of pandemic influenza:

   *The Advisory Group notes the threat of pandemic influenza has not changed. The Advisory Group recommends that efforts to implement the programme of work under the PC should be encouraged.*

**Partnership Contribution: draft guiding principles for use of PC response funds**

24. The Advisory Group reviewed the draft guiding principles and in particular the section relating to “Priority setting” which was clarified based on comments received from industry and other stakeholders. The Advisory Group requested that the revised final draft be shared with industry and other stakeholders who concurred with the final version (found at Annex 5).

25. Advice to the Director-General on Guiding Principles for use of Response funds:

   *“Guiding Principles for the Use of PIP Partnership Contribution Response Funds” are submitted for the consideration and approval of the Director-General.*

**Best process for further discussion and resolution of the issues related to the handling of genetic sequence data as part of the PIP Framework**

26. Under PIP Framework section 5.2.4, Member States requested that the Director-General consult with the Advisory Group on the “best process for further discussion and resolution of the issues related to the handling of genetic sequence data from H5N1 and other influenza viruses with pandemic potential as part of the PIP Framework”.

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27. A Technical Expert Working Group (TEWG) was established in October 2013 to provide background and technical information to the Advisory Group for its examination of the issues related to the handing of genetic sequence data under the PIP Framework. The TEWG report was finalized and submitted to the Advisory Group in October 2014.

28. A technical consultation was held with six database representatives to continue the gathering of technical information. Industry and other stakeholders were invited to attend. Due to a scheduling conflict, the GISAID Initiative met with the Advisory Group the day before the consultation. The GISAID Initiative joined the closing minutes of the consultation by audio-conference.

29. As part of the technical consultation, representatives of databases provided information on their establishments, content, data access, use and transfer policies, monitoring and enforcement policies, and curation procedures. Some general observations included:

- Most databases have an open access policy; access to the EpiFlu™ database hosted by the GISAID Initiative and the Influenza Virus Monitoring On-Line (Indonesia) are open only to registered users who have agreed to their data access policy.
- In general, databases are able to identify the provenance of information that is uploaded; it is difficult, however, for them to forward trace the transfer of data.
- Most GISRS laboratories use GISAID; its value for outbreak response and the biannual seasonal influenza vaccine composition meetings was stressed.
- The databases indicated their willingness to discuss how better to collaborate with each other to improve the sharing of GSD from influenza viruses.

30. The ensuing discussion noted:

- GSD is covered by the Framework (e.g. Section 5.2; Annex 4, Point 9; Annex 5 ‘Guiding Principles’). The spirit of the Framework and the importance of maintaining equal footing for the sharing of viruses and benefits derived therefrom must be kept in mind when considering issues related to the handling of GSD for influenza viruses with pandemic potential.
- There may be some options for identifying GSD that originate from the WHO GISRS other than monitoring databases; however, the process must be feasible, efficient and create legal certainty. Monitoring the end-products generated through the use of GSD was discussed as a potential option.

31. Having taken into consideration the TEWG final report and having interacted with representatives of databases, industry and civil society, the Advisory Group made the following observations:

a. Laboratories should continue to share the GSD of influenza viruses with pandemic potential (IVPP) as soon as it becomes available because it is necessary for timely and comprehensive pandemic risk assessment and response.

b. In accordance with Section 6.3.2, laboratories using GSD will meet appropriate biosafety guidelines (WHO Laboratory Biosafety Manual, 3rd edition) and employ laboratory protection best practices.
c. The objective of benefit-sharing may be met by mechanisms related to monitoring products generated using influenza GSD, rather than by monitoring use of GSD and/or tracing GSD, noting that source identification is critical.6

d. Closer collaboration regarding open sharing of influenza GSD among the many different databases is desirable.

32. Advice to the Director-General on the best process for further discussion and resolution of the issues related to the handling of GSD under the PIP Framework:

In accordance with PIP Framework Section 5.2.4, the Advisory Group recommends for the Director General’s consideration the following as the best process for further discussion and resolution of the issues related to the handling of GSD under the PIP Framework:

- In 2015, the Advisory Group will identify the optimal characteristics of a system for the handling of IVPP GSD under the PIP Framework including consideration of:
  a. Data sharing systems that are best suited to meet the objectives of the Framework considering obligations and timeliness of data submission, quality assurance of data, completeness of data annotation, ease of access to data, sustainability and security of the system.
  b. Systems to monitor use of IVPP GSD in end-products.
- For the foregoing, the Advisory Group will consult with GISRS laboratories, databases, and industry and other stakeholders.
- The results of the above work will be available to the Secretariat for integration into the 2016 review of the Framework and its annexes as provided in Section 7.4.2.

