

**Pandemic Influenza Preparedness Framework for the
sharing of influenza viruses and access to vaccines and
other benefits**

Decision WHA72(12), paragraph 1(a)

Report on influenza virus sharing

Report by the Director-General

February 2020

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INTRODUCTION

1. In May 2019, the Health Assembly, in decision WHA72(12), requested the Director-General, *inter alia*:

“(a) to work with the Global Influenza Surveillance and Response System (GISRS) and other partners, such as Other Authorized Laboratories and relevant institutions, to collect, analyse, and present data on influenza virus sharing in a way that enables a deeper understanding of the challenges, opportunities and implications for public health associated with virus sharing under the GISRS, including by identifying: specific instances where influenza virus sharing has been hindered; and how such instances may be mitigated.”

The present report addresses this request.

BACKGROUND

2. For more than 65 years, the rapid and open sharing of influenza viruses within the WHO Global Influenza Surveillance and Response System (GISRS) has been the foundation of global influenza prevention and control, including support for the development of seasonal influenza vaccines and for pandemic preparedness. Efficient and rapid sharing of influenza viruses is essential for timely risk assessment and mitigation, including production of updated vaccines. The Global Influenza Surveillance and Response System conducts year-round monitoring of constantly changing influenza viruses to identify newly emerging seasonal influenza viruses and influenza viruses with human pandemic potential.
3. The Global Influenza Surveillance and Response System is a network of more than 160 laboratories in 121 countries. Most laboratories are supported by national health ministries. The network currently consists of 147 National Influenza Centres, 14 Other Authorized Laboratories,¹ 12 WHO H5 reference laboratories, six WHO Collaborating Centres and four WHO essential regulatory laboratories.
4. Each year, GISRS laboratories test about 3.5 million human clinical samples for seasonal influenza. National Influenza Centres and Other Authorized Laboratories collect circulating viruses and perform initial analyses. Based on WHO's guidance on timely virus sharing,² they then share a subset of about 40 000 representative viruses and human clinical samples that test positive for influenza with the WHO Collaborating Centres.
5. WHO Collaborating Centres characterize viruses in detail and identify reference viruses that can be used for vaccine development in time for the biannual vaccine virus selection process. Meetings are held in February to determine the recommendations for the composition of the northern hemisphere vaccine and in September for the southern hemisphere vaccine. WHO Collaborating Centres share reference viruses with Essential Regulatory Laboratories and other partner laboratories that develop candidate vaccine viruses. Once the candidate vaccine

¹ This category refers to laboratories that participate in the Global Influenza Surveillance and Response System but are not formally recognized.

² Operational Guidance on Sharing Seasonal Influenza viruses with WHO Collaborating Centres (CCs) under the Global Influenza Surveillance and Response System (GISRS). Geneva: World Health Organization; 2017 (https://www.who.int/influenza/gisrs_laboratory/seasonal_sharing_guide/en/, accessed 10 February 2020)

viruses have been tested by the WHO Collaborating Centres and have been shown to be representative of the original virus, they are made available to all vaccine producers and to other GISRS and non-GISRS laboratories. Certain candidate vaccine viruses will be selected for vaccine production once the vaccine virus selection process has occurred. The timelines for the seasonal influenza vaccine and for virus sharing are shown in Fig. 1. Although virus sharing occurs throughout the year, there is an average of only six months to collect and characterize the most recently circulating viruses and develop candidate vaccine viruses before each vaccine composition meeting. The value of seasonal virus sharing lies not with any individual virus, but with the collection of globally shared viruses. Any delays in virus sharing within the Global Influenza Surveillance and Response System could hinder the availability of an optimal vaccine virus and adversely impact the effectiveness of the seasonal influenza vaccine.

