17 October 2017

III

Implementation of Decision WHA70(10) 8(b)

Evidence for *"Scoping Paper on approaches to seasonal influenza and genetic sequence data under the PIP Framework" ("Scoping Paper")*

Compilation III. PIP Advisory Group work on GSD under the Framework

Recognizing that further work would be needed to resolve the handling of GSD under the Framework, Member States requested that the Director-General consult with the PIP Advisory Group "on the best process for further discussion and resolution of issues relating to the handling of [IVPP GSD] as part of the PIP Framework."[1] The PIP Advisory Group has been working on the matter since 2013. To support its work, the Advisory Group established two technical working groups, and developed several documents. These documents have provided the bases for several recommendations to the Director-General on the handling of GSD under the PIP Framework.

More information on the work of the PIP Advisory Group related to GSD is available at http://www.who.int/influenza/pip/advisory_group/gsd/en/.

This document contains excerpts from PIP Advisory Group documents and meeting Reports on the matter of handling of GSD under the PIP Framework. [2] The excerpts were deemed relevant to Part B of *WHA70(10)(8)(b): Scoping Paper on approaches to seasonal influenza and genetic sequence data under the PIP Framework* ("Scoping paper").[3]

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Every effort has been made to be as inclusive, balanced and thorough as possible while recognizing the need to maintain a focus on the topics relevant to the Scoping Paper. Member States and stakeholders are encouraged to contact the Secretariat at pipanalysis@who.int regarding issues or comments on the content of this document which should be considered to be a living document.

[1] See PIP Framework section 5.2.4.
[2] For information on the PIP Advisory Group's work, see http://www.who.int/influenza/pip/advisory_group/gsd/en/
[3] http://www.who.int/influenza/pip/scopingpaper.pdf ; See also Terms of Reference for the Implementation of decision WHA70(10) 8b), available at http://www.who.int/influenza/pip/8bTORs.pdf?ua=1 .

Table III.1 PIP Advisory Group findings and recommendations to the Director-General

Since 2013, the PIP Advisory Group has been conducting work to develop guidance for the Director-General as requested by Member States under PIP Framework section 5.2.4. The table below contains excerpts from PIP Advisory Group Meeting Reports to the Director-General, related to discussions on the handling of GSD under the PIP Framework. All PIP Advisory Group meeting reports can be found at http://www.who.int/influenza/pip/pip_meetings_consultations/en/