Technical issues: update on the Global Action Plan for Influenza Vaccines (GAP)

33. The Chair of the WHO GAP Advisory Group reviewed the current status of the GAP. GAP was launched in 2006 as a 10 year (2006-2016) initiative aimed at “ensuring the protection of populations worldwide through vaccination in the event of an influenza pandemic.”7 GAP and PIP are complementary in relation to burden of disease studies, enhancement of regulatory capacity, and risk communications.

34. GAP has resulted in a significant increase in the actual and potential global seasonal influenza vaccine production capacity.8 The estimates of influenza burden of disease and the evaluation of the cost-effectiveness of seasonal influenza vaccination are ongoing.

Technical issues: review of GISRS self-assessment report

35. The Advisory Group extended its appreciation to all those who participated in the GISRS self-assessment; their efforts resulted in a high quality and informative report. The report is timely in that the current EVD outbreak reinforces the important role GISRS laboratories can play in responding to public health emergencies through specimen shipping, virological testing, reagent development and other areas of expertise.

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8. Ibid.
36. The assessment identified GISRS’ many strengths as well as some weaknesses and opportunities for improvement. The Advisory Group noted that the self-assessment report provided information that complemented the PC Gap Analyses.

37. Efforts to build and further enhance influenza surveillance and laboratory capacity are being undertaken as part of the PC Implementation Plan. All of the areas for improvement identified in the self-assessment, however, will not be addressed as part of PC implementation activities.

38. The Advisory Group cautioned that the risk of pandemic influenza has not decreased. The global economic crisis, the EVD outbreak and other competing public-health priorities have the potential to impact countries’ support and commitment to National Influenza Centres and other GISRS laboratories.

39. Advice to the Director-General on the GISRS self-assessment report:

The Advisory Group recommends that the Director-General share the self-assessment report with Member States for their review and consideration. In view of the persistent pandemic threat, the Director-General should remind Member States that GISRS plays a pivotal role in pandemic influenza preparedness and response.

The Advisory Group recommends that the report be shared widely with others in addition to Member States.

Advisory Group’s Annual Report to the Director-General

40. The Advisory Group’s Annual Report on its evaluation of the implementation of the Framework can be found in Annex 6 for the Director-General’s consideration.

Review and approval of meeting report

41. The Advisory Group adopted the meeting report after providing comments.

Renewal of Advisory Group members

42. In accordance with the terms of reference of the Advisory Group, the process to renew one-third of its members was started with the drawing of lots to identify members whose names will be added to the Advisory Group roster, and members whose appointments will be extended for one or two years. The results of the drawing can be found in Annex 7. Six new members will join the Advisory Group for the next meeting.

Next steps

43. The Advisory Group will meet in Geneva from 14-17 April 2015.
Annex 1

Pandemic Influenza Preparedness Framework Advisory Group Meeting
21–24 October 2014

List of Advisory Group participants

**Professor Tjandra Y Aditama**, Chairman, National Institute of Health Research and Development, Ministry of Health, Indonesia

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

**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 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, Ministry of Public Health and Social Development, National Influenza Centre, Russian Federation

**Dr Frances McGrath**, Deputy Director of Public Health, Clinical Leadership, Protection and Regulation, 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 P V Venugopal**, Former Director of International Operations, Medicines for Malaria Venture, Public Health Specialist, India

**Dr Yu Wang**, Director General, Chinese Center for Disease Control and Prevention, P. R. China
Annex 2

Pandemic Influenza Preparedness Advisory Group Meeting
21-24 October 2014

Summary of Declarations of Interest by members

In accordance with WHO policy, in advance of the meeting, all PIP Framework Advisory Group members were asked to provide a duly completed Declaration of Interests to inform WHO about real, potential or actual conflicts of interests that they might have in relation to the subject matter of the meeting. Over the course of the meeting, the Advisory Group will:

- Review and discuss their Annual Report to the Director-General
- Interact with manufacturers and other stakeholders regarding the use of the Partnership Contribution (Framework section 6.14.6)
- Consult with genetic sequence database managers on the best process for handling genetic sequence data under the PIP Framework
- Discuss and provide recommendations on the implementation of the Framework, including a) the Partnership Contribution; b) SMTA negotiations; c) other technical matters.

