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. Each year, as part of its terms of reference\(^1\), 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 2021. 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 access of developing countries to vaccines and other pandemic response supplies. This report is structured around seven technical areas specified in Section 7.2.5:

   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.

3. Implementation of the PIP Framework strengthens global preparedness and contributes to broader health outcomes in line with the Global Influenza Strategy 2019-2030, the International Health Regulations (2005), health systems strengthening and Universal Health Coverage, the WHO General Programme of Work 2019-2023, and the Sustainable Development Goals.

4. The Advisory Group typically meets twice a year. As a result of on-going COVID-19 travel restrictions, the PIP Framework Advisory Group has met in a virtual format for both its 2021 meetings (22-26 March and 7-11 October). Both meetings were preceded by Technical Briefings covering the Advisory Group’s work to date on the following topics: 1) Genetic Sequence Data; 2) COVID-19 and influenza virus sharing; and 3) implementation of the Global Influenza Strategy. In addition, the Secretariat welcomed and briefed 6 new members.

5. 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
\(^2\) Available here: https://apps.who.int/iris/bitstream/handle/10665/356918/9789240051706-eng.pdf
b. Briefings which the AG received from the PIP Secretariat, the WHO Global Influenza Programme (GIP) and 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

6. The opening day of WHA 74 in May 2021 marked the 10th anniversary of the adoption of the PIP Framework. The Director-General recognized this in his opening remarks, thanking Member States and stakeholders for their continued commitment to this unique partnership. Several new communication products were developed to commemorate this special event including a feature story posted on the WHO website, an article in the WHO COVID-19 Weekly Operational Update, an article in the UN News Special, and a brochure highlighting key achievements.

7. While the COVID-19 pandemic challenged the PIP Framework’s advocacy efforts for influenza, the Secretariat and the Advisory Group continued to engage with GISRS, industry, civil society, and other relevant groups.

8. COVID-19 has demonstrated the critical importance of GISRS (strengthened with the support of the PIP Framework Partnership Contributions or PC) as the foundation for respiratory pathogen preparedness and response, working in countries around the world. As highlighted in the many ‘Stories from the Field’ published in the Influenza Newsletter the impact of PC investments at the country, regional, and global level, including the collateral benefits PC investments have been significant for the COVID-19 response. A total of 10 monitoring visits both in-person and virtual were conducted, where discussions focused on sustaining High Level Implementation Plan II 2018-2023 (HLIP II) implementation.

9. In 2021, a Mid-Term Review of HLIP II was completed to assess progress and determine if adjustments were needed to improve its implementation. Revisions to the HLIP II monitoring and evaluation framework were completed following the review.

10. 2022-23 biennium workplans were approved in November 2021 after a comprehensive development process including external review by the Partnership Contribution Independent Technical Expert Mechanism. The workplans, targeting 82 PC recipient countries will build on achievements from the previous two biennia and will consider experiences and lessons learned from the COVID-19 pandemic, and continue to leverage national and international investments in pandemic influenza preparedness.

11. From 2020-21, 6 Standard Material Transfer Agreement 2 (SMTA2) were concluded: 1 with a manufacturer of influenza vaccines and 5 with academic and research institutions. A series of meetings were held to discuss pandemic vaccine deployment activities with a view towards operationalizing the SMTA2 supply commitments. The Secretariat started reviewing those SMTA2s signed by manufacturers more than 4 years ago in order to ensure that pandemic vaccine supply agreements are up to date and

3 Previous AG meeting report from March available here: https://cdn.who.int/media/docs/default-source/pip-framework/pip-framework-advisory-group/pip-advisory-group-meeting-report---march-2021.pdf?sfvrsn=4e18cae3_3
can be implemented efficiently during a pandemic. One review with an early signatory has been recently concluded.

12. At the close of 2021, the PC collected from industry was 55% of the expected total (US$ 28M) for the calendar year, consistent with past years. The overall collection rate for the period 2013-2020 is 97.5%.

13. The AG commends the PIP Secretariat, GIP, GISRS and regional offices for their continuous efforts this year as they were called upon to continue their work to strengthen global influenza pandemic preparedness in the midst of the COVID-19 pandemic. The team adapted and demonstrated the importance of their ongoing work on pandemic influenza preparedness planning and capacity building.

