

**Pandemic Influenza Preparedness Framework (“PIP Framework”)
Advisory Group Annual Report to the Director-General
Under PIP Framework Section 7.2.5**

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Acronyms and abbreviations

AOW	area of work
CC	WHO Collaborating Centre
CVV	candidate vaccine virus
EQAP	External Quality Assessment Programme
GAP	Global Action Plan for Influenza Vaccines
GHSA	Global Health Security Agenda
GIP	WHO's Global Influenza Programme
GISRS	Global Influenza Surveillance and Response System
GSD	genetic sequence data
IATA	International Air Transport Association
ICAO	International Civil Aviation Organization
IHR	International Health Regulations
IVPP	influenza viruses with human pandemic potential
IVTM	Influenza Virus Traceability Mechanism
NIC	National Influenza Centre
PC	Partnership Contribution
PIP	pandemic influenza preparedness
PIPB	pandemic influenza preparedness biological material
PCR	polymerase chain reaction
SAGE	Strategic Advisory Group of Experts
SMTA	Standard Material Transfer Agreement
SOP	standard operating procedure
TIPRA	Tool for Influenza Pandemic Risk Assessment
TWG	Technical Working Group
WHA	World Health Assembly
WHO	World Health Organization

EXECUTIVE SUMMARY

1. May 2016 marked the 5th anniversary of the adoption by the World Health Assembly (WHA) of the Pandemic Influenza Preparedness Framework for the sharing of influenza viruses and access to vaccines and other benefits (the “PIP Framework” or “Framework”) which recognized the urgent need to improve global pandemic influenza preparedness and response. Under the Framework, Member States placed on an equal footing the sharing of viruses for global monitoring, risk assessment and development of safe and effective vaccines, and the access to benefits arising from such sharing, recognizing these two measures as equally important parts of the collective action for global public health.

2. The PIP Advisory Group is part of the governance and oversight mechanism of the Framework. Each year, it submits a report on its evaluation of the implementation of the Framework to the Director-General.¹

3. With the exception of GISRS-related data, this Report describes achievements and challenges for the period 1 October 2015–30 September 2016. GISRS-related data cover the period 1 August 2015–31 July 2016. Any exceptions to these time frames are specifically noted in the Report.

4. It is our view that implementation of the Framework is maturing, reflecting in part the increased trust among WHO, Member States, industry and other stakeholders. Gains in benefit sharing achieved through a growing number of concluded Standard Material Transfer Agreements 2 (SMTA 2s) and collection of >90% of the annual USD 28M in Partnership Contribution (PC) resources are testimony to the strength of this unique partnership with influenza vaccine, diagnostic and pharmaceutical manufacturers.

5. Not surprisingly, however, implementation remains a work-in-progress. The decline in the sharing of influenza viruses with pandemic potential (IVPP) compared with the number of confirmed human cases is of particular concern. Efforts to understand and address this decline suggest that improved outreach and communications can play an important role in this and other aspects of implementing the Framework.

6. Taking stock of the achievements and challenges described in this Report, along with the soon-to-be-completed five-year review of the PIP Framework and the development of a new high-level PIP Partnership Contribution Implementation Plan, present opportunities to adjust course as needed to achieve the objectives of the Framework.

1.1 Virus sharing: key findings

7. The Advisory Group noted with concern the marked decrease in the number of H5, H6, H7, H9 and H10 influenza viruses shared with the Global Influenza Surveillance and Response System (GISRS), as compared with the number of confirmed human cases during 2011–2016. Work is underway to understand the reasons for the decline and how to reverse it. Direct communication with GISRS laboratories and countries, along with involvement of WHO regional and country offices is critical and resulted in improved virus sharing recently by one country.

¹ As required under PIP Framework, Section 7.2.5 and Annex 3, Section 2.6.

8. The Advisory Group made its initial recommendations to the Director-General on the optimal characteristics of a genetic sequence data (GSD) sharing system based in part on a report from a Technical Working Group (TWG). The Advisory Group noted that the TWG was unable to reach consensus on terminology and that this remains an unresolved issue. The varying views of databases, Member States and stakeholders suggested that this topic will continue to generate diverse opinions and ongoing discussions.

9. Although GISRS continues to be challenged by gaps in its geographical coverage, basic laboratory capacity has been strengthened as a key element of PC implementation. PC resources also helped support an 81% increase in shipments of IVPP and seasonal influenza viruses using the WHO Shipping Fund Project.

10. The proportion of laboratories participating in the WHO External Quality Assessment Programme that correctly identified 100% of influenza virus samples increased from 71% in 2014 to 82% in 2015.

11. WHO launched and implemented the Tool for Influenza Pandemic Risk Assessment (TIPRA) to provide a standardized and transparent approach to support the risk assessment of influenza viruses with pandemic potential. Version 1 of TIPRA was used to conduct assessments of influenza viruses H5N6, H7N9 and H9N2 in 2016. Continued experience with the Tool will facilitate further refinement as needed in the future.

1.2 Benefit sharing: key findings

12. WHO concluded 22 SMTA 2s, including the fourth with a vaccine manufacturer, the first with a diagnostics manufacturer, and 20 with research and academic institutions. While the pace of concluding SMTAs 2s with vaccine and diagnostics manufacturers accelerated in the last year, it remains a lengthy process and can require two or more years for individual companies. The Advisory Group noted the continued reluctance of some companies to engage in negotiations or commit to sharing benefits.

13. Each year, $\geq 90\%$ of the annual PC of USD 28 M has been collected. The PIP Secretariat is diligent in following up with contributors on funds which are outstanding.

14. By the end of 2015, approximately USD 31 M had been distributed in 73 countries for pandemic preparedness activities in laboratory and surveillance capacity building; measuring the burden of influenza disease; regulatory capacity building; planning for deployment of pandemic supplies; and risk communications. The project is on track to meet most outcome and output targets as defined in the Partnership Contribution High Level Implementation Plan.

1.3 Governance: key findings

15. Industry, in interactions during meetings of the Advisory Group, reiterated its support for the PIP Framework's aims on preparedness and response. This mark of trust building is important for the sustainability of the Framework. GISRS members expressed interest in having increased interaction with the Advisory Group and the Advisory Group welcomed this.