Reference No.	Source	Excerpts from PIP Advisory Group Meeting Reports
A1.	**October 2013 PIP Advisory Group Meeting Report**	5.The Advisory Group agreed that development in synthetic biology raise complex issues with legal, technical, public health and biosecurity implications that require careful review and consideration. 6.To assist the Advisory Group in developing guidance for the Director-General on this matter, technical support from a technical expert working group would be beneficial. The Advisory Group developed Terms of Reference for such an expert group.
A2.	**April 2014 PIP Advisory Group Meeting Report**	4. The Chair of the Technical Expert Working Group presented the Group's method of work and summarized the key elements of the preliminary report (use of genetic sequence data, regulatory and intellectual property issues, monitoring and tracing of genetic sequence data, and biosecurity and biosafety issues). The ensuing discussion noted that: • Genetic sequence data are covered by the PIP Framework. There were different perspectives on whether genetic sequence data are included in the definition of PIP biological materials. • As genetic sequence data fall within the PIP Framework (e.g. Section 5.2; Annex 4, Point 9; Annex 5 "Guiding Principles"), the spirit of the Framework and the importance of maintaining equal footing for the sharing of viruses and benefits derived therefrom must be kept in mind in considering issues related to the handling of genetic sequence data for H5N1 and other influenza viruses with pandemic potential. • Given the many ways that genetic sequence data may be disseminated, it is likely that WHO will not be aware of all instances of the use of genetic sequence data arising out of the WHO Global Influenza Surveillance and Response System. The PIP Framework's objective of benefit sharing, however, must be met. Different approaches are available, including the monitoring and/or tracing of genetic sequence data through electronic databases (e.g. – the Global Initiative on Sharing All Influenza Data or GenBank) or through regulatory approval files and patent applications for influenza-related products. The utility of monitoring to maximize benefit sharing, as well as the feasibility and costs of possible monitoring methods, deserve further investigation. 6. The Advisory Group will meet with electronic database managers for genetic sequence data as well as industry and other stakeholders during its meeting in October 2014 to gather further information with a view to developing advice to the Director-General on genetic sequence data-related issues.
A3.	**April 2014 PIP Advisory Group Meeting Report, recommendations**	5. The Advisory Group reaffirmed the spirit of the Framework and the importance of maintaining equal footing for the sharing of viruses and benefits derived therefrom. It noted that genetic sequence data is a rendering of virus material and its use could accelerate the development of pandemic influenza vaccines. The Advisory Group thanked the Technical Expert Working Group for its work and noted that upon submission of its final report it will have concluded its work. The Advisory Group recommended that the Director-General: • post the final report of the Technical Expert Working Group on the WHO website for informational purposes with an attached cover note describing the process; • inform Members States, industry and other stakeholders about the posting of the report; and • inform the World Health Assembly about progress on the issue of genetic sequence data.
A4.	**October 2014 PIP Advisory Group Meeting Report, Summary of Consultation with database managers**	29. As part of the technical consultation, representatives of databases provided information on their establishments, content, data access, use and transfer policies, monitoring and enforcement policies, and curation procedures. Some general observations included: • Most databases have an open access policy. As explained by a representative of the German Federal Ministry of Food and Agriculture, access to the EpiFlu™ database hosted by the Federal Republic of Germany, based on a co-operation agreement with the GISAID Initiative, is open to anyone who positively identifies himself or herself during registration and accepts the GISAID Database Access Agreement. This Agreement enables fair sharing of GSD, with the goal that all users mutually respect the rights of other users in the relevant data, and facilitates, through the positive identification of each and every user, the tracing of the accession of data. Access to the Influenza Virus Monitoring On-Line (Indonesia) – which has never been used for human influenza viruses – is open only to registered users who have agreed to its data access policy. • In general, databases are able to identify the provenance of information that is uploaded; it is difficult, however, for them to forward trace the transfer of data. • Most GISRS laboratories use GISAID; its value for outbreak response and the biannual seasonal influenza vaccine composition meetings was stressed.