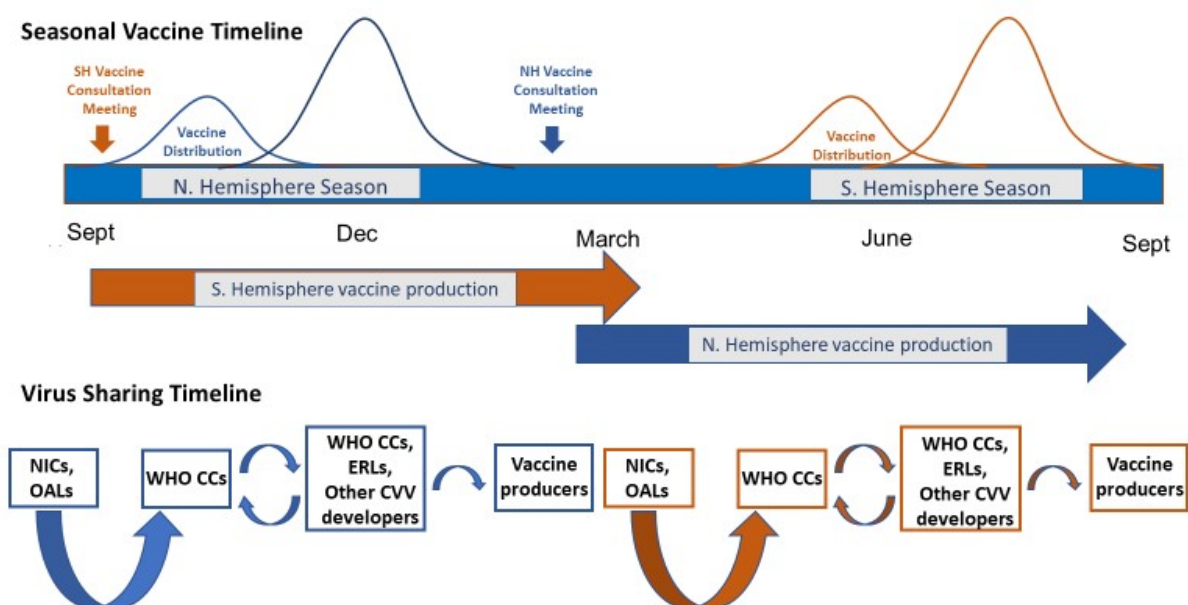


Figure 1: Timeline of Seasonal Vaccine Cycle and Virus Sharing

6. GISRS laboratories also conduct surveillance for influenza viruses with human pandemic potential. These viruses should also be shared with WHO Collaborating Centres according to specific WHO guidance¹ and the Pandemic Influenza Preparedness Framework for the sharing of influenza viruses and access to vaccines and other benefits. WHO Collaborating Centres characterize the viruses and make recommendations on whether candidate vaccine viruses should be developed for pandemic preparedness purposes. These recommendations are also made at the biannual vaccine composition meeting.

¹ Operational guidance on sharing influenza viruses with human pandemic potential (IVPP) under the Pandemic Influenza Preparedness (PIP) Framework. Geneva: World Health Organization; 2017 (https://www.who.int/influenza/gisrs_laboratory/ivpp_sharing_guidance/en/ , accessed 10 February 2020).

7. In recent years, there has been an increasing number of challenges associated with the sharing of both seasonal influenza viruses and influenza viruses with human pandemic potential under GISRS. In response to the request from the Health Assembly,¹ WHO has gathered data from GISRS and non-GISRS laboratories to enable a deeper understanding of the challenges, opportunities and implications for public health associated with virus sharing. This process included identifying specific instances where influenza virus sharing had been hindered and seeking ideas on how to mitigate delays in virus sharing.

DATA COLLECTION METHODOLOGY AND SUMMARY FINDINGS

8. Four questionnaires were distributed to obtain information on virus sharing experiences from different types of GISRS and non-GISRS laboratories. Input was requested on experiences from 2014 onwards, including challenges, concerning the sharing of: (1) seasonal influenza viruses and associated candidate vaccine viruses; and (2) influenza viruses with human pandemic potential and associated candidate vaccine viruses. The questionnaires asked for input on: (1) specific instances where virus sharing had been hindered; (2) reasons for the delay; and (3) possible solutions, and the public health opportunities and implications. Questionnaires were distributed to: (1) GISRS National Influenza Centres and Other Authorized Laboratories that share viruses with WHO Collaborating Centres; (2) GISRS WHO Collaborating Centres and Essential Regulatory Laboratories; (3) non-GISRS industry laboratories; (4) non-GISRS academic and public/private institutions that had received influenza viruses with human pandemic potential under a PIP Framework Standard Material Transfer Agreement 2.
9. A summary of data collected from the questionnaire follows:
 - (a) a total of 119 complete responses were received from GISRS and non-GISRS laboratories;
 - (b) 62 complete responses were received from National Influenza Centres and Other Authorized Laboratories that had shared seasonal influenza viruses since 2014;
 - (c) complete responses were also received from **all** WHO Collaborating Centres and Essential Regulatory Laboratories (nine in total, as one centre is both a WHO Collaborating Centre and an Essential Regulatory Laboratory). The number of responses from GISRS laboratories by WHO region is shown in Fig. 2;
 - (d) overall, 42% of GISRS laboratories submitted complete responses to the questionnaire;
 - (e) nine of the responding GISRS laboratories were also H5 Reference Laboratories;
 - (f) 25 complete responses were received from non-GISRS industry laboratories, including:
 - (i) 19 vaccine manufacturers from Asia, Europe and North America;
 - (ii) four biotechnology companies engaged in vaccine research and development;
 - (iii) two producers of antiviral or diagnostic products;
 - (g) 23 complete responses were received from non-GISRS academic and public/private institutions in Africa, Asia, Europe and North America.

