Pandemic Influenza Preparedness Framework

Advisory Group Annual Report to the Director-General

2022
1. INTRODUCTION

1. The Pandemic Influenza Preparedness Framework ("PIP Framework") Advisory Group (AG) is made up of 18 independent technical experts, who monitor the PIP Framework and advise the WHO Director-General on its functioning. Every year, as part of its terms of reference (TOR)\(^1\), the AG presents a report to the Director-General on its evaluation of progress in the implementation of the PIP Framework. This report covers the period 1 January through 31 December 2022. Previous reports can be found here.

2. The key goals of the PIP Framework are to improve and strengthen the sharing of influenza viruses with human pandemic potential through the WHO Global Influenza Surveillance and Response System (GISRS), and to increase the equitable access of developing countries, particularly affected countries according to public health risks and needs, particularly where those countries that do not have their own capacity to produce or access influenza vaccines, diagnostics and pharmaceuticals. This report is structured around seven technical areas specified in Section 7.2.5 of the TOR:

   i. Necessary technical capacities of GISRS and sharing of influenza viruses (Virus sharing);
   ii. Operational functioning of GISRS;
   iii. GISRS influenza pandemic preparedness priorities, guidelines and best practices (e.g. vaccine stockpiles, capacity building, burden of disease studies);
   iv. Increasing and enhancing surveillance for H5N1 and other influenza viruses with human pandemic potential;
   v. The Influenza Virus Traceability Mechanism;
   vi. The sharing of influenza viruses and access to vaccines and other benefits (benefit sharing);
   vii. Use of financial and non-financial contributions.


5. The PIP Framework Advisory Group typically meets twice a year. In 2022, the Advisory Group met from 14-18 March 2022 via video conference due to COVID-19 travel restrictions and 11-14 October 2022 in person at WHO HQ. Both meetings were preceded by Technical Briefings covering the Advisory Group’s work to update on the following topics: 1. Proportional division of PIP Partnership Contribution Funds, 2. COVID-19 and Influenza, including influenza virus sharing, and 3. development of the High-Level Implementation Plan (HLIP) III. In addition, the Secretariat welcomed and briefed 6 new members.

6. This Annual Report draws on progress reports published by the Secretariat as well as data and information that the AG received at its biannual meetings including:

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\(^1\) Available here: [https://www.who.int/influenza/pip/advisory_group/PIP_AG_Terms_of_Reference.pdf?ua=1](https://www.who.int/influenza/pip/advisory_group/PIP_AG_Terms_of_Reference.pdf?ua=1)

b. Briefings which the AG received from the PIP Secretariat, the WHO Global Influenza Programme (GIP), and representatives of the GISRS, including reports, information and data on the sharing of influenza viruses, both seasonal virus and Influenza Viruses with Human Pandemic Potential (IVPP).

2. SUMMARY

7. Due to the well-established and long-standing expertise, international collaborative connections, and capacity to detect and prepare for a potential influenza pandemic, notably through the GISRS, many countries and the international community benefited from the ability of the partners of the PIP Framework to “pivot” and also address gaps identified during the COVID-19 pandemic.

8. The COVID-19 pandemic has demonstrated the critical importance of laboratory surveillance and GISRS, strengthened with the support of the PIP Framework Partnership Contributions (PC). The support of the Framework has been instrumental in countries around the world in strengthening the broad respiratory pathogen preparedness and response, including the COVID-19 pandemic response. Some of these successes have been highlighted in 20 ‘Stories from the Field’ published in the Influenza Newsletter.

9. Despite the challenges in terms of operational and human resources that the COVID-19 pandemic has caused, WHO and the Advisory Group continue to engage with GISRS, industry, civil society, and other relevant groups. The AG commends the PIP Secretariat, GIP, GISRS, regional and country offices for their continuous efforts this year to strengthen global influenza pandemic preparedness and noted that the overall implementation of the PIP Framework is proceeding well. The teams adapted and demonstrated the importance of their ongoing work on pandemic influenza preparedness planning and capacity building.

10. Nineteen monitoring visits both in-person and virtual were conducted in 2022, where discussions focused on progress achieved and sustaining High Level Implementation Plan II 2018-2023 (HLIP II) implementation.