Reference No.	Source	Excerpts from PIP Advisory Group Meeting Reports
		• The databases indicated their willingness to discuss how better to collaborate with each other to improve the sharing of GSD from influenza viruses.
A5.	**October 2014 PIP Advisory Group Meeting Report**	30. The ensuing discussion noted: • GSD is covered by the Framework (e.g. Section 5.2; Annex 4, Point 9; Annex 5 'Guiding Principles'). The spirit of the Framework and the importance of maintaining equal footing for the sharing of viruses and benefits derived therefrom must be kept in mind when considering issues related to the handling of GSD for influenza viruses with pandemic potential. • There may be some options for identifying GSD that originate from the WHO GISRS other than monitoring databases; however, the process must be feasible, efficient and create legal certainty. Monitoring the end-products generated through the use of GSD was discussed as a potential option. 31. Having taken into consideration the TEWG final report and having interacted with representatives of databases, industry and civil society, the Advisory Group made the following observations: a. Laboratories should continue to share the GSD of influenza viruses with pandemic potential (IVPP) as soon as it becomes available because it is necessary for timely and comprehensive pandemic risk assessment and response. b. In accordance with Section 6.3.2, laboratories using GSD will meet appropriate biosafety guidelines (WHO Laboratory Biosafety Manual, 3rd edition) and employ laboratory protection best practices. c. The objective of benefit-sharing may be met by mechanisms related to monitoring products generated using influenza GSD, rather than by monitoring use of GSD and/or tracing GSD, noting that source identification is critical. d. Closer collaboration regarding open sharing of influenza GSD among the many different databases is desirable.
A6.	**October 2014 PIP Advisory Group Meeting Report, recommendations**	32. Advice to the Director-General on the best process for further discussion and resolution of the issues related to the handling of GSD under the PIP Framework: In accordance with PIP Framework Section 5.2.4, the Advisory Group recommends for the Director General's consideration the following as the best process for further discussion and resolution of the issues related to the handling of GSD under the PIP Framework: In 2015, the Advisory Group will identify the optimal characteristics of a system for the handling of IVPP GSD under the PIP Framework including consideration of: a. Data sharing systems that are best suited to meet the objectives of the Framework considering obligations and timeliness of data submission, quality assurance of data, completeness of data annotation, ease of access to data, sustainability and security of the system. b. Systems to monitor use of IVPP GSD in end-products. For the foregoing, the Advisory Group will consult with GISRS laboratories, databases, and industry and other stakeholders. The results of the above work will be available to the Secretariat for integration into the 2016 review of the Framework and its annexes as provided in Section 7.4.2.
A7.	**April 2015 PIP Advisory Group Meeting Report**	27. The Advisory Group noted the need to quantify and increase the accuracy of results, and narrow the focus of searches to checkpoints that allow identification of end products that are relevant to the PIP Framework (e.g. patents, clinical trials, regulatory approval files, and publications presenting clinical trial data results). 28. The Advisory Group reviewed the next steps for work on GSD sharing systems. Based on discussions with industry, civil society and database representatives, the Advisory Group indicated that the Secretariat should consider initiating discussions with database managers on the possibility of including a statement about the PIP Framework on their website.
A8.	**April 2015 PIP Advisory Group Meeting Report, recommendations**	30. Advice to the Director-General on progress to implement recommendations on handling of Genetic Sequence Data: The Advisory Group recommended that the Secretariat consider initiating discussions with database managers on the possibility of including a statement about the PIP Framework on their website. The Advisory Group recommended that the Secretariat continue its collaboration with the WDCM and WFCC with a view to using the prototype search engine on a pilot basis. The Advisory Group recommended that the TWG start work as soon as possible. They also recommended that the TWG have the same Chair as the TEWG in order to have continuity. The Advisory Group also recommended that the composition of the TWG should include two additional PIP Advisory Group Members.

Reference No.	Source	Excerpts from PIP Advisory Group Meeting Reports
A9.	April 2016 PIP Advisory Group Meeting Report	49. The AG welcomed the TWG revised draft document "Optimal Characteristics of an influenza genetic sequence data sharing system under the PIP Framework" and thanked the TWG for its work. The AG encouraged finalizing the document, taking into consideration the result of the consultation with industry and other stakeholders, and discussion within the AG. 50. The AG reiterated the importance of maintaining equal footing for the sharing of viruses and the sharing of benefits when considering handling of GSD under the Framework. 51. The AG made the following observations regarding GSD and the PIP Framework objectives: a) The system for handling GSD is composed of data providers, data users, and databases. b) Rapid access to the genetic sequence data of influenza viruses with human pandemic potential (IVPP GSD) is necessary for timely and comprehensive pandemic risk assessment and response. c) IVPP GSD can be considered a rendering of virus material, in electronic form. d) The Framework recognizes that there are different approaches to data sharing. e) A diversity of databases is best for optimal data sharing and resilience. f) Technology for traceability has evolved and continues to evolve since adoption of the Framework.
A10.	April 2016 PIP Advisory Group Meeting Report, **recommendations**	53. AG recommends to the Director-General that the following constitutes the initial phase of defining the optimal characteristics of a system to handle IVPP GSD under the PIP Framework: **IVPP GSD sharing** • Ensure rapid and timely sharing of IVPP GSD for pandemic risk assessment and rapid response • Ensure the broad sharing of IVPP GSD with the international scientific and public health community and its availability through publicly-accessible databases • Encourage rapid publication of research relevant to pandemic influenza preparedness and response • Ensure quality in all steps of data management so that the IVPP GSD and its metadata is complete and of high quality • Offer a sufficient degree of redundancy, including through multiple databases, in order to secure sustainability of access to data **Benefit sharing** • Allow identification of commercial end-products developed using IVPP GSD through source identification using accession numbers or self-reporting • Facilitate benefit-sharing through traceability and/or commercial end product identification, data access agreements or database statements about PIP Framework expectations • Ensure appropriate acknowledgement of the contribution of data providers and originating laboratories/countries and strongly encourage their active participation in scientific publication and projects associated with research on the IVPP GSD As a way forward, the AG recommends the development of Standard Operating Procedures for data providers and databases, with a view to implementing some of the optimal characteristics and best practices developed by the TWG. The AG also recommends that the Secretariat continue its collaboration with the WDCM to develop a search engine identifying end-products developed using IVPP GSD and requests that the search engine be implemented on a pilot basis in order to assess its usefulness and feasibility for using data collected for benefit sharing purposes
A11.	October 2016 PIP Advisory Group Meeting Report	13. The AG recalled its discussions during the April 2016 AG meeting and reaffirmed its position that a diversity of genetic sequence databases is best for optimal data sharing and resilience. The AG plans to engage with GISRS members, including the WHO Collaborating Centres, for additional input on the use of databases. 14. The AG considered that development of the guidance document was most urgent. In light of on-going virus sharing issues, the guidance should cover the sharing of materials, GSD, and information, and support the PIP Framework principles and objectives of efficient, fair and equitable access and benefit sharing for pandemic preparedness and response.