¹ See decision WHA72.12, paragraph 1(a) (2019).

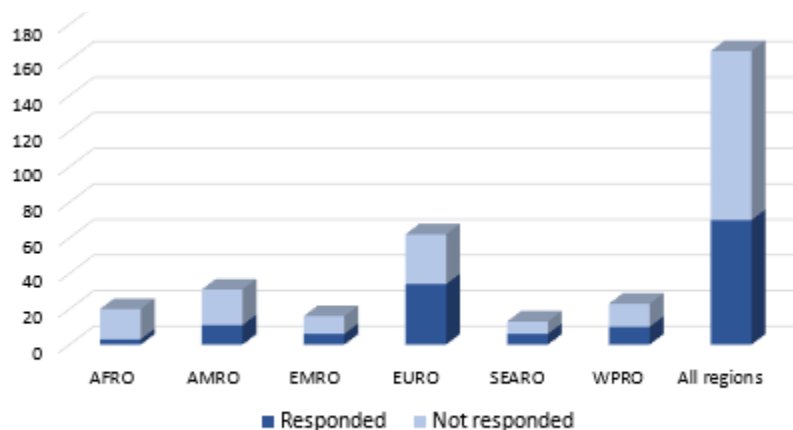


Figure 2: Number of responses from GISRS laboratories by WHO region

SHARING OF SEASONAL INFLUENZA VIRUSES AND ASSOCIATED CANDIDATE VACCINE VIRUSES

GISRS laboratories

10. Key findings from the responses to the questionnaire were:

- (a) of the 62 National Influenza Centres and Other Authorized Laboratories that responded, 24 reported experiences that affected the timely sharing of seasonal influenza viruses with WHO Collaborating Centres;
- (b) 16 laboratories provided specific examples and/or reasons for delayed sharing;
- (c) two WHO Collaborating Centres and one Essential Regulatory Laboratory reported delays in sharing seasonal influenza viruses with other laboratories;
- (d) 13 National Influenza Centres and Other Authorized Laboratories reported experiences that affected the timely receipt of viruses from another GISRS laboratory or a regional laboratory within their own country, but only six laboratories provided examples and/or reasons for the delays;
- (e) three WHO Collaborating Centres and one Essential Regulatory Laboratory reported delays in receiving viruses in time for characterization and the development of candidate vaccine viruses for the biannual vaccine virus selection process.

11. Reasons for delays in the sharing of seasonal influenza viruses within the Global Influenza Surveillance and Response System are summarized in Table 1. National Influenza Centres and Other Authorized Laboratories in some low- and middle-income countries reported that limited or costly courier services delayed virus sharing. In some cases, the cost and availability of courier services between regional laboratories and the National Influenza Centre were a problem. One National Influenza Centre reported delays in virus subtyping, which caused a delay in the shipment of viruses to a WHO Collaborating Centre.

12. A common challenge was the need to obtain national export and import permits from the receiving WHO Collaborating Centre. Each country has its own process for obtaining approval to send and receive biological samples which, when combined, add to the complexity of virus sharing within the Global Influenza Surveillance and Response System.

The time needed to submit applications and receive or renew permits from national authorities delayed shipments of viruses from National Influenza Centres and Other Authorized Laboratories to WHO Collaborating Centres. In some cases, delays in receiving national permits were not because of the viruses themselves, but because the samples also contained animal products. For example, influenza virus samples produced in eggs contain allantoic fluid, an animal product that, in some jurisdictions, requires separate permits or approvals from authorities. In general, delays due to these technical reasons ranged from one week to two months.