The experts participating in the Advisory Group meeting were, by WHO region:

Africa:
- Dr William Kwabena Ampofo (Ghana)
- Dr Hama Issa Moussa (Niger)

Americas:
- Dr Rainer Engelhardt (Canada)
- Mr David E Hohman (United States of America)

Eastern Mediterranean:
- Dr Amr Mohamed Kandeel (Egypt)

Europe:
- Dr Silvia Bino (Albania)
- Professor Didier Houssin (France)
- Professor Oleg Ivanovich Kiselev (Russian Federation)

South-East Asia:
- Professor Tjandra Y Aditama (Indonesia)
- Dr P V Venugopal (India)

Western Pacific:
- Dr Nobuhiko Okabe (Japan)

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1 Dr Rajae El Aouad (Morocco), Dr Rungrueng Kitphati (Thailand), Dr Ziad A Memish (Saudi Arabia), Dr Jarbas Barbosa da Silva Jr, (Brazil) and Dr Adrian Puren (South Africa) were unable to attend.
• Dr Frances McGrath (New Zealand)
• Dr Yu Wang (P.R. China)

Given that discussions in the meeting were on the potential use of Partnership Contribution resources, and in the interest of transparency, the following interests and/or affiliations are relevant to the subject of work and are hereby disclosed:

<table>
<thead>
<tr>
<th>Name</th>
<th>Interest declared</th>
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<tbody>
<tr>
<td>Professor Tjandra Y. Aditama</td>
<td>Civil Servant</td>
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<tr>
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<td>Affiliated with a GISRS laboratory</td>
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<td>Civil Servant</td>
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<tr>
<td>Dr Yu Wang</td>
<td>Civil Servant</td>
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No other interests declared by members of the Advisory Group were deemed relevant to the work of the group.
Annex 3

Pandemic Influenza Preparedness Framework Advisory Group Meeting
21-24 October 2014

Agenda

1. Registration

2. Welcome remarks from the Chair

3. Introductions

4. Declarations of Interest

5. Adoption of agenda

6. Recent developments
   - Remarks on the current Ebola situation
   - Nagoya Protocol

7. Update on SMTAs 2
   - Issues with diagnostic companies
   - Assurances from vaccine producing countries

8. Partnership Contribution
   - Partnership Contribution collection
   - Implementation
   - Communications
   - Critical Path Analysis
   - Draft revised Principles for use of Pandemic Response resources

9. Discussion with GISAID

10. Consultation with database managers
    - Welcome remarks from the Chair
    - Review of the findings of the Technical Expert Working Group (TEWG) on genetic sequence data
    - Technical presentations by database managers

11. Consultation with industry and other stakeholders
    - Update on Partnership Contribution
    - PIP Partnership Contribution Critical Path Analysis
    - Any other business

12. Technical issues
    - Update on Global Action Plan for Influenza Vaccines (GAP)
    - Review of final Global Influenza Surveillance and Response System (GISRS) self-assessment report
13. Review of Advisory Group Annual Report to the Director-General
14. Review of outcomes of consultations and drafting of recommendations
15. Review and approve recommendations and meeting report
16. Renewal of Advisory Group members
17. Next steps
   - Next meeting of the Advisory Group
   - Any other business
18. Close of meeting
Annex 4

Pandemic Influenza Preparedness Framework Advisory Group Meeting
21-24 October 2014

Civil society organizations and other stakeholders:
Participants

- Third World Network

Manufacturers and industry associations:
Participants

- AdvaMedDx
- bioCSL
- Biotechnology Industry Organization (BIO)
- Cepheid
- Fab'entech
- GlaxoSmithKline (GSK)
- Kitasato Daiichi Sankyo Vaccine Co., Ltd.
- International Federation of Pharmaceutical Manufacturers & Associations (IFPMA)
- Novartis
- Novavax
- Sanofi

Genetic sequence database:
Representatives

- GISAID Initiative
- Global Catalogue of Microorganisms
- Influenza Research Database
- International Nucleotide Sequence Database Collaboration (INSDC)
- Influenza Virus Monitoring On-Line (IVMOnline)
- OpenFluDB
Guiding Principles for use of PIP Partnership Contribution “Response” Funds

23 October 2014

I. Background

1. The Partnership Contribution (PC) is an annual payment to WHO from influenza vaccine, diagnostic and pharmaceutical manufacturers using the Global Influenza Surveillance and Response system (GISRS). The Framework specifies that PC resources are to be used for improving pandemic preparedness and response, inter alia, for conducting disease burden studies, strengthening laboratory and surveillance capacities, and access and effective deployment of pandemic vaccines and antiviral medicines. The Framework states that the annual amount to be received by WHO is equivalent to 50% of the running costs of GISRS, which, in 2010, were approximately US$ 56.5 million. Therefore, the annual PC to be received by WHO is US$ 28 million.

2. Recognizing the significant global need for improved preparedness, detailed notably in the IHR Review Committee Report, the PIP Advisory Group (PIPAG) provided the following advice to the Director-General on the proportional allocation of resources between preparedness and response:
   
a) In the early phases of the Framework's implementation, more of the PC should be used for preparedness than response.
   b) Specifically, over the next 5 years (2012 through 2016) approximately 70% of contributions should be used for pandemic preparedness measures and approximately 30% should be reserved for response activities, recognizing the need and usefulness of flexibility in allocating funds.
   c) In order to ensure that the proportional division does not hinder necessary response measures during pandemic influenza emergencies, the Director-General should be able to temporarily modify the allocation of PC resources as required to respond to said emergencies. The Director-General should report on any such modification to Member States.
   d) The proportional division should be reviewed again in 2016.