16. Progress has been made in communications and outreach, including the development of new materials and products. However, the range of actors and varying views on PIP Framework issues, such as GSD, present ongoing challenges. At country level, ministries other than health must be engaged, e.g. agricultural ministries with respect to animal influenza viruses.

17. The PIP Framework continues to gain visibility and was cited “...as a template for creating new agreements for other infectious agents that have caused, or may potentially cause, [public health emergencies of international concern] PHEICs...based on the principle of balancing the sharing of samples and data with benefit sharing on an equal footing.”²

18. The Advisory Group has underscored the importance of synergizing PIP capacity building activities with those related to the International Health Regulations (2005) and the Global Health Security Agenda. More work, however, is required to achieve the desired synergy and coherence.

19. The Advisory Group provided advice to the Director-General on the scope of the five-year review of the PIP Framework and on the Terms of Reference for the members of the PIP Review Group. The review started in January 2016 and is on track for a final report to be submitted to the Director-General at the end of October 2016.

² Implementation of the International Health Regulations (2005). Report of the Review Committee on the Role of the International Health Regulations (2005) in the Ebola Outbreak and Response. Report by the Director-General. Geneva: World Health Organization; 2016 (A69/21)
(http://apps.who.int/gb/ebwha/pdf_files/WHA69/A69_21-en.pdf?ua=1).

1 INTRODUCTION

1. Each year, the Advisory Group submits to the Director-General a report on its evaluation of the implementation of the Pandemic Influenza Preparedness Framework (the “PIP Framework” or “Framework”). The Advisory Group’s findings are organized into three sections: virus sharing, benefit sharing and governance. The Report addresses the seven topic areas (indexed in Annex 1) specified for review in the Framework.³

2. With the exception of data related to the Global Influenza Surveillance and Response System (GISRS), this Report describes achievements and challenges for the period 1 October 2015-30 September 2016. GISRS-related data cover the period 1 August 2015-31 July 2016. Any exceptions to these time frames are specifically noted in the Report.

2 VIRUS SHARING

2.1 Global Influenza Surveillance and Response System

General

3. Improving and strengthening GISRS – the WHO-coordinated international network of public health laboratories – is essential to pandemic influenza preparedness and response at the global, regional and country levels. Global virus detection capacity, as measured through the WHO external quality assessment programme (EQAP), found that the proportion of voluntarily participating National Influenza Centres (NICs) and other national laboratories that correctly identified 100% of influenza virus samples increased from 71% in 2014 to 82% in 2015 (see Annex 2 for more information about EQAP, including performance of participating laboratories from 2007 to the present).⁴ Performance in EQAP is also used as an indicator in the Partnership Contribution Implementation Plan for measuring progress in laboratory and surveillance capacity in those countries that receive Partnership Contribution (PC) resources.⁵

4. No new NICs have been added since the designation of a NIC in Zambia in September 2015. Although GISRS continues to be challenged by gaps in its geographical coverage, basic laboratory capacity has been strengthened in countries without NICs as a key element of PC implementation (see section 3.3).

³ The seven areas specified in PIP Framework, Section 7.2 5 and Annex 3, Section 2.6 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; the sharing of influenza viruses and access to vaccines and other benefits; and the use of financial and non-financial contributions.

⁴ Detection of influenza virus subtype A by polymerase chain reaction: WHO external quality assessment programme summary analysis, 2015. Weekly Epidemiological Record 2016; 9:1–12 (<http://www.who.int/wer/2016/wer9101.pdf>).

⁵ Detailed information about performance indicators for PC implementation can be found in Pandemic Influenza Preparedness Framework. Partnership Contribution 2015 Annual Report. Geneva: World Health Organization; 2016 (http://www.who.int/influenza/pip/benefit_sharing/PC_AnnualReport2015.pdf?ua=1).

Risk assessment and response

5. New human infections with avian and swine influenza viruses continue to be reported; A(H5N1) and A(H7N9) comprise the majority of these infections. Antigenic and genetic analyses performed by the WHO GISRS Collaborating Centres (CCs) are essential for risk assessment and response including the development and updating of zoonotic influenza candidate vaccine viruses (CVVs) (see section 2.2 for more information).⁶

6. After two years of development, the Global Influenza Programme (GIP) launched and initiated use of Version 1 of the Tool for Influenza Pandemic Risk Assessment (TIPRA) in May 2016.⁷ TIPRA, by providing a standardized and transparent approach for risk assessment of IVPP, supports WHO's mandate^{8,9} to provide Member States with pandemic risk assessments during the inter-pandemic and alert phases. GISRS and global experts characterize the risk using an 11-step process based on available information about virus properties, attributes in the human population, ecology and epidemiology. The Tool also helps to identify gaps and steer activities to improve understanding about the virus. TIPRA was used to conduct assessments of influenza viruses H5N6, H7N9 and H9N2 in 2016. Continued experience with the Tool will facilitate further refinement as needed in the future.

7. Other risk assessment and response activities include GIP's monthly risk assessments of the likelihood of sustained human-to-human transmission of IVPP¹⁰ and publication in July 2016 of a document summarizing key information and guidance about avian influenza.¹¹

Shipping Fund Project

8. An important practical consideration for countries to share influenza viruses is having the necessary financial resources and technical knowledge to collect, package and ship infectious substances. Financial support for shipment of both IVPP and seasonal viruses is provided through the WHO Shipping Fund Project. WHO's expanded outreach and communication to GISRS laboratories about the Shipping Fund Project has increased awareness of virus sharing and contributed to the increase in both the number laboratories shipping viruses, and the number of shipments during this reporting period (Table 1).

9. The average cost per shipment increased from USD 1,630 in 2014-2015 to USD 1,736 in 2015-2016 (range USD 500-700 to USD 4,000 per shipment). The availability of reliable and enhanced funding through the PIP PC helps to absorb year-to-year variations in shipping costs such as airport taxes, currency exchange rates and the price of fuel. The weight of the shipment and the logistical complexity, e.g. distance from a country to a CC or need for dry ice, also influence cost.

