Q1: What is the Pandemic Influenza Preparedness Framework?

A1: The Pandemic Influenza Preparedness Framework or ‘PIP Framework’ is an innovative public health instrument that seeks to better prepare the world to respond to pandemic influenza.

Q2: What is pandemic influenza?

A2: Pandemic influenza is a rare and unpredictable event. It occurs when a new influenza virus – to which people have no pre-existing immunity – appears. With nothing to contain it, a pandemic influenza virus can quickly spread to all parts of the world. Some pandemics may result in large numbers of severe infections while others will result in large numbers of milder infections; the reasons behind these differences are not completely understood.

Q3: How is a pandemic different from seasonal influenza?

A3: Seasonal influenza viruses circulate and cause disease in humans every year. In temperate climates, disease tends to occur seasonally in the winter months spreading from person-to-person. People can get infected multiple times throughout their lives. Seasonal viruses have differing degrees of severity and can affect certain people (e.g. the very young, the elderly, pregnant women) in different ways.

Q4: What is pandemic preparedness?

A4: Influenza pandemics are unpredictable but recurring events that can cause severe social, economic, and political stress. Preparedness requires a whole-of-society approach to ensure that when the next pandemic strikes, all countries in the world, working in solidarity, will be able to respond rapidly and effectively to reduce morbidity and mortality.

Preparedness planning should occur at community, national and international levels. At national and community levels, essential elements of preparedness include: early warning systems; good epidemiological surveillance; a strong laboratory network; functioning health systems with well-trained people able to recognize and manage potential pandemic influenza as it emerges; an emergency response system, regularly tested, supported and supplied to respond rapidly and effectively; and good risk communications to explain the nature of the threat and engage communities in behaviors needed to overcome the threat.

Countries also need to be prepared to participate in the international dimension of the response and be ready to work collaboratively within the global architecture.

This is where the PIP Framework comes into play: it is a unique partnership between all the major players able to make the international response to pandemic influenza nimble, flexible, effective and equitable.
Q5: Why was the PIP Framework necessary?

A5: Vaccination is a critically important intervention to prevent infection and severe outcomes caused by influenza viruses – notably pandemic viruses. In order to make an effective pandemic vaccine, manufacturers depend on countries to detect and share influenza viruses that have the potential to cause a pandemic. Many countries, some of whom supply the viruses to make these vaccines, however, are unable to afford or access vaccines and other life-saving measures, such as antiviral medicines. Over time, it became clear to Member States that a formal arrangement was needed:

- to increase the access of developing countries to vaccines and other pandemic related supplies; and
- to improve and strengthen the sharing of influenza viruses with human pandemic potential for global monitoring, risk assessment and the development of safe and effective pandemic influenza vaccines.

Q6: When did the PIP Framework come about?

A6: The emergence of avian influenza A (H5N1) or ‘bird flu’ in 1997 raised concerns that a new human pandemic virus might develop. These concerns increased during outbreaks of human H5N1 influenza in 2006. In 2007, WHO and Member States came together to start negotiating and interacting with industry, civil society organizations and other stakeholders over the next four years to draft the Framework. The PIP Framework was unanimously adopted by the 194 Member States of the WHO during the World Health Assembly on 24 May 2011.

Q7: What are the objectives of the PIP Framework?

A7: The PIP Framework has two objectives which are to be pursued on equal footing:

- improve the sharing of influenza viruses with the potential to cause a human pandemic; and
- establish more predictable, efficient, and equitable access to the benefits that result from the sharing of such viruses, notably vaccines and antiviral medicines.

Q8: What influenza viruses does the PIP Framework cover?

A8: The PIP Framework applies ONLY to influenza viruses with human pandemic potential, such as influenza H5N1. It does NOT apply to seasonal influenza viruses which cause epidemics every year. The Framework also covers other biological materials, termed ‘PIP biological materials’ or ‘PIPBM’, which are defined in Section 4.1 of the Framework.

Q9: How are influenza viruses shared under the PIP Framework?

A9: WHO coordinates the sharing of influenza viruses through an international network of public health laboratories called the ‘Global Influenza Surveillance and Response System’ (GISRS). This network has been collecting and monitoring influenza viruses for more than 60 years. The PIP Framework established Terms of Reference for the GISRS laboratories related to their work with influenza viruses with human pandemic potential.

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4 See http://www.who.int/mediacentre/factsheets/fs211/en/
5 See http://www.who.int/influenza/gisrs_laboratory/en/
Q10: What are some of the key functions of the GISRS network?

A10: More than 140 National Influenza Centres (NICs) in the GISRS collect and test specimens for influenza viruses – both seasonal viruses and those with human pandemic potential. Under the PIP Framework, countries are expected to support their NICs and ensure that they share influenza viruses with pandemic potential in a rapid, systematic, and timely manner with GISRS.

A small number of specialized reference laboratories in GISRS perform molecular testing and other advanced analyses. GISRS laboratories use the viruses to develop candidate vaccine viruses, testing kits and different types of reagents. Moreover, laboratory, clinical and epidemiological data are used to assess the risk that influenza viruses with human pandemic potential might evolve into pandemic viruses.