13. Laboratories also reported difficulties in virus sharing due to individual institutional policies or the international regulations imposed in recent years. Challenges due to the European Union's General Data Protection Regulation¹ were reported by some GISRS laboratories in Europe. Human respiratory samples positive for influenza virus also contain human genetic material, which is considered personal data under the European Union's Regulation and cannot be shared. One National Influenza Centre described the need to encrypt sample numbers and virus strain names in order to share samples with a WHO Collaborating Centre.
14. Sharing of human respiratory samples with WHO Collaborating Centres is critical for the development of influenza vaccines, as only viruses derived directly from these original samples can be used to produce candidate vaccine viruses. Individual institutional policies for sharing viruses or human samples with WHO Collaborating Centres also resulted in delays. In one case, a material transfer agreement between institutions was required and took more than 12 months to complete.
15. Implementation of access and benefit-sharing legislation, such as that on the Nagoya Protocol on Access to Genetic Resources and the Fair and Equitable Sharing of Benefits Arising from their Utilization to the Convention on Biological Diversity, has also contributed substantially to delays in virus sharing between certain countries and WHO Collaborating Centres in the past two years (see Fig. 3). Most cases required lengthy bilateral negotiation of a material transfer agreement between a National Influenza Centre and a WHO Collaborating Centre. New legislation created uncertainty for National Influenza Centres and national access and benefit-sharing focal points, due to a lack of clarity about access and benefit-sharing or Nagoya Protocol requirements. Virus sharing delays related to new legislation and regulations took six to nine months to resolve or remained unresolved as of December 2019.

"Eight years ago only a few GISRS laboratories had problems with sharing clinical samples. Now many more do." (WHO Collaborating Centre)

¹ Regulation (EU) 2016/679 of the European Parliament and of the Council of 27 April 2016 on the protection of natural persons with regard to the processing of personal data and on the free movement of such data (<https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32016R0679&from=EN>, accessed 10 February 2020).

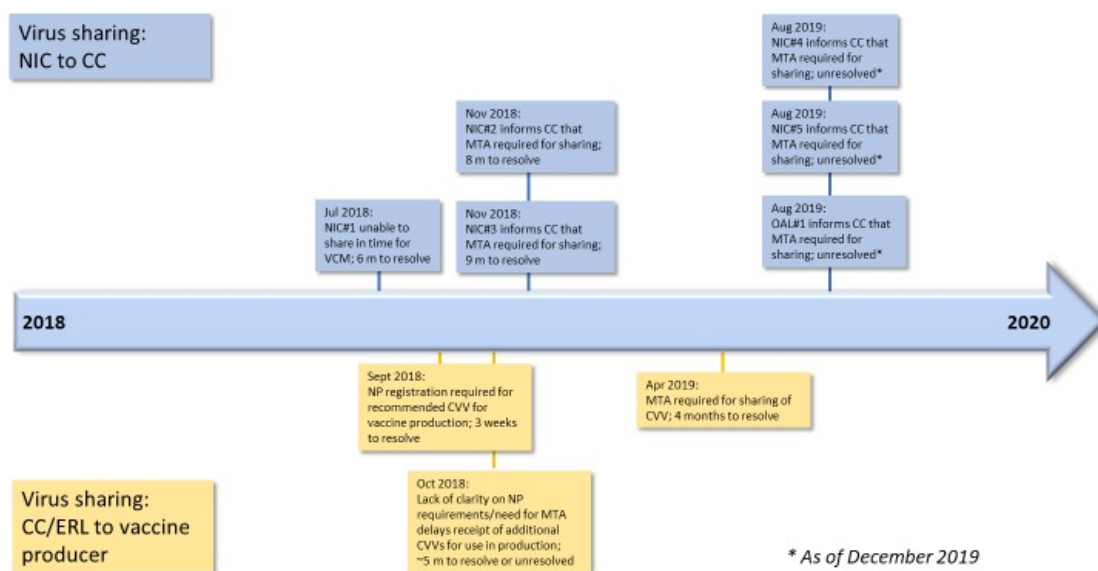


Figure 3: Timeline of Access and Benefit Sharing issues encountered by GISRS and non-GISRS laboratories