11. HLIP III considers the lessons learned from HLIP II implementation and COVID-19 pandemic response experience and other respiratory outbreaks to outline key areas of focus for capacity building efforts. It covers 4 key output areas including: 1) Policies and plans; 2) Collaborative surveillance; 3) Community protection; and 4) Access to countermeasures – also aligning with the Global Architecture for Health Emergency Preparedness and Response. The Advisory Group

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2 Available here: https://apps.who.int/iris/bitstream/handle/10665/372197/9789240076907-eng.pdf?sequence=1&isAllowed=y

3 Previous AG meeting report from March available here: pip-ag-mr-march-2022-25may2022final.pdf (who.int) and October available here: ag-oct2022-meeting-report_11.01.23---with-annexes.pdf (who.int)
endorsed the plan in October 2022 and recommended that it be approved by the WHO Director-General in 2023.

12. At the close of 2022, the PC collected from industry was 68% of the expected total (US$ 28M) for the calendar year, consistent with past years. Timely collection remains a challenge. However, the overall collection rate for the period 2013-2022 is 97.5%.

13. Pandemic influenza and severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) are both respiratory viruses. The synergies between the work done through GIP, GISRS, and the PIP Framework to prepare and respond to an influenza pandemic as well as the COVID-19 pandemic in 2022 will provide essential information for future programmes and help us to better prepare the world for the next emergency, whether that is an influenza pandemic or a pandemic due to another pathogen.

3. SEVEN TOPIC AREAS


3.1 Necessary technical capacities of GISRS and sharing of influenza viruses (Virus sharing)

15. The WHO operational guidance on sharing IVPP continues to be the key guidance in assisting National Influenza Centres (NICs), H5 Reference Laboratories and other National Authorized Laboratories to select and ship IVPP to WHO GISRS Collaborating Centres (CC). The GIP has continued to proactively promote and clarify processes and reinforce the importance of timely sharing of influenza viruses including IVPP. Without the timely sharing of influenza viruses with GISRS – for all public health purposes, including vaccine development – the world will not have access to up-to-date risk assessments or other tools to respond to outbreaks. The AG continue to call on all Member States to timely share viruses with GISRS which remains a cornerstone of pandemic influenza preparedness.

16. The number of countries sharing influenza viruses/clinical specimens at least once with WHO collaborating centres (CCs) rose dramatically to 104 countries (54%), with 53 (27%) sharing two timely shipments with WHO CCs. This compares to 2021 when the figures were 57 countries and 16 countries respectively.

17. Ninety-one (91) countries from all 6 regions made 209 shipments to WHO CCs using the Shipping Fund Project. This is a marked increase in influenza sample sharing compared to previous years (2020 & 2021) during the COVID-19 pandemic where there were significant disruptions. WHO continues to advocate for countries to share influenza samples, through reminders made during

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4 Available here: https://apps.who.int/iris/handle/10665/259402
regional meetings, global webinars and pre-Vaccine Composition Meeting. Many Member States rely on WHO support for training, equipment and the continuous supply of necessary materials.

18. The GISAID Initiative has played an important role in the sharing of data on all influenza viruses and SARS-CoV-2 among the WHO GISRS. This includes the essential bi-annual influenza vaccine virus recommendations made by GISRS.

3.2 Operational functioning of GISRS

19. GISRS continues to operate well and celebrated its 70th anniversary in 2022. The PIP Advisory Group congratulates GISRS on this milestone. In 2022, one NIC joined the network, becoming the 149th recognized by WHO. Increasing access to NICs was the first objective for use of PC funds set by the PIP Advisory Group in 2013 as it improves data representativeness and facilitates a timely and effective response to an influenza pandemic. In addition to the 149 NICs, GISRS includes seven WHO Collaborating Centres (CCs), four Essential Regulatory Laboratories, and 13 H5 Reference Laboratories. The GIP oversees the network and has worked consistently to strengthen the systems, address delays in virus sharing and clarify processes involved herein.

20. GISRS is considering an integrated surveillance system for influenza, SARS-CoV-2, and novel respiratory viruses of epidemic and pandemic potential. GIP is assessing the financial and human resources implications and producing a report for Member States and the AG.

21. A total of 1013 zoonotic influenza viruses and other IVPPs were characterized by GISRS in 2022. The viruses were of 16 influenza A subtypes and originated from 18 countries.