Reference No.	Source	Excerpts from PIP Advisory Group Meeting Reports
A12.	**October 2016 PIP Advisory Group Meeting Report, recommendations**	15. The AG recommended that the Director-General establish a specialized sub-group of the AG to develop the guidance on the sharing of materials, genetic sequence data and information. The sub-group will be composed of up to 10 current or former AG members, with geographical representation, and relevant skill mix and experience. In order to develop the guidance document, the sub-group will work with relevant stakeholders such as, but not limited to: GISRS, databases and initiatives, industry, civil society, academic and research institutions and journals.
A13.	**March 2017 PIP Advisory Group Meeting Report**	26. There was discussion on GSD. It was noted that technology and science are progressing rapidly and their impact on the work of the PIP Framework would need to be considered and anticipated as much as possible. 27. The AG recognized that the topic of GSD had been addressed in the 2016 Review Group recommendations, which will be taken up at the World Health Assembly. The AG has conducted significant work on this topic and will proceed with efforts to develop appropriate guidance. 28. The importance of maintaining Member States' trust in the system was emphasized. The AG reaffirmed its role in safeguarding the objectives of the PIP Framework and its principles of rapid access and equitable benefit sharing. The AG discussed previous work and recommendations on the handling of IVPP GSD and emphasized that the guidance should summarize such work and build upon it. The AG emphasized the need to recognize the contributions of data providers, databases and data users, and to work with them closely to develop the guidance. 29. The AG discussed a possible process for developing the potential guidance on IVPP GSD. The AG plans to develop a draft document which will serve as the starting point for extensive consultations with GISRS, industry, civil society, databases and initiatives, academia and other stakeholders. Mindful of the recommendation of the Review Group on the urgency of the process, the AG decided to consider the document at their next meeting in October 2017. However, conscious of the complexity of the issue, they expressed the need to ensure adequate time for consultations. 30. It was clarified that WHO is not developing a GSD database. WHO further clarified that as recommended by the AG in April 2016, it is "continu[ing] its collaboration with the World Data Centre for Microorganisms (WDCM) to develop a search engine identifying end-products developed using IVPP GSD and [to implement it] on a pilot basis in order to assess its usefulness and feasibility for using data collected for benefit sharing purposes."4 WHO indicated that the development of the search engine is at no cost to the PIP Framework.
A14.	**March 2017 PIP Advisory Group Meeting Report, recommendation**	32. Mindful of the 2016 Review recommendation 15 that the AG "produce with urgency recommendations to clarify the handling of GSD" and with a view to developing guidance on the mechanism to share IVPP GSD and the benefits that result, and recognizing that discussion of this issue at the Seventieth World Health Assembly in May 2017 may lead to further recommendations, the AG recommends a process, to be led by the AG, to develop guidance on this issue. This process should involve close consultation with GISRS, and further consultation with industry, relevant databases, civil society and other interested parties. The AG will review the draft guidance produced by this consultative process at its meeting in October 2017.