14. 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 and the current COVID-19 pandemic will provide essential information for future programmes. Lessons from this ongoing devastating respiratory pandemic will help us to better prepare the world for the next one.

3. SEVEN TOPIC AREAS

15. Illustrative examples of achievements and challenges follow for each of the seven topic areas covered in the AG Annual Report (sections 3.1-3.7).

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

16. The WHO operational guidance on sharing IVPP continues to be the key guidance in assisting National Influenza Centres (NICs), H5 Reference Laboratories and other Nationally Authorized Laboratories to select and ship IVPP to WHO Collaborating Centres (CC). The GIP and GISRS have 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. We continue to call on all Member States to timely share viruses with GISRS which remains a cornerstone of pandemic influenza preparedness.

17. Although the percentage of Member States with zoonotic influenza cases sharing IVPPs with GISRS rose to 80% from 75% in 2021, only 57 (29%) countries shared influenza viruses/clinical specimens at least once with WHO CCs, with 16 (8%) sharing timely two shipments with WHO CCs. The significant decrease in comparison with 2020 (63% and 31% respectively) was due to unusually low influenza virus circulation. This may have resulted from the implementation of public health and social measures (PHSM) to reduce spread of COVID-19.

18. Ninety-six (96) countries from all 6 regions made 259 shipments to WHO CCs in 2020-21 using the Shipping Fund Project. There was also reduced influenza sample sharing compared to the 520 shipments made in the previous biennium, again associated with the disruptions caused by the COVID-19 pandemic and the reduced influenza activity in 2020 and 2021. Despite this, WHO continues to advocate for countries to share influenza samples through regional meetings, global webinars and pre-Vaccine

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4 Available here: https://apps.who.int/iris/handle/10665/259402
Composition Meeting reminders. Many countries rely on WHO support for training and equipment and the continuous supply of necessary materials.

19. The GISAID Initiative\(^5\) has played an important role in the sharing of data on all influenza viruses and the coronavirus causing COVID-19 among the WHO CC and NICs. This includes the essential bi-annual influenza vaccine virus recommendations made by GISRS.

### 3.2 Operational functioning of GISRS

20. GISRS continues to operate well. In 2021, Togo’s National Influenza Centre (NIC) was newly recognized by WHO – bringing the total number of NICs to 148 in 124 countries, as of December 2021. Increasing capacity to NIC recognition was the first objective of using PC funds as set by the PIP Advisory Group in 2013. It improves data representativeness and facilitates a timely and effective response to an influenza pandemic. In addition to the 148 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, addressing delays in virus sharing and clarifying processes involved herein.

21. A total of 1335 zoonotic influenza viruses and other IVPPs were characterized by GISRS in 2021, marking two years of increases. The viruses were of 25 influenza A subtypes and originated from 28 countries.

22. The subsequent characterization through two Vaccine Composition Meetings in 2021, led to the development of four new Candidate Vaccine Viruses (CVVs) for pandemic influenza preparedness. The selection and development of zoonotic CVVs 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. During its October 2021 meeting, the AG proposed to establish an informal sub-group to review the situation, consult with relevant stakeholders and develop options for addressing the issues. The DG accepted the AG proposal and the sub-group started its work in early 2022.

### 3.3 GISRS influenza pandemic preparedness priorities, guidelines and best practices (e.g. vaccine stockpiles, capacity building, burden of disease studies)


#### 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.

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\(^5\) Accessed here: [https://www.gisaid.org/](https://www.gisaid.org/)
26. In the 2020-21 biennium, 9 additional countries published BOD estimates, and 7 updated their previous findings - bringing the number of countries with published estimates based on data collected since 2011 to 48. Of the 48 countries, 69% (33) are low- and middle-income countries. This progress exceeded the biennial indicator target. The increased availability of data from different countries improves geographic and socio-economic data representativeness to inform decision makers.