22. Through the two VCM consultations in 2022, characterization led to the development of three new candidate vaccine viruses (CVV) for pandemic influenza preparedness. The selection and development of a zoonotic CVV is done to maintain a bank of viruses suitable for the immediate development of vaccines, including during a pandemic.

23. However, there continue to be concerns over the implementation of national access and benefit sharing laws, including those to implement the Nagoya Protocol and the implications for systems such as GISRS. Following the October 2021 PIP Advisory Group meeting, an informal PIP Advisory Group Working Group (AGWG) was established to develop guidance for the Director-General on a possible way forward to address the growing concerns around the use of seasonal influenza viruses. The AGWG held several meetings between February and September 2022 and 5 consultations with stakeholders. The group developed a report which was presented to the PIP Advisory Group in October 2022. The PIP Advisory Group agreed with the findings and recommendations of the AGWG and recommended that the Director-General consider these recommendations in moving forward.

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5 Accessed here: https://www.gisaid.org/
3.3 GISRS influenza pandemic preparedness priorities, guidelines and best practices (e.g. vaccine stockpiles, capacity building, burden of disease studies)

24. In 2022, WHO updated and published guidance on the end-to-end integration of SARS-CoV-2 and influenza sentinel surveillance. Taking into account global consultations, this protocol updates the laboratory detection algorithms including the use of multiplex diagnostic methods.

3.3.1 Burden of Disease (BOD)

25. BOD estimates are important for pandemic planning, as national authorities use burden estimates to prioritize the allocation of resources, and plan prevention and control measures such as vaccination programmes and clinical management strategies.

26. In 2022, two additional countries published their BOD estimates and 12 updated their previous findings, bringing the number of countries with published estimates to 50. Of those 50 countries, 68% (34) are low-middle income countries (LMICs). The AG encourages Member States to collect, analyze and publish their influenza BOD data so that the BOD for influenza can be calculated in each country.

27. In April 2022, the Seasonal Influenza Disease Burden Estimator (pyramid tool) was launched online to support countries with limited data to enumerate cases, hospitalizations, and deaths. WHO also developed and piloted an excel-based tool to estimate the burden of influenza illnesses averted through ongoing or planned vaccination programmes. The AG welcomes these new tools and recommends Member States to use these tools to estimate their influenza BOD.

3.3.2 Regulatory Framework

28. In 2022, five PIP-supported countries signed the WHO Collaborative Registration Procedures agreement. As of November 2022, 59 countries have signed this collaborative agreement. Common registration approaches will simplify and streamline regulatory actions at the time of the next pandemic.

29. In 2022, WHO strengthened national regulatory capacities in seven countries for pandemic influenza products through benchmarking assessments, and conducted six technical support activities and regional workshops for 44 countries from four WHO regions. To promote the adoption of regulatory pathways that accelerate approval for use of pandemic influenza products, WHO is updating its emergency regulatory preparedness guidelines through workshop feedback and using the regulatory requirements and challenges experienced through the COVID-19 pandemic. WHO has also conducted two quality management systems (QMS) implementation workshops for 32 countries from two regions.

3.3.3 Risk Communications and Community Engagement
30. OpenWHO continues to grow as a global learning platform for pandemic influenza preparedness and response. Users from 193 countries completed one of 29 influenza courses on OpenWHO. The newest course on seasonal influenza prevention and control for pandemic preparedness, has now enrolled over 16,000 people. This platform has successfully demonstrated utility for pandemic response with over 2.4 million enrolments on 46 COVID-19 courses.

31. During the COVID-19 pandemic, WHO established the Early AI-supported Response and Social Listening system (EARS) to show real time information about how people are talking about COVID-19 online so as to better understand and manage the infodemic and pandemic. EARS now analyzes publicly available data from 32 countries and work is being done to develop a taxonomy on acute respiratory infections including influenza.

3.3.4 Planning for Deployment

32. Needs-estimates for pandemic influenza preparedness products (vaccines, antivirals, diagnostics, and therapeutics) are important for managing global deployment operations. To this end, a series of workshops and expert interviews were held to estimate needs based on different scenarios. A report summarizing the discussions is being developed.

33. The strengthening of seasonal influenza vaccination programmes provides a critical foundation for strengthening pandemic influenza preparedness. WHO participated in five missions in two regions supporting six countries with the aim of strengthening seasonal influenza vaccination programmes and policies.