[4] See Advisory Group meeting Report, April 2016 paragraph 55 http://www.who.int/influenza/pip/ag_april2016_MeetingRpt.pdf

Table III.2 Excerpts from the Technical Expert Working Group ("TEWG") report on GSD

In October 2013, the PIP AG established a Technical Expert Working Group (TEWG) to assess the scientific, technical, operational and intellectual property implications of using GSD to develop vaccines, diagnostic and pharmaceutical products.[5] The TEWG Report can be found at http://www.who.int/influenza/pip/advisory_group/PIP_AG_Rev_Final_TEWG_Report_10_Oct_2014.pdf?ua=1.

Reference No.	Section	Excerpts from AG TEWG Report
A15.	**Current known uses of GSD in relationship to influenza related technologies, products, inventions and patents**	Individual influenza virus genetic sequences can be used as a direct source for the development of products, such as candidate vaccine viruses or vaccines using recombinant proteins. Additionally, bulk sequences are used, inter alia, to gather epidemiological data, to design primers, probes and antibodies as well as for the design of vaccines based on conserved epitopes. Collectively, these approaches, all critical for the development of new and better vaccines, as well as significantly decreasing the time required to manufacture pandemic vaccines, depend crucially on the availability of GSD.
A16.	**Potential regulatory issues that must be resolved before commercialization**	National regulatory authorities would most likely take a similar approach to GSD developed vaccines as they have for approving vaccines made using CVVs prepared by RG technology. Although no additional obstacles for the approval of vaccines based on a CVV generated from synthetic DNA are foreseen, experience during the 2009 H1N1 pandemic suggests that unexpected questions and delays could arise in pandemic situations due to the use of novel products and approaches.
A17.	**Potential intellectual property issues**	In most jurisdictions, influenza GSD would not be considered patentable subject matter. However, innovations from the development of influenza-related products could be protected if the patentability requirements, as applied in the countries where protection is sought, are met. This may lead to a complex IP environment for vaccines and other products using GSD and synthetic DNA. In accordance with SMTA 1, within GISRS neither the provider nor the recipients of GSD should seek to obtain any intellectual property rights on GSD if protection were available.
A18.	**Feasibility of monitoring or tracing the sharing of GSD considering methods to generate, store, retrieve and share GSD**	The objective of benefit-sharing may be met by monitoring use of GSD and/or tracing GSD or by other mechanisms related to influenza-related products. While monitoring and tracing the use of GSD is limited by the medium used to share it, technical mechanisms to trace or monitor downloading of GSD from databases may be implemented. GSD of PIP biological material can also be generated by non-GISRS laboratories. In that case, WHO will likely not know of this, and the sharing of such will be more difficult to monitor. Notwithstanding, there are other potential mechanisms that could be developed to monitor the use of GSD, such as processes related to influenza-related products (e.g. regulatory approval files and patent applications)
A19.	**Issues related to biosecurity**	From a biosecurity perspective, it may be easier to control the custody of a physical object, such as a virus sample, than the custody of data. Large magnitudes of data can be readily disseminated in electronic form, such as through the Internet. However, it is more difficult to convert complex data sequences to malicious use than to use biological materials maliciously. Nonetheless, these issues already exist for all-publicly available GSD and are already under considerable scrutiny within the context of dual-use research of concern. It is hard to see how any PIP GSD would provide an increased risk over what is currently possible.
A20.	**Issues related to biosafety**	From a biosafety standpoint, GSD has potential advantages over the sharing of virus samples, as it mitigates the risk of the inadvertent release of the infectious agent by limiting access to the original biological agent; and by restricting access of dangerous influenza samples to authorized laboratories involved in vaccine development that have adequate high-level security. Furthermore, by reducing the need to transport influenza virus with pandemic potential, the use of GSD could be seen as a way to improve the safety of the production of influenza vaccines, antivirals and diagnostics.

[5] See Terms of Reference, Technical Expert Working Group on genetic sequences under the PIP Framework, available at http://www.who.int/influenza/pip/advisory_group/TEWG_ToRs.pdf?ua=1.