Non-GISRS laboratories

16. Non-GISRS laboratories receive a limited number of seasonal influenza viruses or associated candidate vaccine viruses from WHO Collaborating Centres and Essential Regulatory Laboratories each year for the purposes of vaccine production, vaccine research and development, and other product development or research.
17. Key findings from the responses to the questionnaire were:
 - (a) 11 of the 19 influenza vaccine producers reported experiences that affected the timely receipt of seasonal influenza viruses or associated candidate vaccine viruses from GISRS laboratories, or their ability to use a candidate vaccine virus for vaccine production;
 - (b) eight responses provided specific examples or reasons;
 - (c) two of the four biotechnology companies engaged in vaccine research and development reported delays in receiving viruses from a GISRS laboratory;
 - (d) laboratories that produced antiviral agents or diagnostics, together with academic and other research institutions, did not report any delays in receiving seasonal influenza viruses from GISRS laboratories.
18. The reasons for delays are summarized in Table 1 and include the same issues related to obtaining import or export permits as outlined above. In one case, limited staffing at a WHO Collaborating Centre led to a delay in processing requests and shipping viruses.
19. For vaccine producers, recent legislation implementing the Nagoya Protocol has posed a significant challenge for the timely receipt and use of candidate vaccine viruses (see Fig 3), as explained in detail below.
20. When a new vaccine virus is recommended by WHO, there may be more than one candidate vaccine virus that can be used by vaccine producers. Vaccine producers choose the candidate vaccine virus that works best in their production system. Below are examples of issues that arose in the selection of the 2019 southern hemisphere vaccine viruses.
 - (a) In September 2018, a vaccine virus recommended for the 2019 southern hemisphere vaccine required national authorization and registration under Nagoya Protocol legislation in the country that submitted the virus. However, there was considerable uncertainty and a lack of clarity regarding the process and terms of use of the candidate vaccine virus. These uncertainties resulted in a three-week delay in the use of the candidate vaccine virus for vaccine production.
 - (b) Additional candidate vaccine viruses became available in October 2018 using viruses from a different country that is also a party to the Nagoya Protocol. As with the previous case, similar uncertainty about the registration process and access and benefit-sharing requirements under the laws of that country prevented the use of those candidate vaccine viruses for the production of the 2019 southern hemisphere vaccine. Under the applicable access and benefit-sharing and Nagoya Protocol legislation in that country, one candidate vaccine virus required a material transfer agreement

between the National Influenza Centre and the WHO Collaborating Centre. The negotiation of the material transfer agreement took more than six months.

- (c) These are not isolated cases. In April 2019, another candidate vaccine virus required a material transfer agreement with a different WHO Collaborating Centre so that the Collaborating Centre could transfer the virus to non-GISRS laboratories. The material transfer agreement took four months to negotiate.

Table 1. Summary of findings concerning candidate vaccine viruses

Organization and laboratory type	No. of laboratories responding	No. of laboratories reporting delays in sharing viruses ^a	No. of laboratories reporting delays in receiving viruses	Major reasons for delays	Impact
GISRS National Influenza Centres and Other Authorized Laboratories	62	16	6	<ul style="list-style-type: none"> Limited or costly courier services for National Influenza Centres in some regions Complex and restrictive national import and/or export permits, including restrictions on shipping samples with animal product content National access and benefit-sharing and Nagoya Protocol legislation Institutional policies on sharing viruses National policies on sharing human specimens (i.e. General Data Protection Regulation) 	<p>Delays due to couriers or permits generally ranged from one or two weeks to one to two months</p> <p>Delays due to access and benefit-sharing and Nagoya Protocol legislation ranged from six to nine months or remain ongoing</p>
WHO Collaborating Centres and Essential Regulatory Laboratories	9 ^b	3	4		
Non-GISRS vaccine producers ^c	19	N/A ^d	8		<p>Delays due to permits were generally two to eight weeks</p> <p>Delays due to access and benefit-sharing and Nagoya Protocol legislation generally ranged from three weeks to more than eight months or remain ongoing</p>
Non-GISRS other industry laboratories	6	N/A	2		
Non-GISRS academic and public/private institutions	23	N/A	0		

^a Laboratories that provided examples and/or reasons for delays.

^b One organization is both a WHO Collaborating Centre and an Essential Regulatory Laboratory. Of the six WHO Collaborating Centres, only five routinely receive and share seasonal influenza viruses.

^c Vaccine producers reported delays in receiving a seasonal influenza viruses or associated candidate vaccine viruses or in their ability to use them in vaccine production.

^d N/A, not applicable; non-GISRS laboratories do not routinely share viruses with other laboratories.

Opportunities and implications for public health

21. There is an opportunity to improve the timeliness of virus sharing within the Global Influenza Surveillance and Response System by improving communications between WHO Collaborating Centres and National Influenza Centres in order to clarify optimal virus sharing practices and address specific courier or export/import permit issues.
22. Lengthy delays in virus sharing due to national access and benefit-sharing and Nagoya Protocol legislation and regulations have public health implications because they jeopardize the vaccine virus selection process and the timely development of candidate vaccine viruses and access to vaccines. The need to navigate a system in which each country has different access and benefit-sharing requirements that have to be negotiated on a bilateral basis is extremely burdensome and inefficient and could cause inequities in benefit sharing and limit virus access for the research and development of improved influenza vaccines. There is an opportunity for the public health sector to work towards harmonizing administrative and access and benefit-sharing processes and procedures for sharing influenza viruses.