27. In 2021, a survey aimed at learning whether BOD studies inform policy found that authors from 14 of the 20 countries surveyed shared their findings with government officials. However, just five reported their results being considered in vaccine policy fora. WHO is exploring different ways to increase the prominence of BOD data to inform country policies and decisions on influenza prevention and control.

3.3.2 Regulatory Framework
28. As of December 2021, 24 PIP-supported countries signed the Collaborative Registration Procedure agreement, of which 2 signed in 2020-21. This brings the global total to 59 countries by December 2021, representing 24 PIP-supported countries and 25 other countries. Common registration approaches will simplify and streamline regulatory actions at the time of the next pandemic. The number of PC recipient Member States that have implemented a regulatory approach (41/48) was almost double the target for 2021 (23). By 30 June 2021, 47 out of the 48 PIP PC recipient countries had authorized one or more COVID-19 vaccines (one country did not seek COVID-19 vaccines for non-technical reasons). For the 45 countries with data, 39 (87%) provided timely Marketing Authorization within 15 days of emergency use listing by WHO.

3.3.3 Risk Communications and Community Engagement
29. OpenWHO continues to grow as a global learning platform for pandemic influenza preparedness and response. Over 228,000 users from 193 countries completed one of 23 influenza courses on OpenWHO. The platform is also used in support of other emergencies including for the COVID-19 pandemic knowledge transfer, with over 6.35 million enrollments across 42 different COVID-19 relevant courses.

30. A new course on Influenza Prevention and Control was launched in 2021. Targeted towards health workers, it provides an overview of influenza vaccination and its importance. This launch was coupled with advocacy events to promote uptake and use of the platform.

31. In 2020-21, 56 webinars and meetings were conducted to strengthen key Risk Communication and Community Engagement (RCCE) capacities relevant for COVID-19 and pandemic influenza - including influencing risk perceptions, using evidence for strengthening community resilience systems, and COVID-19 stigma. Additionally, regions tailored their support activities to regional and country contexts. In the WHO Western Pacific Region, webinars focused on using multi-source listening systems and social media for assessment of essential information about at-risk populations; and in the WHO Region of the Americas, workshops stressed the role of risk communications in the roll-out of relevant guidelines for country-level adaption. Despite these achievements, technical assistance to strengthen RCCE capacities still requires further investment.

3.3.4 Planning for Deployment
32. In 2021, WHO initiated a project to estimate national, regional, and global needs for pandemic influenza preparedness medical products, and identify gaps in global preparedness for availability and access of such medical countermeasures. Using foresight methodologies, this analysis will also inform
product allocation and deployment strategies, and the development of operational plans for product deployment.

33. Guidance and tools developed through PC implementation were leveraged to facilitate country planning and deployment of COVID-19 vaccines. Lessons learned from the development of COVID-19 National Deployment and Vaccination Plans (NDVPs) are being used to adapt and update guidance on developing influenza and COVID-19 NDVPs. Vaccine Post-Introduction Evaluations are being done in 34 countries, which will be used to update guidance, operational protocols and deployment practices.

34. WHO continues to provide technical resources, including the influenza vaccination toolbox, to support Member States with developing or strengthening their influenza vaccination programmes. Quality influenza prevention and control programmes at country level serve as an important foundation for pandemic influenza preparedness.

35. WHO plans to document COVID-19 lessons learned such as the impact of advanced technologies and the establishment of additional production capacities, information on sustainable influenza vaccine procurement and production activities moving forward, and results from the sustainability assessment checklist. In 2021, for example, Serbia completed its sustainability assessment, thus allowing the country to identify opportunities and challenges for sustaining its local production of influenza vaccines.

3.3.5 Influenza Pandemic Preparedness Planning (IPPP)

36. Of the 63 IPPP PC recipient countries in the 2020-21 biennium, 37 (59%) had a plan based on WHO’s Pandemic Influenza Risk Management guidance by the end of 2021. This is an increase of 4 PC recipient countries with an up-to-date plan in 2020-21. Twenty-four (24) more countries are in the process of developing or updating their plans. This progress in the biennium shows that despite the primary focus being on the COVID-19 response, countries are sustaining operational planning for an influenza pandemic.