3. The guidance was accepted by the Director-General and submitted to the 131st Executive Board that likewise accepted it, in accordance with PIP Framework Section 6.14.5.

4. Annual contributions received have been divided according to the decision of the Executive Board.

5. This document outlines the Guiding Principles for use of PIP PC Response funds. Use of “Preparedness” funds is covered in the PIP PC Implementation Plan 2013-2016 approved by the Director-General on 17 January 2014.

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9 See PIP Framework Section 6.14.3
10 See PIP Framework Section 6.14.4
11 See PIP Framework Section 6.14.3 and 6.14.4
6. PIP Framework Section 6.14.6 states that “the Director-General, based on advice from the ‘Advisory Group’, will decide on the use of [Partnership Contribution] resources. The Director-General and the ‘Advisory Group’ will interact with manufacturers and other stakeholders.”

7. The decision on the use of “Preparedness” resources was taken by the Director-General following several significant consultations with the PIP Advisory Group, and interaction with industry and other stakeholders. These took place over several months and meetings, from February 2012 to October 2013.

8. At the time of a pandemic, time will be of the essence and there will be limited or no opportunities to convene the Advisory Group or hold interactions with industry and other stakeholders to discuss the use of “Response” resources.

9. The Guiding Principles will provide the basis for the Director-General to decide on the use of the PC for response purposes without further advice from the Advisory Group, or interaction with industry and other stakeholders.

II. Guiding Principles governing use of PIP PC Response funds

1) Authority: Using the Guiding Principles outlined herein, the Director-General shall decide on the allocation and use of PC “Response” funds.

2) Release of PC Response funds: The release of PC Response funds will be based on the following:

- **Determination of a Public Health Emergency of International Concern (PHEIC) under the International health Regulations (2005)(IHR):** The responsibility of determining a PHEIC lies with the WHO Director-General under IHR Article 12. This requires the convening of an Emergency Committee of experts under IHR Article 48. In accordance with the IHR, the Director-General shall consider the following when determining whether an event constitutes a PHEIC:
  - information provided by the State Party;
  - the decision instrument contained in IHR Annex 2;
  - the advice of the Emergency Committee;
  - scientific principles as well as the available scientific evidence and other relevant information; and
  - an assessment of the risk to human health, of the risk of international spread of disease and of the risk of interference with international traffic.

- **Declaration of a pandemic:** During the spread of human influenza caused by a new subtype, and appropriate to the situation, the Director-General may make a declaration of a pandemic.

- In some instances, the Director-General may allocate some funds to pandemic response activities that would take place in advance of a pandemic declaration, such as for instance, to secure access to antiviral medicines or other essential supplies and equipment.

3) **Priority setting:** In accordance with PIP Framework section 6.0.2 (iii) WHO will prioritize and provide access to “important benefits, such as and including antiviral medicines and vaccines […] as high priorities, to developing countries, particularly affected countries, according to public health risk and needs and particularly where those countries do not have their own capacity to produce or access influenza vaccines, diagnostics and pharmaceuticals. Prioritization will be based on assessment of public health risk and need, by experts with transparent guidelines.”

- **Criteria to allocate benefits:** Development of criteria will be based on assessment of public health risk and need, by experts with transparent guidelines, provided in the Framework (see above). This will require information about, *inter alia*, the level and extent of disease transmission, clinical and virological characteristics of the pandemic virus, its spread, and the development status of countries. Additionally, at the time of the pandemic event, updated information on the production capacities of manufacturers of pandemic products will be necessary. Allocation of benefits will also take into account national pandemic preparedness plans, e.g. regulatory capabilities and plans for deployment of vaccines, antivirals, diagnostics and other pandemic-related products.

- **Coordination with Standard Material Transfer Agreements 2 (SMTAs 2):** SMTAs 2 will provide WHO with real-time access to critical pandemic response products (e.g. pandemic vaccines, antivirals, diagnostics and other pandemic-related products). PC Response funds will be used to ensure that WHO can access all such products secured under SMTAs 2 on a donation or reserve basis. While many products will be accessed on a donation basis, funds will be necessary to ship many of these goods to recipient countries. Additionally, funds will be necessary to access goods reserved for purchase at an affordable price.

4) **Fairness and Equity:** WHO shall ensure that fairness and equity, as well as public health risk and need, govern access to pandemic response products and services provided by WHO.