“Public health can be positively impacted by doing all that is necessary to limit bureaucracy and the administrative burden involved in virus sharing. If public health is to be supported by the best choice of strains for seasonal vaccines, then minimizing barriers must be a priority.” (vaccine producer)

Proposed solutions for mitigating hindrances to seasonal influenza virus sharing

23. The following solutions were proposed by GISRS and non-GISRS laboratories to mitigate influenza virus sharing delays.
 - (a) WHO and WHO Collaborating Centres should provide enhanced guidance to individual National Influenza Centres and Other Authorized Laboratories as needed to clarify the specific number of viruses and optimal timing of shipments.
 - (b) GISRS laboratories should improve communications with vaccine producers about the availability of candidate vaccine viruses.
 - (c) GISRS laboratories within each country should work with regulatory authorities to establish requirements for timely import/export approvals.
 - (d) The Secretariat should raise awareness among Member States of the critical need for rapid, streamlined virus sharing, including the need to share human clinical samples in order to support global public health security. Health ministries should raise awareness of this need with the national authorities responsible for access and benefit sharing and Nagoya Protocol implementation.
 - (e) The Secretariat should encourage countries that have not yet implemented national access and benefit-sharing and Nagoya Protocol legislation to give special consideration to processes that facilitate the rapid sharing of influenza viruses (and

- other pathogens) and ideally exclude seasonal influenza viruses from access and benefit-sharing requirements.
- (f) Countries not requiring benefit sharing should provide documentation of this as legal certainty for vaccine producers.
 - (g) WHO and Global Influenza Surveillance and Response System members should implement a standardized WHO material transfer agreement between WHO Collaborating Centres and National Influenza Centres to provide harmonized and timely sharing of viruses, outlining GISRS benefits and providing transparency as to how viruses may be shared and used.
 - (h) The Secretariat and Member States should work together to gain international recognition of the Global Influenza Surveillance and Response System as a specialized international access and benefit-sharing instrument.

SHARING OF INFLUENZA VIRUSES WITH PANDEMIC POTENTIAL AND ASSOCIATED CANDIDATE VACCINE VIRUSES

GISRS laboratories

24. Key findings were as follows:

- (a) seven of 62 National Influenza Centres and Other Authorized Laboratories reported experiences that affected the timely sharing of influenza viruses with pandemic potential, but none provided examples or reasons for the delays. Most National Influenza Centres and Other Authorized Laboratories that gave this response had not had the opportunity to share influenza viruses with pandemic potential within GISRS since 2014, so it is likely that this specific question was misunderstood;
- (b) eight National Influenza Centres and Other Authorized Laboratories reported delays in receiving influenza viruses with pandemic potential or associated candidate vaccine viruses but only four provided specific examples or reasons. Some of the examples included delays in sharing H7N9 viruses in 2013 and 2014;
- (c) three of the nine WHO Collaborating Centres and Essential Regulatory Laboratories reported challenges in sharing influenza viruses with pandemic potential with other GISRS laboratories;
- (d) six of the nine WHO Collaborating Centres and Essential Regulatory Laboratories reported challenges in receiving influenza viruses with pandemic potential.

25. Table 2 summarizes the major reasons for delays in sharing influenza viruses with pandemic potential. Biosafety and biosecurity issues are a key source of difficulties in sharing influenza viruses with pandemic potential within the Global Influenza Surveillance and Response System. Influenza viruses with pandemic potential are typically animal viruses that cause zoonotic infections and are regulated by agricultural or veterinary authorities.

26. The classification of many influenza viruses with pandemic potential as “select agent” or “dual use” viruses in some countries has resulted in complex and restrictive national

approval and import/export permit processes that take many months, even years, to complete. Each country has a different set of requirements for obtaining approval to export or import influenza viruses with pandemic potential, which may involve multiple national authorities and ministries. Permits and licenses are typically quite restrictive; they may only cover certain viruses and be time-limited, requiring regular renewals. The conditions for virus sharing may prohibit further distribution of viruses to other GISRS laboratories. There may be heightened laboratory biosafety requirements, especially for work with influenza viruses with human pandemic potential of the H5 and H7 subtype, and these conditions are difficult to meet for some laboratories. Some institutions required lengthy negotiation of a bilateral material transfer agreement, including for candidate vaccine viruses that were developed using a patented genetic engineering process. One country required requests for sharing influenza viruses with human pandemic potential to be supported by specific non-technical justifications of the public health need to receive viruses, particularly when multiple viruses of a given subtype or outbreak are requested. Some countries have insufficient or no regulatory guidance for importing or exporting influenza viruses with pandemic potential.