Table III.3 Excerpts from the PIP Advisory Group Technical working group (TWG) on the sharing of GSD – "*Optimal Characteristics of an influenza GSD sharing system under the PIP Framework*"

The PIP Advisory Group established a Technical Working Group ("TWG") in April 2015 to support its work on GSD under the PIP Framework. The TWG was asked to develop optimal characteristics of an influenza GSD sharing system that is best suited to meet the objectives of the Framework, for the Advisory Group's consideration.[6] The TWG report "*Optimal Characteristics of an influenza genetic sequence data sharing system under the PIP Framework*" can be found at **http://www.who.int/influenza/pip/advisory_group/twg_doc.pdf?ua=1**.

The table below contains the excerpts from the TWG Report to the PIP Advisory Group.

Reference No.	Section	Excerpts from TWG Report
A21.	**Obligations and expectations of data submission**	- OC I.1: IVPP GSD should be accessible to the international scientific and public health community as well as other stakeholders as widely and rapidly as possible after first identification of an IVPP. This accessibility should however take into account the need to share benefits arising from the use of IVPP GSD. - OC I.2: *3 options proposed for AG's consideration*: o Option 1: Data providers should submit IVPP GSD to a database without registered user access/open access database (DWRUA/OAD) (such as GenBank, ENA, or DDJB) or a database with registered user access/controlled access databases (DRUA/CAD) (such as GISAID EpiFluTM). DRUA/CADs (such as GISAID EpiFluTM) are better supportive of the benefit-sharing objectives of the PIP Framework because of their potential for traceability o Option 2: IVPP GSD should be submitted to a publicly-accessible database that is implementing a data access and use agreement that supports the principles and objectives of the PIP Framework and should be shared freely between all such databases. o Option 3: IVPP GSD should be submitted to a publicly-accessible database that supports the principles and objectives of the PIP Framework and should be shared freely between all such databases. - OC I.3: The IVPP GSD sharing system should support the ability of GISRS laboratories to fulfil their Terms of Reference under the PIP Framework.
A22.	**Timeliness of Data submission**	- OC II.1: Data providers should upload IVPP GSD to a publicly accessible database in a timely manner but no later than one month after sequencing is completed. - OC II.2: Databases should aim to provide public access to submitted IVPP GSD within 24 hours of data submission. - OC II.3: The IVPP GSD sharing system should include a mechanism whereby newly submitted IVPP GSD can be put under a temporary submission embargo. During that period, data users should not submit manuscripts involving the newly submitted IVPP GSD for publication in peer-reviewed scientific journals without the original data provider's authorization. - OC II.4: *2 options proposed for the AG's consideration:* o Option 1: In order to encourage timely IVPP GSD sharing, data users should acknowledge the contribution of data providers and the originating laboratories in scientific publications and other works. o Option 2: In order to encourage timely IVPP GSD sharing, data users should acknowledge the contribution of data providers and the originating laboratories in scientific publications and other works. The requirement for proper acknowledgement should be part of a data access and use agreement.
A23.	**Quality assurance of data**	- OC III.1: All entities that contribute to the IVPP GSD sharing system are jointly responsible for quality assurance and quality control of IVPP GSD. IVPP GSD and its metadata should be accurate, complete and of high quality. - OC III.2: Timeliness of data sharing is a priority. Therefore, in certain instances, data providers may submit initial data that is incomplete or has not been fully quality assured. It is understood that quality assurance and quality control is a dynamic layered process that may require several updates to the data. Data providers should update the data as often as necessary. - OC III.3: The IVPP GSD sharing system should provide quantifiable metrics for accuracy, completeness and quality to data users such that they can judge appropriateness of the data for downstream use. These metrics may change overtime in response to the needs of data providers and users. Therefore, the system should be flexible enough to adapt to these

[6] See Technical Working Group (TWG) on the sharing of influenza genetic sequence data, Terms of reference, available at http://www.who.int/influenza/pip/advisory_group/twg_tors.pdf?ua=1