5) **Transparency:** Information on the allocation and use of PC response funds will be shared in a timely manner with Member States, the PIP Advisory Group, industry and other stakeholders.

6) **Accountability:** WHO will be fully accountable for the use of all PC funds used by WHO for response activities.

7) **Leverage through the Director-General’s Good Offices:** The Director-General will leverage the positive impact of the use of PC funds and encourage further contributions for pandemic response activities. No PC Response funds will be used to achieve this end.

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13 See PIP Framework Section 6.02 (iii).
Annex 6

Annual Report from the Advisory Group to the Director-General

1 INTRODUCTION

This is the third Annual Report of the Pandemic Influenza Preparedness Framework (PIP Framework) Advisory Group (AG) to the Director-General on its evaluation of the implementation of the Framework as provided under Section 7.2.5 and Annex 3, Section 2. It covers the 12-month period beginning 1 October 2013 through 30 September 2014 and is organized into three sections: virus sharing, benefit sharing and governance. It addresses the seven topic areas specified in the Framework; these topics are indexed at the end of the report.

The Framework aims to ensure an equitable and transparent balance between sharing of influenza viruses that have pandemic potential and distributing the benefits that result. Since the 2013 Annual Report, steady progress has been made to implement the many components of the Framework. Highlights include:

- the number of Contributors to the Partnership Contribution has increased with 25 manufacturers contributing more than USD 27 million to the Partnership Contribution;
- additional Standard Material Transfer Agreements 2 (SMTAs 2) have been concluded;
- a Partnership Contribution Implementation Plan 2013-2016, with supporting Gap Analyses, was approved by the Director-General in January 2014 and detailed implementation plans for the use of these funds were finalized by WHO headquarters and regional offices. The main focus of these Partnership Contribution implementation plans is capacity building which is foundational to pandemic preparedness and accords with the Executive Board’s decision that:
  - The greatest impact can be achieved by building capacity in countries where it is lowest.
  - Preparedness requires long-term investment, particularly when capacity building requires training and transfer of knowledge.
- funds have been disbursed to all areas of work in the Implementation Plan and staff has been hired; implementation of activities has started and is poised to accelerate in the upcoming months;
- The Technical Expert Working Group (TEWG) on genetic sequence data (GSD) completed its assessment of the scientific, technical, operational and intellectual property implications of using the GSD of influenza viruses with

14 Global Influenza Surveillance and Response System (GISRS)-related data cover the 12-month period 1 August 2013 through 31 July 2014. This allows for continuous reporting of GISRS data (i.e. GISRS data in the 2013 Annual Report concluded on 31 July 2013), and for time to tabulate and analyze data.

15 The seven areas specified in PIP Framework, Section 7.2.5 and Annex 3, Section 2 are: necessary technical capacities of the WHO GISRS; operational functioning of WHO GISRS; WHO GISRS influenza pandemic preparedness priorities, guidelines and best practices (e.g. vaccine stockpiles, capacity building); increasing and enhancing surveillance for H5N1 and other influenza viruses with human pandemic potential; the Influenza Virus Traceability Mechanism (IVTM); the sharing of influenza viruses and access to vaccines and other benefits; and the use of financial and non-financial contributions.

pandemic potential (IVPP) thereby facilitating the work of the Advisory Group.

- The Global Influenza Surveillance and Response System (GISRS) self-assessment was concluded and the accompanying report outlined the strengths, weaknesses, opportunities, threats, and trends of GISRS that will allow for further improvement of the system.

2 VIRUS SHARING

2.1 Global Influenza Surveillance and Response System

The GISRS network of public health laboratories is foundational to pandemic preparedness and response. The rapid sharing and analysis of influenza viruses with human pandemic potential and associated clinical and epidemiological information allow GISRS to conduct risk assessments, and develop and distribute laboratory tests, reagents, testing kits and candidate vaccine viruses. The response to the emergence of the A(H7N9) virus in China in March 2013 is a recent example of the global benefits of virus sharing.

GISRS is closely monitoring other zoonotic viruses of concern such as H5N1, H3N2v, and H9N2. There is enhanced surveillance for non-seasonal subtypes of influenza in both humans and animals in China, the countries neighbouring China and globally.

The WHO Shipping Fund Project continues to play an important role for countries that require technical training and financial support to share influenza viruses with GISRS in a timely fashion. In October 2011, due to decreased funding, restrictions were placed on the maximum number of shipments that could be supported under the Project. In July 2013 additional funds were received from partners and these restrictions were lifted. From August 2013 through July 2014, the WHO Shipping Fund Project supported 122 shipments from 82 laboratories in 73 countries, areas and territories at a cost of USD 209,577. GISRS organized two training workshops on the proper handling and packaging of infectious substances for international shipment in two WHO regions (African Region and Region of the Americas) during this same period.