⁶ Antigenic and genetic characteristics of zoonotic influenza viruses and development of candidate vaccine viruses for pandemic preparedness. Geneva: World Health Organization; February 2016 (http://www.who.int/influenza/vaccines/virus/201602_zoonotic_vaccinevirusupdate.pdf?ua=1).

⁷ See http://www.who.int/influenza/areas_of_work/human_animal_interface/tipra/en/.

⁸ See PIP Framework Section 6.2.3.

⁹ Pandemic Influenza Risk Management: WHO interim guidance. Geneva: World Health Organization; June 2013 (http://www.who.int/influenza/preparedness/pandemic/influenza_risk_management/en/).

¹⁰ See http://www.who.int/influenza/human_animal_interface/HAI_Risk_Assessment/en/.

¹¹ Summary of Key Information Practical to Countries Experiencing Outbreaks of A(H5N1) and Other Subtypes of Avian Influenza. First Edition. Geneva: World Health Organization; July 2016 (http://www.who.int/influenza/publications/avian_influenza_packagev1/en/).

Table 1. WHO Shipping Fund Project activities, 2013 - 2016

	Reporting period		
	2013-2014	2014-2015	2015-2016
Number of shipments (seasonal viruses and IVPP)	122	118	213
Number of participating countries, areas and territories	73	74	95
Number of participating laboratories	82	83	112
Funds expended (USD)	209,577	192,341	369,783
Number of GISRS training workshops on infectious substances	2	11	7
Number of participants	NA	259	165
Number (%) of participants awarded certificates	NA	205 (79)	139 (84)

10. In addition to the GISRS training workshops, WHO's Department of Global Capacities, Alert and Response, in collaboration with the International Air Transport Association (IATA) and International Civil Aviation Organization (ICAO), developed a training course on the transport of infectious substances as part of its ongoing efforts to strengthen health security by implementing the International Health Regulations (IHR) (2005). The on-line training course comprises eight modules and is available in all six WHO official languages.¹² Since 2007, IATA-trained WHO staff have led in-person training sessions in the shipping of infectious substances for more than 1500 laboratory workers, including many from NICs.

Antiviral susceptibility surveillance

11. GISRS' technical capacity and operational functioning were enhanced by expert input and consultation. The Expert Working Group on Surveillance of Antiviral Susceptibility provided advice which led to the development of WHO guidance for NICs on antiviral susceptibility surveillance.¹³

Pandemic vaccine preparedness

12. In 2016 WHO released the report of an informal consultation held 29 June – 1 July 2015 with public and private sectors, including national policy makers and vaccine manufacturers. The consultation considered the complexities of pandemic vaccine response at the start of a pandemic.¹⁴ Outcomes included:

- a draft operational framework for pandemic vaccine response at the start of a pandemic when seasonal influenza might still be circulating;
- timelines for pandemic vaccine production; and
- an outline of WHO's process for vaccine response to an influenza pandemic or potential pandemic.

¹² See http://www.who.int/ihr/iss_shipping_training/en/.

¹³ Practical guidance for National Influenza Centres establishing or implementing neuraminidase inhibitor susceptibility surveillance. Geneva: World Health Organization; 2016 (http://apps.who.int/iris/bitstream/10665/205703/1/9789241510158_eng.pdf).

¹⁴ Influenza Vaccine Response during the Start of a Pandemic. Report of a WHO Informal Consultation held in Geneva, Switzerland: 29 June - 1 July 2015. Geneva: World Health Organization; 2016 (http://apps.who.int/iris/bitstream/10665/207751/1/WHO_OHE_PED_GIP_2016.1_eng.pdf?ua=1).

Burden of Disease

13. GIP is working to produce credible global burden estimates of influenza mortality, morbidity and hospitalization through literature reviews and special studies. A consultation on influenza burden was held in July 2016 to:

- review national and regional methods and estimates;
- identify gaps in influenza burden of disease studies; and
- agree on next steps to develop national, regional and global estimates.

Pilot testing of a standardized tool for measuring the associated economic burden due to influenza will be completed by the end of 2016.

Severity assessment

14. The Expert Working Group on Pandemic Influenza Severity Assessment met in November 2015 to discuss the use of different methods to set severity-related thresholds and to propose parameters for indicators of pandemic influenza severity. Work to define the minimum data required for modelling of pandemic severity and to explore the validity of the moving epidemic method of data analysis for severe acute respiratory infections datasets and datasets from tropical and subtropical countries is being undertaken.

Further information about GISRS capacities and functioning is in Annex 2.

2.2 Influenza Virus Traceability Mechanism

Tracking of PIP biological materials

15. An electronic, internet-based tool, the Influenza Virus Traceability Mechanism (IVTM), is used to track the sharing of PIP biological materials (PIPBM).¹⁵ The sharing of PIPBM, as recorded in the IVTM, contributes towards transparency in global public health surveillance. One human case can generate multiple PIPBM recorded in the IVTM. This can happen if multiple materials of human origin are collected; additionally, GISRS laboratories may generate new PIPBM, e.g. virus isolates and CVVs.

16. The initial entry of PIPBM into GISRS, as well as new PIPBM, and the subsequent transfer of PIPBM to other GISRS laboratories and to external entities, such as manufacturers of vaccines and research and academic institutions, are recorded in the IVTM. Basic information, e.g. shipment dates and virus subtype, is also recorded in the IVTM.

17. Since August 2011, a total of 863 records were entered in the IVTM: 759 for viruses and 699 for shipments.¹⁶ During this five-year period, a total 16 subtypes of IVPP (and 3 H9 viruses without the neuraminidase subtype specified) were recorded in the IVTM. The number of PIPBM for the current reporting period is shown in Table 2. The GIP has noted that improved understanding and usage of the IVTM is needed; work is underway to enhance the usability of the IVTM and to train users of the tool.

¹⁵ See PIP Framework, Section 4.1 for definition of PIPBM.

¹⁶ Virus data recorded through 31 July 2016 and shipment data recorded through 10 October 2016.