Q11: How are influenza viruses with human pandemic potential tracked in GISRS?

A11: An electronic, internet-based tool called the Influenza Virus Traceability Mechanism (IVTM)\(^6\) is used to track viruses with human pandemic potential and PIPBM. The IVTM records their entry into the GISRS, as well as their subsequent transfer to other GISRS laboratories and to external entities, such as manufacturers of vaccines. The results of molecular analyses and tests on these viruses and materials are also recorded in the IVTM. The IVTM helps to make the work of GISRS and the sharing of viruses with pandemic potential more transparent – a key principle of the Framework.

Q12: What is the role of a Standard Material Transfer Agreement 1 in virus sharing?

A12: A Standard Material Transfer Agreement 1 (SMTA 1) is a binding contract that establishes the conditions under which laboratories in GISRS exchange viruses with human pandemic potential and other PIPBM among themselves. An SMTA 1 covers many matters including:

- handling of PIPBM in accordance with WHO guidelines and national bio-safety standards
- transfers of PIPBM to entities outside GISRS
- use of the IVTM
- research and publications
- intellectual property rights
- dispute resolution

Q13: How are benefits accessed under the PIP Framework?

A13: The Framework establishes two mechanisms to facilitate access to the benefits that result from the sharing of viruses with human pandemic potential:

- the Partnership Contribution\(^7\)
- the Standard Material Transfer Agreement 2\(^8\)

Q14: What is the Partnership Contribution (PC) and who contributes to it?

A14: The Partnership Contribution is an annual contribution to WHO from influenza vaccine, pharmaceutical and diagnostic manufacturers that use the WHO GISRS. Manufacturers ‘use GISRS’ for example, by using data and information generated by GISRS (see Question 10), or requesting PIPBM to make pandemic-related products, such as vaccines. Under the Framework, WHO is to receive a total of USD 28 million each year in contributions; the amount is based on the estimated costs to run the WHO GISRS.

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Q15: How is the amount of each company’s portion of the Partnership Contribution decided?

A15: Every year WHO issues a questionnaire to identify potential contributors. The Questionnaire is uploaded to the PIP Framework webpage and the link is sent to all previous year contributors, all companies and institutions that conduct research and development in the field of influenza, and all recipients of PIPBM recorded in the IVTM, with a request that they complete the Questionnaire. WHO has developed a set of standard operating procedures and a formula for calculating an individual company’s payment into the Partnership Contribution.

Q16: Who decides how the Partnership Contribution will be used?

A16: The Director-General decides how the contributions will be used. The decision is based on advice and consultation with the PIP Advisory Group, as well as interaction with industry and civil society. The WHO Executive Board plays a central role in deciding how to divide resources between pandemic preparedness and response.

Q17: What is the Partnership Contribution being used for?

A17: The Executive Board decided that for the first five years (2012-2016), approximately 70% of the Partnership Contribution resources should be used for pandemic preparedness activities and 30% should be reserved for use at the time of the next pandemic for response purposes. In addition a portion of Partnership Contribution funds, not exceeding 10% averaged over 2013-2016, is available to the PIP Secretariat to support implementation of the Framework.

Q18: What pandemic preparedness activities are funded by the Partnership Contribution?

A18: There are currently five broad areas of work for pandemic preparedness:

1) strengthening laboratory and surveillance capacities;
2) conducting burden of disease studies;
3) strengthening regulatory capacities;
4) strengthening risk communications; and
5) planning for deployment.

Activities in each of these areas are described in the PIP Partnership Contribution Implementation Plan. A Critical Path Analysis outlines the scope and scale of the preparedness programme.

Q19: How were countries selected to receive Partnership Contribution resources for preparedness activities?

A19: Countries were prioritized by WHO region using the results of the Partnership Contribution Gap Analyses which reviewed the risks and needs in each area of work. Prioritization of countries was based on many factors including WHO knowledge of the status of capacities in countries; the self-reported readiness and capacity of countries to absorb support; the capacity of WHO to provide support; and sustainability of the proposed efforts.

Q20: What is the status of pandemic preparedness activities being implemented using Partnership Contribution resources?

A20: Detailed information about the implementation of capacity building activities and associated financial data can be found in the PIP Partnership Contribution Annual Report and the PIP Partnership Implementation Portal which is updated quarterly.

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9 See http://www.who.int/influenza/pip/benefit_sharing/pc_collection_sop.pdf?ua=1
10 See http://www.who.int/influenza/pip/pc_distribution.pdf?ua=1
11 See http://www.who.int/influenza/pip/pip_pcimpplan_17jan2014.pdf?ua=1
12 See http://apps.who.int/iris/bitstream/10665/161368/1/WHO_HSE_PED_GIP_PIP_2015.1_eng.pdf?ua=1
13 See http://www.who.int/influenza/pip/pip_pc_ga.pdf?ua=1
14 See http://www.who.int/influenza/pip/benefit_sharing/PC_AnnualReport2015.pdf?ua=1
15 See https://extranet.who.int/pip-pc-implementation/
Q21: How will Partnership Contribution resources be used for pandemic response activities?