34. Guidance and tools developed through PIP PC implementation were leveraged to facilitate country planning and the deployment of COVID-19 vaccines. Guidance on updating national deployment and vaccination plans for influenza and other respiratory viruses, with input from the COVID-19 experience, has recently been published for public comment. This guidance was presented to 11 countries at a regional meeting in the Americas with the aim of linking the development of national deployment and vaccination plans (NDVP) to pandemic influenza preparedness planning.

3.3.5 Influenza Pandemic Preparedness Planning (IPPP)

35. WHO is supporting countries through multisectoral planning workshops and conducting simulation exercises. Of the 65 IPPP PC recipient countries in the 2022-23 biennium, 37 (59%) now have a plan based on WHO guidance, of which five updated their plan in 2022. Additionally, five countries conducted simulation exercises, two of which used a simulation exercise package developed by WHO, focusing on outbreak response, multi-sectoral coordination, RCCE and the triggers for decision making. As influenza is one of the few known pandemic prone pathogens, the AG strongly encourages all Member States to conduct IPPP exercises. For example, the Islamic Republic of Iran is drafting its national IPPP, using a three-phased approach defined by WHO’s essential steps in...
developing or updating a national pandemic influenza preparedness plan, and incorporating lessons learned from the COVID-19 pandemic.

36. WHO has developed a respiratory module as part of the Preparedness and Resilience for Emerging Threats (PRET) initiative. Within this module, updated guidance on preparedness for a pandemic due to a respiratory pathogen, including influenza, has been published. Complementing this is the development of a checklist aimed at supporting national authorities to develop and/or revise existing pandemic preparedness plans. This checklist builds on the WHO checklist for pandemic influenza risk and impact management: building capacity for pandemic response and lessons learned from the COVID-19 pandemic.

3.4 Increasing and enhancing surveillance for H5N1 and other influenza viruses with human pandemic potential

37. Data sharing is critical to monitor influenza activity and to inform risk assessments. Of 194 WHO MS, 146 reported to FluNet and 123 reported to FluiD. Most of these (141 to FluNet and 114 to FluiD) reported consistently during the influenza season. In 2022, two countries started reporting for the first time to FluNet, and six countries started reporting for the first time to FluiD. The participation of more countries increases the data representativeness, or completeness, of circulating influenza viruses.

38. There has been a rapid rise in the number of countries integrating SARS-CoV-2 into their influenza sentinel surveillance systems and using an established platform to share data. Numbers rose from 76 countries in December 2021 to 103 countries a year later – indicating countries’ desire to increase efficiency in surveillance.

39. In 2022, the yearly External Quality Assurance Program (EQAP) test panels were sent by the Global Influenza Programme to 134 participating countries to monitor, sustain, and drive improvements in virus detection capacity. In 2022, the panels covered both influenza and a SARS CoV-2 Omicron variant of concern. Of the participating countries, 120 (90%) correctly identified all non-seasonal viruses, and 128 (95%) correctly identified all seasonal viruses. In 2022, 1 country participated for the first time. In 2022, 68 countries from six regions benefited from 37 laboratory training activities. These activities help improve and sustain quality of the national influenza virus detection capacity.

40. Outbreak detection and response trainings are critical for pandemic influenza readiness. In 2022, 133 outbreak detection and response trainings were conducted in 27 countries from five regions. Additionally, 28 country-level human-animal interface risk assessments, coordination meetings, and joint investigations were conducted in seven countries from four regions. These activities strengthen national capacity for influenza detection and readiness to respond to emerging outbreaks.

41. Risk and severity assessments are critical to inform national and global pandemic preparedness. In 2022, 10 WHO influenza human-animal interface risk assessments were published and a total of 58 trainings completed by seven countries in five regions on the pandemic influenza severity
assessment (PISA) tool. The PISA tool and guidance is currently under revision and will be published and rolled out in the coming biennium.

42. The AG strongly encourages further training and workshops for Member States in all regions in outbreak detection and response. This will reinforce the vital role Member States play in preventing and managing a pandemic through surveillance and response within their respective regions and globally.

3.5 The Influenza Virus Traceability Mechanism (IVTM)

43. Tracing the evolution of viruses and virus subtypes is essential to determine their risk to public health. IVTM works as a transparent tracking system and the large number of virus subtypes recorded each year. From 1 January 2022 to 31 December 2022, 105 virus subtypes were recorded, bringing the total number to 1,476 virus subtypes since 1 December 2012. Overall, the AG notes that a good amount of biological material is shared and the laboratories are sharing in a reasonable manner enabling the tracking of viruses.

