THIRD WORLD NETWORK
19 October 2015

Comments on: “Options to monitor the use of genetic sequence data from influenza viruses with human pandemic potential (IVPP GSD) in end-products”, PIP Secretariat draft dated 29 September.

Summary

All users of GSD should be subject to a PIP Data Access Agreement implementing the Framework's benefit sharing provisions. This Agreement cannot be implemented with a “notice” type approach, but rather must be explicitly applied before data access is granted.

This Agreement should include provisions requiring the user to sign an SMTA2 and, as applicable, make a Partnership Contribution if the user synthesizes or intends to synthesize materials from PIP sequence data. It should also require disclosure of use of PIP GSD in intellectual property claims and publications.

While downstream monitoring may be part of the Framework's approach to genetic sequence data (GSD), there are numerous substantial weaknesses in the available methods. These mean that it will not be possible to reliably track use of PIP GSD using downstream methods alone. Moreover, downstream methods may be difficult and complex to implement, and will require significant human inputs, e.g. to manually review and assess patent claims and sequences.

On the other hand, more efficient and effective downstream monitoring will be facilitated by a strong PIP Data Access Agreement. For example, by requiring a user to disclose use of GSD in intellectual property applications and publications, measures that are otherwise decidedly impractical or impossible to implement.

A. „Upstream Options”

1. All users of GSD should be subject to a PIP Data Access Agreement implementing the Framework’s benefit sharing provisions. This PIP GSD access agreement should be the same at all databases, and its execution digitally recorded and transmitted to WHO.

2. Implementation of the PIP Data Access agreement at databases with existing access agreement procedures, e.g. GISAID, may initially be easiest, however, the same PIP Access Agreement should be implemented at all other databases with PIP GSD.

3. Databases that are unable or unwilling to require their users’ agreement with the PIP Data Access Agreement should not host PIP GSD.

4. The PIP Data Access Agreement should include requirements for the user to:

   A) Sign an SMTA2 and, as applicable, make a Partnership Contribution if the user synthesizes, or intends to synthesize, materials from sequence data; and,
B) Disclose use of PIP GSD in any intellectual property claim arising from use of PIP GSD; and,

C) Disclose use of PIP GSD in all publications of research that involves use of PIP GSD.

4. The Framework should have rules for the implementation of the Agreement, to ensure it is consistently applied across all databases hosting PIP GSD.

5. Concepts such as a “notice” will not suffice to ensure the user’s compliance or enforceability of the Access Agreement. Notice is likely to be inadequate in facilitating identification of users as it very much depends on whether the user contacts the PIP Framework.

B. “Downstream Options”

1. It is sensible for the Framework to build a capacity to monitor downstream use of GSD, but the limitations of such systems need to be fully understood and acknowledged.

2. Many of the serious limitations for downstream monitoring might be addressed by use of a PIP Data Access Agreement that includes the provisions described above.

3. Downstream monitoring may identify cases where an SMTA2 and Partnership Contribution have been required for some years but were not made. The Working Group should give thought to how to assess the PC in cases where years have passed and payments that should have been due were not made.

4. In the absence of a PIP GSD Access Agreement, it can only be suggested that user clearly and consistently identify GSD in publications and patent applications, i.e. it is optional.

5. Patent applications may deliberately or inadvertently claim PIP BM without any indication or acknowledgement. This complicates downstream monitoring and indicates the need for active human evaluation of patent applications. For example:

- Patent claims commonly claim a specified sequence, and any other materials with a certain degree of homology, e.g. 90% or 95%. A patent claim that lists the sequence of an animal virus but which also claims homologous sequences may cover quite a bit of GSD without mentioning a PIP BM strain or listing its exact sequence.

- Applicants may hide their use of GSD by lack of identification. For example, the recently published WO2015023461 from the University of Pennsylvania and private company Inovio claims a “consensus HA sequence” of H7 (SEQ ID: 40), indicated as synthetic, but which in fact is the exact sequence of a 2013 H7 isolate from a human infection in China. The patent application does not divulge the origin of the GSD.
6. The single most useful way to identify relevant patents and patent applications for downstream monitoring is the International Patent Classification (IPC), which is not mentioned in the paper. The IPC has a specific class for influenza-related vaccines, and classes related to diagnostics and anti-virals. Identification of influenza-related patent applications with the IPC and human analysis of each and every match will yield much higher quality results for patent searches than any automated system.

7. Sequences associated with patent applications or other regulatory filing identified, even if they are labeled as artificial or as belonging to a non-PIP BM strain, will need to be intelligently and recursively compared (due to introduced mutations, e.g. WO201599609) to PIP GSD in order to determine if the Framework is applicable. That is, PIP BM with introduced mutations will not necessarily exactly match the sequence of a PIP virus, therefore, downstream searches for PIP GSD will need to take this into account by searching shorter segments or using a “fuzzy logic” that will return hits that closely, but not precisely, match PIP BM.

8. The paper contains omissions in discussing the Budapest Treaty, which is disconcerting in view of the fact that the Framework's prospective partner in developing a search system (WFCC) is an organization that is dominated by Budapest Treaty Depositories. The Budapest Treaty is problematic for downstream tracking of use of GSD. Under the Treaty's Article 6, and implementing Rule 9.2, Budapest Depositories are required to be highly secretive about patent-related deposits and are prohibited from releasing any information about them, except to pertinent patent offices. Therefore, while patent applicants may deposit materials generated from GSD in Budapest Treaty Depositories, WHO can be fully assured of an unhelpful wall of silence about those deposits from Budapest Treaty Depositories.

9. An international GSD disclosure of origin requirement under patent law would obviously be desirable but is not presently realistic. While creation of such a requirement for GSD under national law, in some countries, may be theoretically possible, the disclosure of information under such a requirement would have to be public (i.e. not only to national authorities), and WHO would need access to its declarations, and need to consistently search all national filings in those countries, in their respective languages and formats, and analyze results. This does not seem practical (however, see below).

10. On the WHO ICTRP it appears that inclusion of a GSD indicator would be up to each individual contributing (national) clinical trial database and, as such, it seems difficult to ensure that the ICTRP would be a reliable source of information for Framework GSD tracking purposes. A provision in the PIP GSD Data Access Agreement might be helpful.

11. As TWN previously noted, and this paper acknowledges, there are substantial problems with reliance on regulatory files, which may come late, redacted, or incomplete. While regulatory files may occasionally be useful in monitoring of use of GSD, their information will frequently only come available after the fact, or not at all.