WHO and GISRS have updated information and/or laboratory guidance and best practices in areas related to improving influenza vaccine virus selection and molecular diagnostic

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18 During 1 August 2013 through 31 July 2014, four summaries were published on the status of development and the availability of candidate vaccine viruses and potency testing reagents for A(H5N1) (http://www.who.int/influenza/vaccines/virus/candidates_reagents/a_h5n1/en/); six summaries for A(H7N9) (http://www.who.int/influenza/vaccines/virus/candidates_reagents/a_h7n9/en/); and one summary for A(H9N2) (http://www.who.int/influenza/vaccines/virus/candidates_reagents/a_h9n2/en/).


20 See http://www.who.int/influenza/vaccines/virus/201402_h5h7h9h10_vaccinevirusupdate.pdf?ua=1.


protocols for detection of seasonal and pandemic potential influenza viruses. A WHO PCR Working Group met in May 2014 to review PCR technologies relevant to GISRS’ public health responsibilities, including gaps and quality assessment issues. An antiviral expert Working Group met in June 2014 to finalize pending guidance on antiviral susceptibility testing and review the status of neuraminidase inhibition susceptibility of circulating viruses, including A(H7N9). To assist countries in improving the quality of epidemiological surveillance, WHO published *WHO Global Epidemiological Surveillance Standards for Influenza* in January 2014 after a lengthy consultative process.

In February 2012, the AG recommended that a self-assessment of GISRS laboratories be undertaken to consider GISRS’ role, function and capacities in relation to the Framework. The assessment was completed in September 2014. Key findings included:

- GISRS is a robust network with strong technical foundations;
- it has the expertise to respond to and conduct surveillance for other infectious pathogens;
- significant geographical gaps remain in Africa, the Middle East and eastern Europe;
- due to the economic constraints and “flu fatigue” many National Influenza Centres (NICs) are challenged by insufficient funding and government commitment; and,
- while understanding of the Framework is generally good, NICs could benefit from more information.

### 2.2 Influenza Virus Traceability Mechanism

Transfers of PIP biological materials are monitored through the Influenza Virus Traceability Mechanism (IVTM). From August 2013 through July 2014, 252 shipments of PIP biological materials were sent and recorded in the IVTM; 213 (84%) of these were sent to 75 non-GISRS laboratories. During this same period, a total of 77 human IVPP (i.e. A(H3N2), A(H5N1), A(H7N7), and A(H7N9) viruses) were recorded in the IVTM by 9 different countries.

### 2.3 Genetic sequence data

Several manufacturers have been using GSD to develop vaccines and other influenza-related products. The use of biosynthetic technologies in influenza product development is anticipated to increase. To assist the AG in developing guidance for the Director-General on the best process to further discuss and resolve issues related to the handling of GSD from A(H5N1) and other IVPP as part of the PIP Framework, a TEWG was established in late 2013. The TEWG’s report to the AG addressed, *inter alia*, the uses of GSD, regulatory and intellectual property issues, monitoring and tracing of GSD, and biosecurity and biosafety issues.

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26 See PIP Framework, Section 5.4.2.
During its April 2014 meeting, the AG affirmed that as GSD falls within the PIP Framework (e.g. Section 5.2; Annex 4, Point 9; Annex 5 “Guiding Principles”), the spirit of the Framework and the importance of maintaining equal footing for the sharing of viruses and benefits derived therefrom must be kept in mind in considering issues related to the handling of GSD for H5N1 and other IVPP. There were different perspectives, however, on whether GSD are included in the definition of PIP biological materials.

3 BENEFIT SHARING

3.1 Status of agreements entered into with industry

SMTAs 2 are individually negotiated contracts between WHO and companies and institutions that receive PIP biological materials. They are a key mechanism to ensure that vaccines, antivirals and other supplies are delivered to WHO for use in countries that need them during a pandemic. GlaxoSmithKline (GSK) and the Serum Institute of India have each committed to providing WHO 10% of pandemic influenza vaccines as they come off the production line; Sanofi Pasteur will provide 15% of its pandemic vaccine production. GSK has also committed to providing access to 10 million treatment courses of antiviral medicine. Discussions are on-going with two large vaccine manufacturers and have been initiated with 12 manufacturers of other products needed during a pandemic (e.g. diagnostic manufacturers). Three SMTAs 2 have been concluded with non-manufacturing entities: Harvard College, Public Health England Porton Down and the University of Florida; several more are in process.

During SMTA 2 negotiations, several vaccine manufacturers expressed concern about their ability to export influenza vaccine to WHO in real-time during a pandemic if the country where the vaccine is produced does not authorize its export. In April 2014, the AG recommended that the Director-General seek periodic assurances from Member States that they would enable companies to fulfil their SMTA 2 commitments to supply pandemic vaccine to WHO on a real-time basis.