3.6 The sharing of influenza viruses and access to vaccines and other benefits (Benefit Sharing)

44. Virus sharing and access to benefits are at the center of the PIP Framework. Virus sharing has been previously addressed (see Sections 3.1). Benefit sharing is covered through two benefit sharing mechanisms: the annual Partnership Contribution (PC)\(^6\) and the Standard Material Transfer Agreement 2 (SMTA2)\(^7\). The Secretariat manages the collection of the PC as well as the negotiation and review of SMTA2s. Work initiated in 2020 is ongoing to better understand the use of PIP biological material by the diagnostic sector.

3.6.1 The PIP Partnership Contribution

45. The PC is collected annually from influenza vaccine, diagnostic, and pharmaceutical manufacturers that use GISRS. Funds are allocated for: (a) pandemic preparedness capacity building; (b) response activities during the time of an influenza pandemic; and (c) PIP Secretariat for the management and implementation of the Framework. As mentioned earlier, timely collection of the PC in the year of invoice continues to be a challenge despite overall collection continuing to be very satisfactory. In October 2022, the PIP AG recommended to implement the new PC level adjusted for inflation starting in 2024, and to work with relevant stakeholders to develop SOPs. The PIP Secretariat is working closely with the industry associations to update the amount of PC due each year from each manufacturer identified as a contributor, and to determine how such amount is divided amongst the

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\(^6\) For more on the Partnership Contribution, see here: [Partnership contribution (who.int)](http://www.who.int)

\(^7\) For more on SMTA2, see here: [who.int/initiatives/pandemic-influenza-preparedness-framework/standard-material-transfer-agreement-2-smta2](http://www.who.int/initiatives/pandemic-influenza-preparedness-framework/standard-material-transfer-agreement-2-smta2)
contributors through the use of the PC formula. The AG welcomed the progress achieved through these discussions.

46. The Secretariat developed and submitted a draft decision on the proportional division of PIP PC funds for the period 2023-2030 to the Executive Board in January 2023. The draft decision was based on the Advisory Group recommendation to maintain the current proportional division of the PC funds (70% for preparedness and 30% for response) through 2030 and it was subsequently approved by the Executive Board.

3.6.2 The PIP SMTA2

47. The purpose of Standard Material Transfer Agreements is to secure access to pandemic products for future pandemic response. Fourteen agreements have been signed with large, medium, and small vaccine manufacturers since 2013, securing access by WHO to around 10% of future global production of pandemic influenza vaccine, in real time. Using current technologies and average yields, this translates to over 420 million vaccine doses. The agreements also secure access to 250,000 diagnostic test kits, and 25 million syringes. A further 76 SMTA2 agreements have been signed with academic and research institutions. These agreements have also led to 29 offers of benefit-sharing from academic and research institutions.

3.7 The use of financial and non-financial contributions

48. Overall PC budget implementation improved with 34% implementation in 2022 compared to 21% in 2020, i.e. at the end of first year of the previous biennium. This is due to an increase in travel, in-person meetings and trainings as COVID-19 control measures were progressively relaxed.

49. PIP PC Preparedness approved budget for the 2022-2023 biennium was USD 27.9 million, initially USD 14.6 million distributed out of which USD 9.4 million implemented by 31 Dec 2023 representing 34% implementation on the approved budget and 64% on the funds distributed for 2022.

50. The total PC collection between 2012 and 2022 stood at US$ 282.9 million. As of 31 December 2022, there is a balance of USD 44.8 million allocated to preparedness (net funds available for implementation) and USD 76.7 million allocated to the Response Fund (inclusive of programme support costs). This latter figure includes an accrued interest of $4 million for the period 2018-2022.

51. Overall, the AG believes that the funding allocations are well managed and monitored. The PIP PC collection is being done in a fair manner and is well managed by the Secretariat, despite some challenges. The programme provides financial implementation data at the deliverable level which provides more detail and enables greater oversight compared to the standard WHO reporting done at the output level. The accounts are reviewed on an annual basis by the WHO financial department and a Certified Financial Statement are issued each year and included in the PIP Framework annual and biennial progress reports.