Table 2. Number of PIPBM recorded in the IVTM, by influenza virus subtype, 1 August 2015 - 31 July 2016

Influenza virus subtype	Human origin PIPBM	All PIPBM
A (H10N8)	2	2
A (H1N1)v	6	6
A (H3N2)v	12	12
A (H5N1)	42	64
A (H5N3)	0	2
A (H5N6)	4	4
A (H5N8)	0	8
A (H7N7)	2	3
A (H7N9)	17	17
A (H9N2)	5	5
Total	90	123

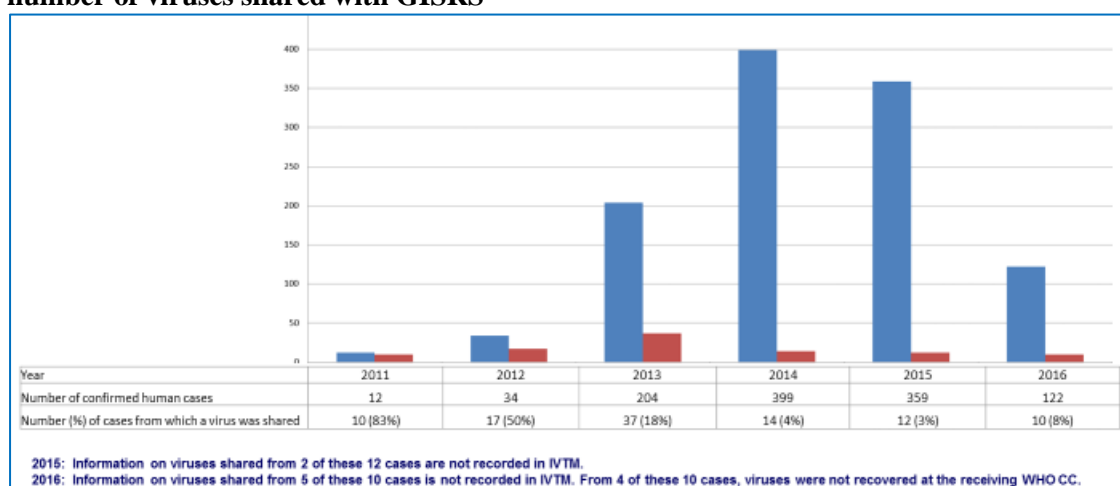
Virus sharing trends

18. Since 2013 there has been a marked decrease in the number of H5, H6, H7, H9 and H10 viruses shared with GISRS as compared with the number of confirmed human cases (Figure). During the current reporting period (1 August 2015 through 31 July 2016), four countries shared 22 viruses. This decrease was not observed in all WHO regions. At the April 2016 meeting of the Advisory Group, the Secretariat noted possible reasons for the decline including 1) a lack of understanding among NICs that sharing IVPP genetic sequence data (GSD) does not replace sharing biological material; 2) different interpretations of the phrasing of the PIP Framework that all IVPP should be shared “as feasible”; 3) export procedures that can be lengthy and involve ministries other than health; and 4) lack of clarity by laboratories with dual roles as both a NIC and a WHO CC about their international sharing responsibilities. Also, in some instances there may be insufficient material to share after confirmatory testing is completed or transport of material is sub-optimal.

19. The Advisory Group recommended in April 2016 that the Secretariat investigate the reasons for the decline in IVPP / PIPBM sharing in recent years. The Secretariat developed a questionnaire that was shared through the regional offices with the NICs in countries where viruses are not being systematically shared; findings will be presented at the October 2016 Advisory Group meeting. It has been observed that direct communication with GISRS laboratories and countries, along with involvement of WHO regional and country offices can have tangible effects. Following such communication efforts, virus sharing by one country recently increased.

20. The Advisory Group also recommended that the Secretariat (with guidance from GISRS) develop technical operational guidance and engage with WHO country and regional offices and national Ministries of Health to address barriers to sharing IVPP / PIPBM.

Figure. Confirmed human cases of influenza H5, H6, H7, H9 and H10 by year of onset and the number of viruses shared with GISRS^a



^aBlue bars = confirmed human case; red bars = cases from which a virus was shared

Candidate Vaccine Viruses

21. The development of CVVs, coordinated by WHO, remains an essential component of the overall global strategy for pandemic preparedness and is the first step towards timely vaccine production. WHO CCs shared 17 H5 and 5 H9 CVVs with GISRS and non-GISRS laboratories during 1 August 2015 - 31 July 2016, as recorded in the IVTM.

2.3 Genetic sequence data under the PIP Framework

22. Multiple work streams have assisted the Advisory Group in developing guidance for the Director-General on the best process for handling IVPP GSD under the Framework.¹⁷ These are detailed below and illustrated in the “GSD Timeline”.¹⁸

1) Survey of data sharing systems (August 2015 - December 2015)

The objective of this work stream was to gain a better understanding of how IVPP GSD are generated, shared and used by GISRS laboratories, academia, public health laboratories and industry. The Questionnaire was sent to 190 entities from GISRS, public health institutions, academia, and industry and completed by 41 data providers and data users. A report analysing results was published in April 2016.¹⁹ The Advisory Group noted that although most providers share IVPP GSD either through a database or public reports, sharing also occurs via email or other private means with the result that not all sequences are publicly accessible. The Advisory Group also noted that timely access to new GSD, completeness of data and acknowledgement of data providers could be improved; and that most laboratories do not have standard operating procedures (SOPs) for posting GSD.

2) Options to monitor use of IVPP GSD in end-products (February 2015 – April 2016)

The objective of this work stream was to identify different options for monitoring the use of IVPP GSD to develop end-products, such as vaccines, antivirals and diagnostics. Member States and

¹⁷ See PIP Framework, Section 5.2.4.

¹⁸ See http://www.who.int/influenza/pip/advisory_group/GSD_timeline.pdf?ua=1.

¹⁹ WHO survey on the sharing of genetic sequence data of influenza viruses with human pandemic potential. Results and analysis of data received 27 April 2016. Geneva: World Health Organization; 2016 (http://www.who.int/influenza/pip/advisory_group/GSDSurveyResults.pdf?ua=1).

stakeholders were invited to provide comments on the draft paper which was published in October 2016.²⁰ The paper concluded that monitoring the use of IVPP GSD to develop commercial products would likely: a) require a combination of upstream and downstream tools and approaches; b) depend on publicly accessible source identification using unique identifiers such as accession numbers; and c) require collaboration with a number of entities, including databases, GISRS laboratories, industry and other stakeholders.