3.2 Financial report on the Partnership Contribution

A methodology and formula to calculate how much each Contributor should pay, as well as standard operating procedures for the Partnership Contribution, were previously established.

The PIP Secretariat issues an annual questionnaire to identify entities that should contribute to the total annual Partnership Contribution of USD 28 million. The 2013 questionnaire identified 36 companies; as of 30 September 2014, 25 companies have contributed USD 27,201,025. It has been challenging for some companies to pay their share of the Partnership Contribution in a single payment. Following guidance from the AG, the PIP Secretariat gave such companies, on an exceptional basis, the option of paying in installments.

3.3 Use of the Partnership Contribution

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31 See [http://www.who.int/influenza/pip/2013_PC_Final_Results_30May2014.pdf?ua=1](http://www.who.int/influenza/pip/2013_PC_Final_Results_30May2014.pdf?ua=1).
The WHO Secretariat collaborated with the AG, industry and other stakeholders to develop the Partnership Contribution Implementation Plan, 2013 – 2016 which was approved by the Director-General in January 2014.\textsuperscript{32} The plan provides outcomes, outputs, key deliverables, indicators and estimated budgets for use of Partnership Contribution resources in the areas of influenza laboratory and surveillance; burden of disease studies; regulatory capacity; risk communications and planning for deployment of pandemic supplies. The Implementation Plan is underpinned by the Pandemic Influenza Preparedness Partnership Contribution, 2013-2016: Gap Analyses.\textsuperscript{33} The analyses provide a global and regional snapshot of gaps and needs for pandemic preparedness; they were used as the basis for regional offices to prioritize countries for receipt of Partnership Contribution resources.

From May to September 2014, USD 17.36 million was allocated to technical programmes in WHO regional offices and headquarters against detailed work plans for implementation in 2014 across 43 priority countries. Approximately 70% of the funds were allocated for laboratory and surveillance activities; the remaining 30% were distributed between burden of disease (5%), risk communications (10%), planning for deployment (5%), and regulatory capacity building activities (10%).

Work in 2014 has focused on a range of normative activities such as development of guidelines, standards, tools, common procedures, coalition building, country level capacity and needs assessments leading to country level actions plans, procurement of some laboratory supplies, and training. (Note: a report of all implementation activities in 2014 and their impact will be issued in January 2015 and will include priority areas and targets for the 2015 work plan.)

3.4 Global influenza vaccine production capacity

The Global Action Plan for Influenza Vaccines (GAP) is a comprehensive strategy to reduce the shortage of influenza vaccines for seasonal epidemics and pandemic influenza. Its focus, building vaccine production capacity, works in synergy with the pandemic influenza preparedness capacity building activities supported by the Partnership Contribution. Since 2006, GAP has helped to increase potential global vaccine production capacity from 500 million doses in 2006 to 1.5 billion doses in 2013; manufacturing capacity is projected to reach five billion doses by 2016.\textsuperscript{34}

3.5 Vaccine stockpiles

In November 2013, the Strategic Advisory Group of Experts (SAGE) on Immunization, at the request of WHO, reviewed its 2007 recommended policies for the establishment and use of influenza A(H5N1) vaccine stockpiles during a pandemic. Based in part on increased access to pandemic vaccine production afforded by the PIP Framework and the unchanged global epidemiological picture for A(H5N1), SAGE agreed that WHO should not create a stockpile of influenza A(H5N1) vaccine, but should ensure immediate access to pandemic vaccines under the PIP Framework.\textsuperscript{35} SAGE also highlighted the need for WHO to ensure equitable

\textsuperscript{33} See http://www.who.int/influenza/pip/pip_pc_ga.pdf?ua=1.
\textsuperscript{34} See http://apps.who.int/iris/bitstream/10665/112307/1/9789241507011_eng.pdf?ua=1.
access to pandemic vaccine by low- and middle-income countries and to develop a strategy for timely communication of any delays in pandemic vaccine availability.

5 GOVERNANCE

Section 7.4.2 requires that “[t]he Framework and its Annexes […] be reviewed by 2016 with a view to proposing revisions reflecting developments as appropriate, to the World Health Assembly in 2017, through the Executive Board.” The AG and PIP Secretariat undertook preliminary discussions regarding the objectives of the review and the process to conduct the review.

A new Chair (Dr William Kwabena Ampofo from Ghana) and Vice-Chair (Professor Rajae El Aouad from Morocco) assumed responsibilities for the AG in October 2013 as required by the PIP Framework (Annex 3, Section 3.2). In 2015, six new members will join the AG to replace one-third of the existing AG members, in accordance with AG Terms of Reference sections 3.2 and 3.3. The process to identify members to be renewed will commence at the end of the October 2014 meeting.