27. Broader national security issues also adversely affected the sharing of influenza viruses with pandemic potential. Freight embargoes imposed on certain countries have prevented direct shipment of influenza viruses with pandemic potential, and some national policies do not allow viruses to be shipped outside of a country.
28. GISRS laboratories do not have sufficient resources to address all these issues.
29. In February 2019, WHO convened an informal consultation to discuss the rapid risk assessment for influenza emergencies. Representatives from countries with WHO Collaborating Centres outlined their national processes and timelines for sharing influenza viruses with pandemic potential. For “select agent” or “dual use” viruses, countries reported that it took a minimum of four to six months to obtain all regulatory approvals and coordinate shipments. One country reported an expedited approval process, or a “green channel”, that could reduce the time for approval to one or two weeks. However, this process is apparently only used in exceptional situations.
30. Overall, delays in sharing influenza viruses with pandemic potential, once requested, ranged from two months to more than three years. Many requests for influenza viruses with pandemic potential remained ongoing as at December 2019.

Table 2. Summary of findings concerning the reported reasons for delays in sharing influenza viruses with pandemic potential and associated candidate vaccine viruses

Organization and laboratory type	No. of laboratories responding	No. of laboratories reporting delays in sharing viruses ^a	No. of laboratories reporting delays in receiving viruses	Major reasons for delays	Impact
National influenza centres and Other Authorized Laboratories	62	0	4	<ul style="list-style-type: none"> • Biosafety and biosecurity issues: classification of many influenza viruses with pandemic potential as "select agent" or "dual use" viruses • Complex and restrictive national import or export permit or license requirements • National or institutional policies on sharing influenza viruses with pandemic potential and/or human specimens • Requirement to have bilateral material transfer agreements • Freight embargoes due to security concerns 	Delays in sharing viruses ranged from two months to more than three years or remain ongoing
WHO Collaborating Centres and essential regulatory laboratories	9 ^b	3	6		
Non-GISRS vaccine producers ^c	19	N/A ^d	6	<ul style="list-style-type: none"> • Biosafety and biosecurity issues: testing requirements to lower biosafety level of candidate vaccine viruses • Complex and restrictive import or export permit or license requirements • Additional permit/approval requirements for candidate vaccine viruses that are genetically modified organisms 	Delays in sharing viruses ranged from two to 11 months or remain ongoing
Non-GISRS other industry laboratories	6	N/A	1		
Non-GISRS academic and public/private institutions	23	N/A	2		

^a Laboratories that provided examples and/or reasons for delays.

^b One organization is both a WHO Collaborating Centre and an Essential Regulatory Laboratory.

^c Vaccine producers reported delays in receiving an influenza virus with pandemic potential or the associated candidate vaccine virus or in the ability to use it in vaccine production.

^d N/A, not applicable; non-GISRS laboratories do not routinely share viruses with other laboratories.

Non-GISRS laboratories

31. Key findings were as follows:

- (a) eight of 19 influenza vaccine producers reported experiences that affected the timely receipt of influenza viruses with pandemic potential or associated candidate vaccine viruses from GISRS. Six of the responses included specific examples or reasons;
- (b) one biotechnology company engaged in vaccine research and development also reported challenges, stating, “We gave up on receiving the H7N9 candidate vaccine virus due to the paperwork required for the process”;
- (c) two academic institutions provided reasons for delays in receiving influenza viruses with pandemic potential and associated candidate vaccine viruses from GISRS laboratories. Complex regulatory issues and import/export approvals were a key reason for delayed sharing or an inability to receive influenza viruses with pandemic potential;
- (d) vaccine producers described delays in receiving candidate vaccine viruses for influenza viruses with pandemic potential due to the requirement for safety testing of candidate vaccine viruses. This is a WHO requirement in order to be able to downgrade biocontainment for use in vaccine production. WHO has recently updated safety-testing requirements for vaccine viruses for influenza viruses with pandemic potential in order to address this issue;⁶
- (e) furthermore, almost all candidate vaccine viruses for influenza viruses with pandemic potential are genetically modified organisms. Some countries require additional approval or permits to import and work with such viruses;
- (f) delays in sharing influenza viruses with pandemic potential ranged from two to 11 months or remain ongoing.