A21: The Partnership Contribution funds that have been set aside for pandemic response will allow WHO to access the products and services covered under Standard Material Transfer Agreements 2. These include pandemic vaccines, antiviral medicines and diagnostics. During a pandemic there will be limited or no opportunities to convene the PIP Advisory Group or meet with industry and other stakeholders to discuss the use of ‘response’ resources. In view of this, the PIP Advisory Group, with input from industry and other stakeholders, developed ‘Guiding Principles for Use of PIP Partnership Contribution Response Funds’ 16. They will provide the basis for the Director-General to decide on the use of the Partnership Contribution for response purposes.

Q22: What is the role of a Standard Material Transfer Agreement 2 in accessing benefits?

A22: A Standard Material Transfer Agreement 2 (SMTA 2) is a legally binding agreement between WHO and non-GSIRS entities (including manufacturers, biotechnology firms, and academic and research institutions) that receive PIPBM from GSIRS. Entities commit to provide specified benefits based on the nature of their work and their capacities. Benefits include pandemic influenza vaccines, antiviral medicines or other pandemic-related products or technologies. The agreements specify that the products will be delivered at the time of the next pandemic to WHO for use in countries that need them. Up-to-date information about signed SMTAs 2 17 can be found on the PIP website.

Q23: Do all countries have access to benefits? For example, if a country does not have any viruses with pandemic potential to share, will it still have access to benefits?

A23: All countries have access to collective benefits such as global risk assessment analyses and information, and materials such as candidate vaccine viruses, subject to applicable rules and regulations. Targeted benefits, such as Partnership Contribution funds to support capacity building projects, and pandemic response products, such as vaccines, antivirals and other products, are allocated according to public health risk and need. A country may be identified to receive targeted support even if it has not shared any viruses with pandemic potential.

Q24: What is the relationship between the PIP Framework and the International Health Regulations?

A24: The International Health Regulations (IHR) are an international agreement under the WHO Constitution that is binding on 196 States Parties, including all WHO Member States. First adopted as the International Sanitary Regulations in 1951, the IHR underwent significant revisions throughout their history and more recently in 2005 to address a range of issues brought to the global fore by major outbreaks of disease such as Ebola in the 1990s and the emergence of severe acute respiratory syndrome (“SARS”) in 2003. The Regulations now include:

(a) an “all-hazards” approach covering “an illness or medical condition, irrespective of origin or source, that presents or could present significant harm to humans”; they are not limited to specific diseases or modes of transmission;
(b) the obligation for States Parties to develop certain minimum core public health capacities;
(c) the obligation for States Parties to notify WHO of events that may constitute a public health emergency of international concern (PHEIC) according to defined criteria and
(d) specific human rights provisions.

The spread of a new influenza virus could be determined by the WHO Director-General to constitute a public health emergency of international concern under the IHR.

Ensuring that PIP Partnership Contribution funds are implemented in a manner that achieves coherence, complementarity and synergy with IHR activities is fundamental to achieving the greatest impact with limited public health resources.

15 See http://www.who.int/influenza/pip/guiding_principles_pc_response_funds.pdf?ua=1
17 See http://www.who.int/influenza/pip/benefit_sharing/smta2_signed/en/
Q25: Who oversees the implementation of the PIP Framework?

A25: Under the provisions of the Framework, three different bodies play a role in overseeing implementation of the Framework: 1) the World Health Assembly oversees implementation; 2) the Director-General promotes implementation; and 3) an Advisory Group – a group of eighteen independent experts from all six WHO regions – monitors implementation of the Framework and provides recommendations to the Director-General on its evaluation of implementation. In formulating advice to the Director-General, the Advisory Group interacts with industry and other stakeholders.

Q26: What is the structure and composition of the Advisory Group?

A26: The Advisory Group is comprised of 18 members, drawn from three Member States in each WHO region, and appointed by the Director-General. The members are experts in health policy, public health, or influenza. The biographies of current and previous Advisory Group members can be found under the Advisory Group section of the website. Members serve three-year terms. They select from among themselves a Chairperson and a Vice-Chairperson who serve for two years. The Director-General regularly accepts nominations of representatives and draws from this list to replace outgoing members.

Q27: How are potential conflicts of interest among Advisory Group members assessed?

A27: Prior to being appointed, each nominee completes a WHO Declaration of Interests (DOI) which is reviewed and assessed using WHO standard procedures. Prior to each meeting, all Advisory Group members complete a new DOI form to inform WHO about real, potential or actual conflicts of interests related to the subject matter of the meeting. Any conflicts of interests and/or affiliations that are relevant to the meeting are disclosed and reported in the meeting report; Advisory Group meeting reports can be found on the PIP website.

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18 See http://www.who.int/influenza/pip/advisory_group/members/en/
19 See http://www.who.int/influenza/pip/pip_meetings_consultations/en/