Reference No.	Section	Excerpts from TWG Report
		changing metrics. - OC III.4: Databases should provide tools to support quality assessment and quality control and to detect the presence of potential sequence artefacts, including extraneous sequences in IVPP GSD that are not of viral origin.
A24.	**Upload and completeness of data annotation**	- OC IV.1: The IVPP GSD sharing system should support the collection and validation of a minimum set of core sequence metadata annotations and additional optional metadata using standard vocabularies for all eight IVPP gene segment. - OC IV.2: Tools for uploading metadata should have high usability and present to the GISRS laboratories as few obstacles to data sharing as possible. - OC IV.3: The IVPP GSD sharing system should support the curation of submitted metadata. - OC IV.4: The IVPP GSD data system should support subsequent revision and/or editing of sequence metadata. - OC IV.5: Provided metadata should not infringe applicable patient confidentiality requirements. - OC IV.6: In order to maintain metadata quality, the IVPP GSD sharing system should ensure interoperability.
A25.	**Ease of access to and use of IVPP GSD**	- OC V.1: DRUA/CADs should provide IVPP GSD users with a data access and use agreement that contains PIP Framework expectations regarding the use of IVPP GSD and benefit sharing associated with its use, and requires users to agree to the terms of the data access and use agreement. - OC V.2: DWRUA/OADs should publish a statement that contains PIP Framework expectations regarding the use of IVPP GSD and benefit sharing. - OC V.3: The IVPP GSD sharing system should ensure that the various stakeholders receive information about the PIP Framework. - OC V.4: IVPP GSD and its metadata should be provided for download and use in a variety of standard data formats for use with third-party bioinformatics analysis software tools. - OC V.5: The data sharing system should provide for programmatic access and use of IVPP GSD and associated metadata by external database resources that provide for the processing and analysis of these data in a manner that is consistent with the data access and use agreement. - OC V.6: Whenever possible, the system should support the linkage between sequence data (and their metadata) with epidemiological data based on WHO reports, OIE reports, FAO reports, national reports of influenza cases, outbreaks or surveillance activities. This can be implemented based on interoperability strategies between databases, as is already in place between EMPRES-I/OpenFlu/IRD for animal, environmental and human zoonotic influenza.
A26.	**Sustainability and security of the system**	- OC VI.1: The IVPP GSD sharing system should be secure and able to ensure that the GSD and metadata provided cannot be altered substantively by outside parties without assent by the data provider or their designated representative. - OC VI. 2: The IVPP GSD sharing system should be sustainable and provide IVPP GSD and its metadata for download in perpetuity.
A27.	**Source identification**	- OC VII.1: Data providers should identify sequences from IVPPs as PIP Framework IVPP GSD at the time of upload or at the earliest opportunity so that users are aware of their status. - OC VII.2: Data users should properly identify the origin of IVPP GSD using accession numbers in scientific publications, intellectual property applications, clinical trial files, product inserts and regulatory filings.
A28.	**Support to the regulatory process**	- OC VIII.1: Appropriate IVPP GSD quality assurance and quality control systems may be useful to facilitate the process to obtain regulatory approval of pandemic influenza preparedness products. - OC VIII.2: To ensure timely regulatory approval of pandemic influenza products, data access and use agreements should facilitate access to IVPP GSD by regulatory authorities.

Table III.4 ***Options to monitor the use of genetic sequence data from influenza viruses with human pandemic potential (IVPP GSD) in end-products***

This document was developed by the Secretariat at the request of the PIP Advisory Group. The document identifies options for monitoring the use of GSD in the development of influenza products, such as vaccines, antivirals and diagnostics. The document was developed in consultation with Member States and stakeholders. The Options paper can be found at http://www.who.int/influenza/pip/advisory_group/gsdoptionspaper_revised.pdf?ua=1.

This table contains excerpts relevant to the Part B of the Scoping Paper.