Opportunities and implications for public health

32. The timely and unrestricted sharing of influenza viruses with pandemic potential is critical for public health risk assessment and pandemic preparedness, including the development of diagnostic tools and vaccines and confirming antiviral effectiveness. In a pandemic response situation, delayed receipt of influenza viruses with pandemic potential or release of candidate vaccine viruses will have an impact on vaccine development and production and quality release, all of which will delay vaccine availability for the public. Unfortunately, the challenging country-specific regulations and biosafety concerns that surround influenza viruses with pandemic potential and associated candidate vaccine viruses currently result in inadequate sharing of influenza viruses with pandemic potential within the System and with non-GISRS partners.

“Clearly efficient and rapid sharing of viruses is a cornerstone of GISRS and the global response to influenza. Anything that impedes this has a potential public health impact.” (WHO Collaborating Centre)

⁶ Guidelines for the safe development and production of vaccines to human pandemic influenza viruses and influenza viruses with pandemic potential. In: WHO Expert Committee on Biological Standardization: sixty-ninth report. Geneva: World Health Organization; 2019: Annex 3 (WHO Technical Report Series, No. 1016; https://www.who.int/biologicals/expert_committee/Annex_3_WHO_TRS_1016_web3.pdf, accessed 13 February 2020)

Proposed solutions for mitigating hindrances to sharing of influenza viruses with pandemic potential

33. The following solutions were proposed by GISRS and non-GISRS laboratories for mitigating delays or the lack of sharing of influenza viruses with pandemic potential and associated candidate vaccine viruses:
- (a) WHO and GISRS should clarify the regulatory approval process for exporting influenza viruses with pandemic potential in relevant countries, including the criteria for using an expedited or “green channel” approval process.
 - (b) The Secretariat should prepare a document that explains to non-technical Member State partners the public health need to share influenza viruses with pandemic potential and in particular the need to share multiple representative influenza viruses with pandemic potential resulting from outbreaks.
 - (c) The Secretariat and GISRS members should develop and maintain a central database that provides requirements for importing and exporting influenza viruses with pandemic potential and candidate vaccine viruses from different countries.
 - (d) WHO Collaborating Centres, essential regulatory laboratories and H5 Reference Laboratories should ensure that up-to-date permits and licenses are in place to share and receive influenza viruses with pandemic potential. They should work with the national authorities responsible for regulating the import and export of influenza viruses with pandemic potential to develop approaches to ensure more rapid and streamlined virus sharing and to address restrictions on sharing;
 - (e) Vaccine producers should ensure that approvals for the use of genetically modified candidate vaccine viruses for influenza viruses with pandemic potential are in place.

CONCLUSIONS

34. Influenza is a unique, vaccine-preventable disease; efforts to tackle it rely on regular and timely access to viruses to ensure that the public health sector has access to up-to-date vaccines. The WHO Global Influenza Surveillance and Response System has efficiently and openly shared influenza viruses for the purposes of risk assessment and response for more than 65 years.
35. In recent years, the sharing of influenza viruses within the Global Influenza Surveillance and Response System and with non-GISRS partners has become increasingly complex. For seasonal influenza viruses, both technical issues and international legislation contribute to delays in virus sharing. Delays in seasonal influenza virus sharing due to technical reasons were resolved in a shorter time frame than delays due to international legislations.
36. Legislation relating to access and benefit sharing, the Nagoya Protocol and human data protection have introduced great uncertainty into the sharing process and, in some cases, have meant that influenza virus and candidate vaccine virus cannot be shared until after the vaccine virus selection and vaccine production process has ended. In September and October 2018, the uncertainties and delays in virus sharing caused by Nagoya Protocol legislation for the first time had a direct impact on vaccine production. If such sharing issues are not resolved, it is likely that GISRS laboratories will become severely limited in their ability to share, receive and forward viruses within the Global Influenza Surveillance and Response System, restricting the availability of optimally protective vaccine viruses and the timely availability of life-saving influenza vaccines.
37. Biosafety and biosecurity issues are largely responsible for delays in the sharing of influenza viruses with pandemic potential, which is critical for risk assessment, pandemic preparedness and timely vaccine development in a pandemic situation. The complex, multisectoral approval process, and lack of transparency in some cases, has severely hampered the sharing of influenza viruses with pandemic potential. Unless this issue is resolved, the global public health sector may fall far short in responding to the next pandemic.
38. Solutions to issues relating to the sharing of seasonal influenza viruses and influenza viruses with pandemic potential require commitment and action from the Secretariat, the Global Influenza Surveillance and Response System and Member States.

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