3) “Optimal characteristics of a GSD sharing system best suited to meet the objectives of the Framework” (April 2015-June 2016)

To support its work on GSD, in April 2015, the Advisory Group recommended establishment of a Technical Working Group (TWG) that would bring together experts with knowledge and expertise in fields such as influenza research, bioinformatics and regulatory policy. The TWG was established in July 2015 and held three meetings. It consulted broadly with Member States, industry, civil society organizations and academia. The TWG posted its draft report on the PIP webpage on 20 November 2015, inviting Member States and stakeholders to submit comments through 31 January 2016;²¹ 14 submissions were received. Several journal editors were also consulted to discuss their opinion on the pros and cons of publication embargoes, as proposed in the draft document. The TWG met again in February 2016 to revise its document taking into account input received from Member States, industry and other stakeholders, academia and research institutions and databases. The TWG draft was discussed by the Advisory Group and stakeholders during its April 2016 meeting and the document was revised again by the TWG taking into consideration the result of the consultation with industry and other stakeholders, and discussion within the AG. The topic of GSD generates diverse opinions and the Advisory Group will continue to work on the issue. The TWG submitted its final report to the Advisory Group in June 2016.²²

23. In April 2016, upon consideration of a draft of the TWG report, the Advisory Group made initial recommendations²³ on the optimal characteristics of a GSD sharing system. It also recommended that the Secretariat work with relevant partners to develop guidance for data providers and databases and continue its collaboration with the World Data Center for Microorganisms to develop and pilot test a search engine for identifying commercial products developed using IVPP GSD.

²⁰ Best process to handle genetic sequence data from influenza viruses with human pandemic potential (IVPP GSD) under the PIP Framework. Options to monitor the use of genetic sequence data from influenza viruses with human pandemic potential (IVPP GSD) in end-products. Revised 6 May 2016. Geneva: World Health Organization; 2016 (http://www.who.int/influenza/pip/advisory_group/gsoptionspaper_revised.pdf?ua=1).

²¹ Pandemic Influenza Preparedness (PIP) Framework Advisory Group Technical Working Group (TWG) on the sharing of influenza genetic sequence data. Draft optimal characteristics of an influenza genetic sequence data sharing system under the PIP Framework. Draft document for discussion 20 November 2015. Geneva: World Health Organization; 2015 (http://www.who.int/influenza/pip/advisory_group/draft_twg_doc.pdf?ua=1).

²² Pandemic Influenza Preparedness (PIP) Framework Advisory Group Technical Working Group (TWG) on the sharing of influenza genetic sequence data. Optimal characteristics of an influenza genetic sequence data sharing system under the PIP Framework. Geneva: World Health Organization; 2016 (http://www.who.int/influenza/pip/advisory_group/twg_doc.pdf?ua=1).

²³ See http://www.who.int/influenza/pip/ag_april2016_MeetingRpt.pdf?ua=1.

3 BENEFIT SHARING

3.1 Status of agreements entered into with industry and academic / research institutions

24. In order to rapidly secure real-time access to a predictable supply of pandemic influenza vaccine, the Secretariat has prioritized its negotiations of Standard Material Transfer Agreements 2 (SMTAs 2) with industry based on several factors that include production capacity, prequalification status, and export experience.²⁴ The Secretariat has also sought to strike a balance between developed and developing country manufacturers. At the same time, the Secretariat has concluded several SMTAs 2 with academic and research institutions, many of whom have offered to provide benefits that should help strengthen preparedness through laboratory and surveillance capacity building.

25. Since 1 October 2015, an SMTA 2 was signed with the first Chinese influenza vaccine manufacturer, China National Biotech Group Company (CNBG).²⁵ CNBG committed to donating 8% of its real-time pandemic vaccine production to WHO, and will reserve another 2% of its pandemic production at affordable pricing to WHO. This is the fourth SMTA 2 which WHO has signed with a vaccine manufacturer. The first agreement with a diagnostics manufacturer was concluded with Quidel Corporation²⁶ which committed to reserving at least 250,000 diagnostic test kits for WHO at affordable pricing. Of the 46 agreements signed to date with research and academic institutions, 20 were concluded during this reporting period; 22 of these institutions have offered to provide a benefit under the SMTA 2. These offers have typically been training in laboratory and / or surveillance capacity; work is under way to operationalize these offers.²⁷

26. Formal negotiations are proceeding with eight vaccine manufacturers (four Japanese, one South Korean, one Chinese, one United Kingdom / United States of America company and one large multinational company). Preliminary discussions and negotiations are under way with two other vaccine manufacturers. Discussions and negotiations are also underway with several research and academic institutions, as well as biotechnology companies.

27. Concluding SMTAs 2 with vaccine or diagnostics manufacturers can be a lengthy process, sometimes requiring up to two years from initial contact with the company to signing of the agreement, regardless of company size. The Secretariat has reported previously that many small- and medium-size companies are not familiar with the PIP Framework, do not have prequalification or export experience, and, therefore, require considerable additional preparation time and background information. Additionally, some companies have been reluctant to engage in the SMTA 2 negotiation process or commit to sharing benefits.

²⁴ Briefing Note for the PIP Advisory Group Special Session 13-14 October 2015. 5 October 2015. Geneva: World Health Organization; 2015

(http://www.who.int/influenza/pip/advisory_group/Briefing_NoteAGSS.pdf?ua=1).

²⁵ The agreement was signed on 23 May 2016

http://www.who.int/influenza/pip/benefit_sharing/SMTA2_CNBG.pdf?ua=1

²⁶ See http://who.int/influenza/pip/benefit_sharing/SMTA2_Quidel.pdf.

²⁷ A complete listing of signed SMTAs 2 can be found at

http://www.who.int/influenza/pip/benefit_sharing/smta2_signed/en/.

28. In view of these challenges, the Advisory Group recommended in April 2016 that WHO apply the “stepwise approach” previously agreed in October 2015²⁸ with a handful of companies if negotiations failed to progress; the Secretariat followed this advice and this has resulted in negotiations moving forward with several companies. To assist smaller companies that do not export, the Secretariat is working with WHO technical experts to develop informational packages on prequalification and other technical requirements under the SMTA 2, as recommended by the Advisory Group.