37. By the end of 2021, three PIP recipient countries had conducted simulation exercises to assess their IPPPs with a focus on laboratory readiness, outbreak response, and multi-sectoral coordination. These exercises will support the iterative improvements of emergency preparedness and response protocols with lessons from the COVID-19 response.

38. In 2021, WHO continued the collaborative process initiated in 2020 to update the Pandemic Influenza Risk Management guidance with a broader respiratory pathogen focus. A policy brief to guide Member States on updating their national pandemic preparedness plans has been published. Additionally, WHO published two papers describing its country-level support during the first year of the COVID-19 pandemic showcasing the operational breadth and intensity of cooperation. Key lessons and recommendations from the COVID-19 pandemic response including WHO’s actions will inform updated guidance.

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

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6 Available [here](#) and [here](#)
39. Data sharing is critical to monitor influenza activity and to inform risk assessments. In 2021, of 194 WHO Member States, 142 (73%) reported influenza surveillance data to FluNet and 116 (68%) reported to FluID. Most of these (96% and 88% respectively) reported consistently during their influenza season. Of the 41 PIP PC L&S recipient countries, the proportion reporting to FluNet (90%) and FluID (71%) exceeded the indicator targets. By the end of 2021, 3 new countries had started reporting for the first time to FluNet, and 3 countries started reporting for the first time to FluID. The participation of more countries increases the data representativeness of the circulating influenza viruses.

40. As of December 2021, 76 countries integrated COVID-19 into their sentinel surveillance systems for influenza and used an established influenza platform to share COVID-19 data.

41. In 2021, the yearly External Quality Assurance Program (EQAP) panels were sent to 127 participating countries to monitor, sustain, and drive improvements in virus detection capacity. Of these, 105 (83%) correctly identified all non-seasonal influenza viruses, and 120 (95%) correctly identified all seasonal viruses. By the end of 2021, 4 new countries had participated for the first time. Similarly in 2020, when the 1st WHO EQAP panel for SARS-CoV-2 was distributed using the GISRS EQAP system, the 2021 EQAP included a panel for influenza antiviral susceptibility testing. These innovations showcase the continued efforts to meet emerging needs from influenza and other respiratory viruses of public health importance. By the end of December 2021, 105 countries from 6 regions had benefited from 122 laboratory training activities. These activities along with the yearly participation in the EQAP help improve and sustain quality national influenza virus detection capacity.

42. Outbreak detection and response trainings are critical for pandemic influenza readiness. By the end of 2021, 430 outbreak detection and response trainings were conducted in 61 countries from all 6 regions over the course of the biennium. This represents a significant increase of 71% in trainings conducted compared to the previous biennium.

43. In 2021, a total of 7 WHO risk assessments of human infections with non-seasonal or animal influenza viruses were published.

3.5 The Influenza Virus Traceability Mechanism (IVTM)

44. IVTM is working as a transparent tracking system for IVPP. From 1 January 2020 to 31 December 2021, 168 virus subtypes were recorded, bringing the total number to 1,373 virus subtypes since 1 December 2012.

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

45. 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)\(^7\) and the Standard Material Transfer Agreement 2 (SMTA2). The Secretariat diligently manages the collection of the PC as well as the negotiation and

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\(^7\) The PIP PC funding model is described in HUP II, Section 6
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

46. The PIP 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, collection of the PIP in the year of invoice continues to be a challenge despite overall collection continuing to be very satisfactory. With respect to the amount of PIP due each year from each manufacturer identified as a contributor, industry continued to work together with a view to developing a new formula. The AG welcomed the progress on this work.

47. A PC Independent Technical Expert Mechanism (PCITEM) was established in 2017, with a view to increasing the transparency of the process that seek to approve technical projects for funding using PIP Framework Partnership Contribution (PC) funds. The PCITEM, comprising of eight experts from a variety of relevant disciplines, with regional and gender balance, meets in person once per biennium to review work plans submitted for funding under the PC. It reviews and provides scientific and technical guidance and advice to support, improve and finalize the PC funded biennial work plans. It also assesses the appropriateness of projects to contribute to the Outcome and Output targets in the High Level Implementation Plan 2018-2023 (HLIP II). Finally, it provides inputs to implementing unit focal points, and submits its report to the Director, Department of Global Infectious Hazards (GIH).