The AG met in October 2013 and April 2014. Consultations with industry and other stakeholders occurred at each meeting; both groups noted the importance of communications and transparency and how this might be improved.

Following each AG meeting, two Information Sessions led by the AG Chair were held: one for the Permanent Missions in Geneva and the other for industry and other stakeholders.

Table 1. Distribution of reverse transcription polymerase chain reaction (RT-PCR) kits for diagnosis and surveillance of influenza viruses (seasonal and viruses with human pandemic potential), 1 August 2013 through 31 July 2014

<table>
<thead>
<tr>
<th>Virus type</th>
<th>No. of kits</th>
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<tbody>
<tr>
<td>H5</td>
<td>56</td>
</tr>
<tr>
<td>H7</td>
<td>38</td>
</tr>
<tr>
<td>Other (seasonal)</td>
<td>444</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>538</strong></td>
</tr>
</tbody>
</table>

Table 2. Performance of participating laboratories in the annual external quality assessment of PCR testing, April-June 2013

<table>
<thead>
<tr>
<th>No. of correct results (10 samples tested)</th>
<th>No. (%) of laboratories (N=158 participating laboratories)</th>
</tr>
</thead>
<tbody>
<tr>
<td>10 samples correct</td>
<td>130 (82.3)</td>
</tr>
<tr>
<td>9 samples correct</td>
<td>7 (4.4)</td>
</tr>
<tr>
<td>6-8 samples correct</td>
<td>19 (12.0)</td>
</tr>
<tr>
<td>&lt;6 samples correct</td>
<td>2 (1.3)</td>
</tr>
</tbody>
</table>

Note: Among 140 participants reporting influenza A(H5) results, 120 (86%) correctly identified all four influenza A(H5) samples. Compared with the six most recent surveys, the ‘all correct’ rate remained stable at around 88% for influenza A(H5). Proficiency in detecting less commonly circulating influenza viruses such as the A(H9) subtype increased.

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37 GISRS-related data cover the 12-month period 1 August 2013 through 31 July 2014. This allows for continuous reporting of GISRS data (i.e. GISRS data in the 2013 Annual Report concluded on 31 July 2013) and for time to tabulate and analyze data.

38 During this time, the WHO Collaborating Centre (Atlanta) distributed 538 RT-PCR kits to 96 GISRS laboratories in 87 countries.

Table 3. Characterization of influenza viruses with human pandemic potential by WHO Collaborating Centres, 1 August 2013 through 31 July 2014

<table>
<thead>
<tr>
<th>Influenza virus</th>
<th>No. of viruses characterized</th>
<th>No. of countries providing viruses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Influenza A(H5N1)</td>
<td>14</td>
<td>4</td>
</tr>
<tr>
<td>Influenza A(H5N6)</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Influenza A(H7N9)</td>
<td>89</td>
<td>3</td>
</tr>
<tr>
<td>Influenza A(H9N2)</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Influenza A(H10N8)</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Influenza A(H3N2)v</td>
<td>2</td>
<td>1</td>
</tr>
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</table>
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1 See PIP Framework, Section 7.2 5 and Annex 3, Section 2 for the seven areas to be covered by the annual report.
Annex 7

Results of the process to renew one-third of Advisory Group members

African Region:
- Dr Adrian Puren’s name will be added to the Roster for a possible future second appointment
- 1-year term extension: Dr William Ampofo
- 2-year term extension: Dr Hama Issa Moussa

Region of the Americas:
- Mr David Hohman’s name will be added to the Roster for a possible future second appointment
- 1-year term extension: Dr Rainer Engelhardt
- 2-year term extension: Dr Jarbas Barbosa da Silva Jr

Eastern Mediterranean Region:
- Prof Rajae El Aouad’s name will be added to the Roster for a possible future second appointment
- 1-year term extension: Dr Amr M. Kandeel
- 2-year term extension: Prof Ziad Memish

European Region:
- Dr Silvia Bino’s name will be added to the Roster for a possible future second appointment
- 1-year term extension: Prof Oleg I Kiselev
- 2-year term extension: Prof Didier Houssin

South-East Asia Region:
- Dr Rungrueng Kitphati’s name will be added to the Roster for a possible future second appointment
- 1-year term extension: Prof Tjandra Y. Aditama
- 2-year term extension: Dr P.V. Venugopal

Western Pacific Region:
- Dr Nobuhiko Okabe’s name will be added to the Roster for a possible future second appointment
- 1-year term extension: Dr Fran McGrath
- 2-year term extension: Dr Yu Wang

1 Lots were drawn by region