3.2 Partnership Contribution collection

28. The PIP Secretariat uses a set of SOPs,²⁹ including an annual questionnaire, to identify manufacturers using GISRS and divide up the payment of the PC among companies. Following a suggestion from industry, the 2016 PC Collection Questionnaire was simplified to include a check box for entities to tick if there was “no change from last year”; 50% of respondents have used this feature. Additionally, a pilot questionnaire was translated and is now available in Chinese.

Table 3. Summary of Partnership Contribution Collection, 2013-2016, as of 30 September 2016

Questionnaire year	No. of entities contacted	No. of questionnaire responses	No. of contributors identified	No. of contributors that paid	Amount received in USD
2013	194	89	32	30	27,538,586
2014	250	102	42	38	26,966,861
2015	256	90	39	32	25,213,738 ^a
2016 ^b	249	82	40	22	19,740,090

^a As of 1 December 2016 ^b As of 1 December 2016; PC collection in process

29. Collection results for 2013-2016 are summarized in Table 3. Over the last three years, the number of entities contacted and the number of contributors identified has remained about the same. The amount received each year has been >90% of the total annual PC (USD 28M). One large company has not made its 2015 PC payment in full as of the end of the Annual Report reporting period.

30. Several challenges have been identified in the PC collection scheme.

- From the perspective of companies:
 - receipt of invoices from the Secretariat late in the fiscal year;
 - the unpredictability of the amount due;
 - the inclusion of 2009 as a base year in the annual calculation;
 - local tax barriers;

²⁸ See http://www.who.int/influenza/pip/ag_meetingreport_october2015.pdf?ua=1.

²⁹ Partnership Contribution Standard Operating Procedures June 2015. Geneva: World Health Organization; 2015 (http://www.who.int/influenza/pip/benefit_sharing/pc_collection_sop.pdf?ua=1).

- differences in the “level of use of GISRS” by different types of manufacturers, e.g. vaccine and diagnostic companies; and
- the inability to pay in one instalment can impede their making full and timely annual payments.
- From the perspective of the Secretariat:
 - receipt of PC funds is not well aligned with WHO’s timetable for formulating and funding the PC work plans;
 - delays in receiving funds exacerbate this cash-flow problem.

31. As a first measure to address the alignment issues and industry’s request for receipt of invoices earlier in the fiscal years, for 2016, the Secretariat issued PC invoices in August 2016 instead of November. This has enabled WHO to receive funds earlier which will allow the 2017 work plan review and funding decisions to also be taken earlier.

32. At its April 2016 meeting, the Advisory Group recommended that the Secretariat explore with industry how the PC collection process might be modified and simplified. The Secretariat is currently working with industry to explore possible options. The Advisory Group also recommended that the Director-General consider mechanisms to advance funds to the PIP Secretariat, e.g. to enable PC activities to go ahead as planned in anticipation of receipt of PC funds; identification of possible mechanisms is still under way.

3.3 Partnership Contribution implementation

Pandemic preparedness activities: implementation and assessment

33. The 2015 PC Annual Report was issued in June 2016 and provided technical and financial information concerning progress to implement activities outlined in the PC Implementation Plan.³⁰ Activity funds have been distributed to all five Areas of Work (Table 4) and have been used in 73 countries.

Table 4. Allocation of PC funds by Area of Work, (as of 30 June 2016³¹)

Area of work	Allocated (USD)
Laboratory and surveillance	37,202,059
Burden of disease	2,641,367
Regulatory capacity building	1,969,974
Risk communication	5,883,091
Planning for deployment	2,582,438

34. In recent months, there has been an effort to improve the robustness of implementation and assessment. Performance measurements have started to shift from financial metrics to programmatic performance and progress on achieving strategic objectives. The third semi-annual PIP PC Implementation Global Planning Workshop, bringing together PIP staff in regional offices and

³⁰ Pandemic Influenza Preparedness Framework. Partnership Contribution 2015 Annual Report. Geneva: World Health Organization; 2016

(http://www.who.int/influenza/pip/benefit_sharing/PC_AnnualReport2015.pdf?ua=1).

³¹ See <https://extranet.who.int/pip-pc-implementation/budget.aspx?year=2012>.

headquarters was held on 14-15 July 2016. The purpose was to review results and to improve planning, implementation, monitoring and reporting of activities in countries and at all three levels of WHO.

Pandemic response funds

35. Response funds are set aside for use during a pandemic to deploy (and in some cases, purchase at affordable prices) vaccines, antivirals, diagnostics and other pandemic-related products secured through SMTAs 2 and in accordance with previously adopted “Guiding Principles.”³² As of 30 June 2016, US\$ 23,416,948 have been allocated and held in reserve for responding to an influenza pandemic.

Development of a new PC Implementation Plan

36. At its April 2016 meeting, the Advisory Group recommended that decisions relating to PC implementation be extended to 31 December 2017 including i) Executive Board decision 131/4 on the proportional allocation of PC resources between preparedness and response and ii) the “Partnership Contribution Implementation Plan 2013-2016”. This would allow development of a new multi-year PC implementation plan and a proposal on the proportional distribution of PC funds to take into account the PIP Review and the findings and recommendations of the 2017 WHA.

37. The Advisory Group also recommended that the Director-General start the process to develop a new implementation plan by updating the Gap Analyses from 2013. As a first step, the Secretariat has developed a proposed approach which the Advisory Group will review at its October 2016 meeting.

3.4 Global influenza vaccine production capacity

38. The Global Action Plan for Influenza Vaccines (GAP) has propelled the potential global vaccine production capacity for pandemic influenza vaccines from an estimated 1.5 billion doses in 2006 to 6.372 billion doses in 2015.³³ The 10-year GAP initiative will conclude in 2016. A third and final consultation will be held in Geneva in November 2016. In preparation of this meeting, WHO solicited information through an online questionnaire during December 2015 – February 2016 from key stakeholders to measure views on progress and remaining work to be conducted. It is anticipated that a summary of the survey results will be published in peer-reviewed literature and made available on the GAP website in late October 2016.