48. The eight PCITEM members met virtually on 31 August – 3 September 2021 to review progress and the project work plans for 2022-2023. PCITEM provided the following summary conclusions to the GIH Director:

1. Overall, there has been remarkable progress since 2018 on HLIP II implementation. The capacities strengthened are well aligned with the high-level outcome of the Global Influenza Strategy to have stronger country capacities that contribute to national and global preparedness, response and health security.

2. The COVID-19 pandemic highlighted: i. The critical contribution of influenza systems and capacities – including human resource capacities in-country and within WHO - to support pandemic response; ii. The valuable role of PC investments to strengthen country, regional and global preparedness systems, knowledge and capacities as a foundation for response in the different areas of work; iii. The importance of addressing barriers so that the equitable access of developing countries to vaccines and other pandemic related supplies is ensured.

3. In 2020-2021, the risks to HLIP II work plan implementation due to the COVID-19 pandemic were managed to minimize impact, where progress was made on the majority (14 out of 19) indicators. As the COVID-19 pandemic continues, human resources for influenza preparedness remain constrained. This poses an ongoing challenge to HLIP II implementation and may become more acute with staff turnover or continued repurposing to COVID-19.

4. Lessons continue to be learnt from the COVID-19 pandemic. The 2022-2023 work plans reflect the contextual needs of countries and regions while remaining aligned with HLIP II’s deliverables and outputs. The learnings and gaps identified to date were noted and accounted for further consideration in the development and revision of work plans.
3.6.2 The PIP SMTA2

49. Thirty-two (32) percent of influenza vaccine and antiviral manufacturers have concluded an SMTA2. Fourteen agreements have been signed with large, medium, and small vaccine manufacturers since 2013, securing access by WHO to 11.25% of future global production of pandemic influenza vaccine, in real time; using current technologies and average yields, this translates to over 400 million vaccine doses. The agreements also secure 10 million treatment courses of antivirals, 250 000 diagnostic test kits, and 25 million syringes. A further 75 SMTA2 agreements have been signed with academic and research institutions-including 2 that were signed in 2021. These agreements have led to 29 offers of benefit-sharing from academic & research institutions.

50. To implement the WHA’s 2019 amendment to the PIP Framework (Decision WHA72(12) OP2), a process has been developed and is being implemented to amend the 84 SMTA2s signed prior to the Decision to add a new reporting obligation for indirect use of PIP biological materials. 18 out of 70 Category C agreements have been amended.

51. In 2021, a series of meetings were held to discuss pandemic vaccine deployment activities with a view towards operationalizing the SMTA2 supply commitments.

3.7 The use of financial and non-financial contributions

52. Overall budget implementation was low this year, no doubt due to the continued impact of the COVID-19 pandemic. However, it is important to note that implementation of activities adapted to new conditions such as no non-essential travel, multi-tasking human resources working to maintain progress, and the use of newly developed capacities to respond to the pandemic.

53. The PIP PC Preparedness budget for the 2020-2021 biennium was USD 31.4 million, and as of 31 December 2021 USD 23.4 million (74.5%) had been funded and USD 16.8 million (53.5%) had been implemented. The WHO Programme Budget Portal provides updated, detailed and transparent information on PIP contributions, budget allocations, technical and financial implementation, and progress across three level of the organization against specific objectives across the six outputs of the High-Level Implementation Plan II 2018-2023.

54. As of 31 December 2021, the total PC collection (2012-2021) stood at US$ 252 million. Of this, a total of US $ 126.93 million was allocated to preparedness (net funds available for implementation) and US$ 71.6 million was allocated to the Response Fund (inclusive of programme support costs). An additional amount of $3.58 million, representing accrued interest was added to the response funds.

55. Overall, the AG believes that the funding allocations are well managed and monitored. 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.

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8 Accessed here: [https://open.who.int/2020-21/our-work/category/14/programme/14.003/about/about](https://open.who.int/2020-21/our-work/category/14/programme/14.003/about/about)