Reference No.	Reference	Excerpts from the "Options" document
A29.	**Options paper, p. 4**	[…] promoting the sharing of benefits generated using IVPP GSD will likely require a combination of both upstream and downstream options.11 Upstream options should focus on informing entities and individuals accessing GSD of potential obligations and/or expectations under the PIP Framework. This would give more legal certainty to users of the data and could facilitate identification of users of IVPP GSD for benefit-sharing purposes. In contrast, downstream options would involve implementing mechanisms to monitor use of IVPP GSD to develop end-products, such as vaccines, antivirals and diagnostics. This would allow WHO to identify entities that have used IVPP GSD to generate benefits and result in more transparency for providers of the data.
A30.	**Options paper, p.15**	[…]comprehensive monitoring will depend on publicly-accessible source identification from multiple sources. As highlighted in this paper, there is currently no consistent practice of identifying use of IVPP GSD in publicly available downstream documents, such as patents, research trial documentation, and regulatory files.
A31.	**Options paper, p. 15**	[…] implementing this system will require cooperation by a number of entities, including databases, GISRS laboratories, industry and other stakeholders. Best practices or guidance could therefore be developed in consultation with these entities.

Table III.5 WHO Survey on the sharing of GSD

In July 2015 the Secretariat conducted a survey to understand better how GSD of influenza viruses with human pandemic potential is generated, shared and used by laboratories in WHO GISRS, academia, public health institutions and industry. The Report, which contains the ***analysis of responses received***, can be found at http://www.who.int/influenza/pip/advisory_group/GSDSurveyResults.pdf?ua=1. Each reference to "provider" or "user" is understood to refer to the survey respondents.

The table below contains excerpts from the Survey relevant to Part B of the Scoping Paper.

Reference No.	Section	Excerpts from WHO Survey
A32.	**Mechanisms to share IVPP GSD**	Data providers and users rely on 4 different databases to share and access IVPP GSD: GISAID EpiFluTM, INSDC, IRD and OpenFluDB. A majority of data providers use GISAID EpiFluTM and several providers use more than one platform to share IVPP GSD. Data providers cited two main reasons for choosing GISAID EpiFluTM: convenience of data upload and user interface, and data access and usage policy. Providers who upload to INSDC, IRD or OpenFluDB indicated choosing these databases mainly because they are perceived as offering the broadest access possible to the research and public health community. A majority of users access IVPP GSD through more than one database. Individual comments from users of IVPP GSD indicate that they favour different databases depending on the nature of their work. For example, laboratories that promptly need new sequences for risk assessment during outbreaks praised GISAID EpiFluTM, in particular in relation to H7N9 sequences. On the other hand, several respondents have pointed out OpenFluDB's flexibility for sequence data parsing, or IRD's tools and their value for users with limited bioinformatics capabilities. Taken together, these observations suggest that the various databases each fulfil different needs of users, whether it is rapid availability of data for public health purposes, bioinformatics features for academic research projects, or convenience. A significant number of data providers indicated that they do not upload all IVPP GSD to publicly-accessible databases. Several GISRS laboratories mentioned that they will not upload IVPP GSD unless they receive permission from the sample-submitting laboratory. Therefore, some IVPP GSD are shared only with the originating laboratory, GISRS, and/or WHO via emails, reports or other means; they are not uploaded to any database.
A33.	**Timely access to IVPP GSD**	Several data users reported being unsatisfied with timeliness of access to new IVPP GSD. Many of these laboratories are involved in risk assessments during outbreaks, in which case timely access may be more important than in other contexts. Many users, however, explained that this was only true for a limited number of viruses and that the majority of IVPP GSD are available when needed. Data providers indicated that pending publications and approval from originating laboratories or ministries of health were the main reasons for delays in sharing.
A34.	**Completeness and quality of IVPP GSD**	- Almost all users reported being satisfied with the general quality of the data available. - Completeness of metadata could be improved, especially for clinical data.
A35.	**Traceability**	- When publishing results, almost all users indicated they identify the origin of the data using database accession numbers, which is very useful in order to trace use of IVPP GSD. However, results from the survey indicate that data users cannot always find information on the origin of the data (e.g. the laboratory that sequenced or detected the virus)
A36.	**Acknowledgement and collaboration**	- The majority of providers reported that their contributions were not properly acknowledged in publications that used IVPP GSD generated by their laboratories. - Although a majority of data users indicated that they collaborate with the data provider, many users mentioned that it was sometimes difficult to develop a project or to find funding for such collaborations.