39. The Advisory Group is exploring how the PIP Framework might support relevant GAP activities. The Advisory Group noted that some of the PIP implementation activities, e.g. burden of disease studies and regulatory capacity building, are in line with GAP activities.

³² Guiding Principles for use of PIP Partnership Contribution “Response” Funds. 23 October 2014. Geneva: World Health Organization; 2014

(http://www.who.int/influenza/pip/guiding_principles_pc_response_funds.pdf?ua=1).

³³ McLean KA, Goldin S, Nannei C, Sparrow E, Torelli G. The 2015 global production capacity of seasonal and pandemic influenza vaccine. *Vaccine* 2016; 34:5410-5413

(<http://www.sciencedirect.com/science/article/pii/S0264410X16306764>).

3.5 Vaccine stockpiles

40. In November 2013, the Strategic Advisory Group of Experts (SAGE) on Immunization agreed that WHO should not create a stockpile of influenza A(H5N1) vaccine, but should ensure access to pandemic vaccines under the PIP Framework.

4 GOVERNANCE

Interactions with stakeholders and communications

46. Interactions with stakeholders and communication activities help to maintain support for the Framework's objectives and to combat "flu fatigue". Industry, in interactions during meetings of the Advisory Group, reiterated its support for the PIP Framework's aims on preparedness and response. This mark of trust-building is important for the sustainability of the Framework. GISRS members have expressed interest in having increased interactions with the Advisory Group and the Advisory Group welcomed this.

47. The Secretariat has continued to produce an increased range of communications and outreach materials for a diverse array of audiences. New products included graphics such as a PIP poster;³⁴ two sets of Frequently Asked Questions^{35,36} a video on SMTAs 2,³⁷ and a publication in the Eastern Mediterranean Health Journal.³⁸ In addition, the Secretariat held regular informal teleconferences with industry and civil society organizations and continued its targeted outreach on specific topics, e.g. SMTA 2 and GSD. The range of actors and their different views on PIP Framework issues, such as GSD, nonetheless, present ongoing challenges and require further strengthening efforts to improve communications.

48. At its April 2016 meeting,³⁹ the Advisory Group made a number of recommendations aimed at strengthening and broadening communications to Ministries of Health and other relevant ministries; scientific communities; government officials and policy makers; and working through the WHO country offices and Regional Committees. In response to this, the regional offices have developed communications action plans in consultation with countries.

Linkages and synergies of PIP Framework with other agreements and activities

49. The Advisory Group noted that PIP Framework continues to gain visibility and was cited "...as a template for creating new agreements for other infectious agents that have caused, or may potentially cause, [public health emergencies of international concern] PHEICs...based on the principle of balancing the sharing of samples and data with benefit sharing on an equal footing."⁴⁰

50. The Advisory Group has underscored the importance of ensuring that capacity-building activities intrinsic to the PIP Framework, the IHR (2005) and the Global Health Security Agenda

³⁴ See http://www.who.int/influenza/pip/PIPF_Poster.pdf?ua=1.

³⁵ See http://www.who.int/influenza/pip/QA_Flyer.pdf?ua=1

³⁶ See http://www.who.int/influenza/pip/benefit_sharing/smta2_FAQs.pdf?ua=1.

³⁷ See <https://www.youtube.com/watch?v=RM9R9ZbYN7I>.

³⁸ Huvos A, Khan W. A new paradigm in global health security. EMHJ 2016;22:562-3.

³⁹ See http://www.who.int/influenza/pip/ag_april2016_MeetingRpt.pdf?ua=1.

⁴⁰ Implementation of the International Health Regulations (2005). Report of the Review Committee on the Role of the International Health Regulations (2005) in the Ebola Outbreak and Response. Report by the Director-General. Geneva: World Health Organization; 2016 (A69/21) (http://apps.who.int/gb/ebwha/pdf_files/WHA69/A69_21-en.pdf?ua=1).

(GHSA), are synergistic. In April 2016, the Advisory Group recommended that synergistic work should be promoted across relevant departments and units across all three levels of the Organization and with entities implementing IHR core capacities, including GHSA. Implementation of this recommendation is incomplete and more work is required to achieve the desired synergy and coherence.

PIP Review

51. In October 2015, the Advisory Group held a special session to harvest views of Member States and stakeholder on the PIP Review. The Advisory Group provided advice to the Director-General on the scope of the five-year review of the PIP Framework in accordance with the Framework's provisions and suggested Terms of Reference for Review Group members.⁴¹

52. The PIP Review started in January 2016 and is on track for a final report to be submitted directly to the Director-General at the end of October 2016. As part of the process to review the PIP Framework, the PIP Advisory Group was interviewed by the PIP Review Group. The PIP Advisory Group will look forward to reading the final report to the Director-General and to taking actions, as appropriate in response thereto.

New members and meetings of the Advisory Group

53. In April 2016, six new members joined the Advisory Group to replace one-third of the existing members, as provided under the Framework.⁴² Dr Jarbas Barbosa da Silva, Jr (Brazil) was selected as the Chair and Professor John M Watson (United Kingdom) was selected as the Vice Chair.⁴³

54. The Advisory Group met in October 2015 and April 2016. Consultations with industry and other stakeholders occurred at each meeting. Information Sessions for the Permanent Missions in Geneva, led by the Chair, were held following the meetings.

⁴¹ http://www.who.int/influenza/pip/advisory_group/ag_spec_session_report.pdf?ua=1

⁴² See PIP Framework, Annex 3, Sections 3.2 and 3.3.

⁴³ A complete listing of Advisory Group members can be found at http://www.who.int/influenza/pip/advisory_group/members/en/.

INDEX OF TOPICS COVERED IN THE 2016 ANNUAL REPORT

Topic area for Annual Report ¹	Location in report
1. Necessary technical capacities of the WHO Global Influenza Surveillance and Response System (GISRS)	Section 2.1 Annex 2
2. Operational functioning of WHO GISRS	Section 2.1 Annex 2
3. WHO GISRS influenza pandemic preparedness priorities, guidelines and best practices (e.g. vaccine stockpiles, capacity building)	Section 2.1 Section 3.3 Section 3.4 Section 3.5
4. Increasing and enhancing surveillance for H5N1 and other influenza viruses with human pandemic potential	Section 2.1 Section 3.3
5. Influenza Virus Traceability Mechanism (IVTM)	Section 2.2
6. Sharing of influenza viruses and access to vaccines and other benefits	Section 2.1 Section 2.2 Section 2.3 Section 3.1 Section 3.4
7. Use of financial and non-financial contributions	Section 3.2 Section 3.3 Section 4

¹ See PIP Framework, Section 7.2 5 and Annex 3, Section 2 for the seven areas to be covered by the annual report.

**TECHNICAL CAPACITIES AND OPERATIONAL FUNCTIONING
OF THE WHO GLOBAL INFLUENZA SURVEILLANCE AND RESPONSE SYSTEM**

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 2015 through 31 July 2016¹

Virus type	No. of kits
H5	65
H7	60
Other (seasonal)	406
Total	531

Table 2. Number and subtype of IVPP obtained from humans, characterized by WHO Collaborating Centres, (1 August 2015 -31 July 2016)²

Influenza virus	No. of viruses characterized	No. of countries providing viruses
Influenza A(H5N1)	11	3 (China, Egypt, Bangladesh)
Influenza A(H5N6)	7	1 (China)
Influenza A(H7N9)	41	1 (China)
Influenza A(H9N2)	9	2 (China, Bangladesh)
Influenza A(H1N1)v	3	2 (China, USA)
Influenza A(H1N2)v	4	2 (USA, Brazil)
Influenza A(H3N2)v	19	2 (USA, Vietnam)

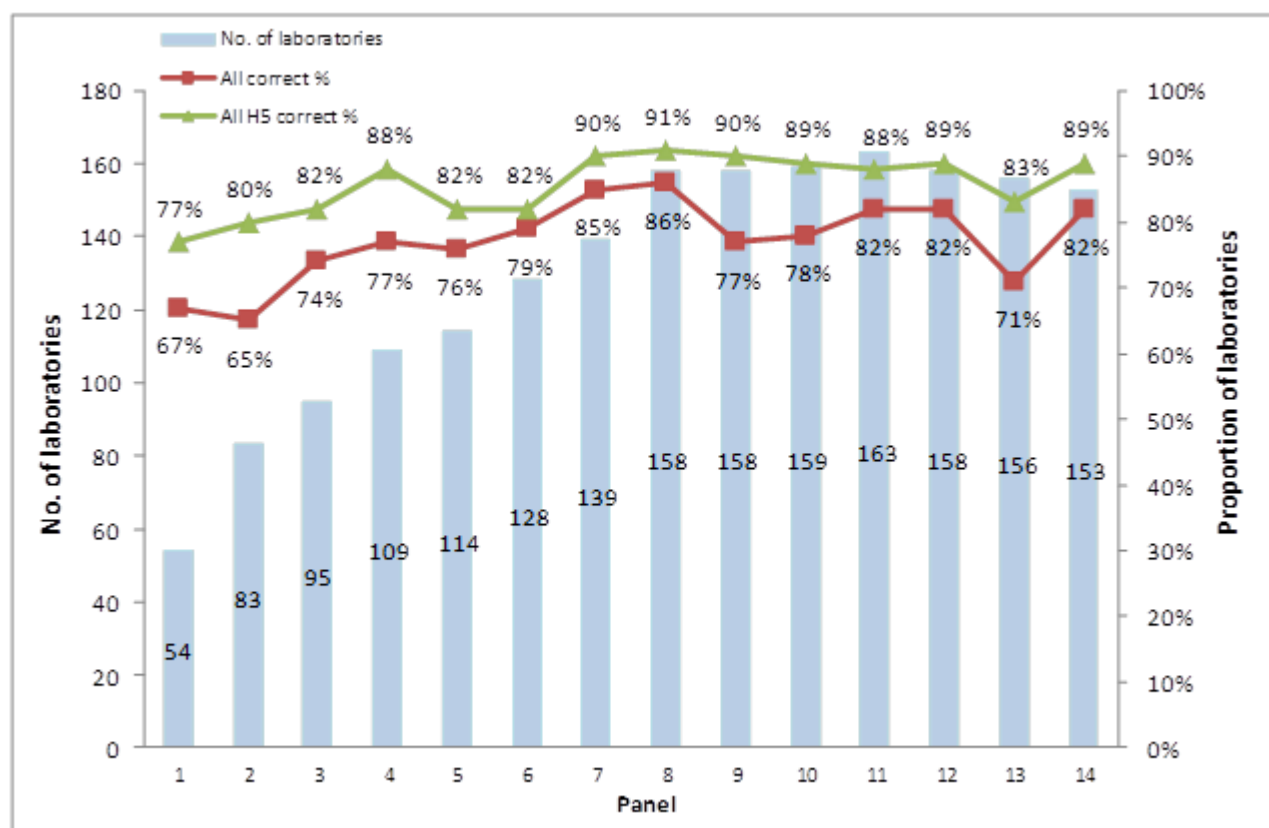
¹ During this time, the WHO Collaborating Centre (Atlanta) distributed 531 RT-PCR kits to 84GISRS laboratories in 82 countries.

² An additional 637 IVPP obtained from environmental and avian sources were characterized by WHO Collaborating Centres.

Table 3. Assessment of PCR testing performance by laboratories participating in the WHO external quality assessment programme (EQAP), April-June 2015¹

No. of correct results (10 samples tested)	No. (%) of laboratories (N= 153 participating laboratories)
10 samples correct	125 (81.7)
9 samples correct	15 (9.8)
6-8 samples correct	11 (7.2)
<6 samples correct	2 (1.3)

Figure. Performance of laboratories participating in the WHO external quality assessment programme (EQAP) for detection of influenza A and B viruses, panels 1-14, 2007-2015¹



¹ Detection of influenza virus subtype A by polymerase chain reaction: WHO external quality assessment programme summary analysis, 2015. *Weekly Epidemiological Record* 2016; 9:1–12 (<http://www.who.int/wer/2016/wer9101.pdf>).