WHO R&D Blueprint meeting on pathogen genetic sequence data (GSD) sharing in the context of public health emergencies, 28-29 September 2017

Introduction

The World Health Organization’s May 2016 Policy Statement on Data Sharing in the Context of Public Health Emergencies\(^1\) states that: “WHO will advocate that pathogen genome sequences be made publicly available as rapidly as possible through relevant databases and that benefits arising out of the utilization of those sequences be shared equitably with the country from where the pathogen genome sequence originates.”

This policy clearly defines two elements: rapid sharing of pathogen genetic sequence data (GSD) and equitable sharing of benefits resulting from sharing those sequences. It was developed after a 2015 WHO R&D Blueprint meeting of international stakeholders where there was consensus that data sharing norms must change during public health emergencies to facilitate rapid information sharing that could be crucial to outbreak response.\(^2\) While sample sharing is not included in this policy statement, it is being considered in a parallel workstream of the Blueprint.\(^3\) Among the action items produced in the 2015 meeting was the need to develop a code of conduct for pathogen GSD sharing during emergencies.\(^4\) This is an issue with growing relevance in outbreak response, demonstrated in both the Ebola and Zika public health emergencies.

In December 2016, The Parties to the Convention on Biological Diversity (CBD) and the Nagoya Protocol established an Ad Hoc Technical Expert Group (AHTEG) on Digital Sequence Information on Genetic Resources to examine the potential implications of the use of digital sequence information on the implementation of the Nagoya Protocol and the CBD. The report of the AHTEG will be considered by CBD and Nagoya Parties in 2018. These discussions have potential consequences for GSD sharing in the context of public health. WHO’s policy already explicitly includes benefit sharing elements in its policy on pathogen GSD sharing in the context of public health emergencies, in alignment with the Nagoya Protocol, and any future guidance should include elements of benefit sharing.\(^5\)

---

\(^1\) [http://www.who.int/ihr/procedures/SPG_data_sharing.pdf](http://www.who.int/ihr/procedures/SPG_data_sharing.pdf)


\(^5\) WHO provided comments expanding on this policy to the Convention on Biological Diversity study on “The emergence and growth of digital sequence information in research and development: implications for the conservation and sustainable use of biodiversity, and fair and equitable benefit sharing”: [http://www.who.int/un-collaboration/partners/whocommentscbdds.pdf?ua=1](http://www.who.int/un-collaboration/partners/whocommentscbdds.pdf?ua=1)
Meeting aims and objectives

Against this background, the Blueprint convened representatives from the pathogen genome sequencing academic community with experience of pathogen GSD in the Ebola, Zika and MERS-CoV outbreaks amongst others, together with research funders’ representatives. As pathogen GSD has not yet become broadly embedded within surveillance data streams including IHR reporting, the research community is a critical enabler for generation of pathogen GSD in outbreaks.6

The purpose of the meeting was to gather participants’ perspectives as a first step towards developing specific guidance for pathogen GSD sharing in outbreaks and public health emergencies that, as articulated in the WHO policy statement referenced above, provides principles underpinning rapid public sharing of outbreak pathogen GSD, while facilitating that benefits from utilization of those sequences be shared equitably with the country from where the GSD originated (originating country). This is the first step in a larger consultation process to gather views from other relevant institutions and communities.

Participants were asked to identify any added value of pathogen GSD in outbreaks and discuss aspects of existing global frameworks which can be built upon or used to encourage GSD sharing while ensuring equitable benefits.

The value of pathogen GSD in outbreaks

As stated in the WHO guidelines for Managing Ethical Issues in Infectious Disease Outbreaks,7 during outbreaks there is a “moral obligation to learn as much as possible as quickly as possible, in order to inform the ongoing public health response, and to allow for proper scientific evaluation of new interventions being tested... The ethically appropriate and rapid sharing of data can help identify etiological factors, predict disease spread, evaluate existing and novel treatment, symptomatic care and preventive measures, and guide the deployment of limited resources.” In addition to the moral imperative to share data broadly when it is available, the practical value of pathogen GSD as a tool to improve public health in the context of outbreaks was discussed. Participants identified the following specific use cases:

Uses of pathogen GSD in outbreaks

1. Characterizing an outbreak pathogen directly or through the identification of the pathogen’s common ancestor if it is a novel pathogen;

2. Determining the molecular epidemiology of the pathogen, including its diversity, virulence, transmission routes and timelines, and possible mutation;

---

6 https://www.glopid-r.org/
7 http://apps.who.int/iris/bitstream/10665/250580/1/9789241549837-eng.pdf
3. Identifying hotspots of transmission and helping to pinpoint outbreaks to map where emergency response measures are needed most,

4. Providing clarity on contentious aspects of a given outbreak by specifying the route of transmission within humans and between humans and potential zoonotic reservoirs. This can help target response measures effectively to the most affected or at risk areas, and trace the origin of an outbreak more accurately;

5. Validating and improving molecular diagnostic tool development (i.e. PCR-based assays) based on up to date, relevant genomic data of given pathogen, especially early in the outbreak;

6. Underpin R&D to better understand the immunopathology of the disease, and to identify and/or develop useful interventions (therapeutics and vaccines) for immediate or future outbreak control and prevention;

7. Identify sources and sinks of infections, distinguish locally-transmitted versus imported cases;

8. Improve epidemiological models predicting disease transmission.

**Benefit sharing: public health benefits**

Over the longer term (beyond one emergency or outbreak), availability of pathogen GSD also facilitates scientific advances and positive public health outcomes, by:

9. Improving disease surveillance in human and animal hosts. Genome-based surveillance through portable technology can improve diagnostic capabilities in resource-poor (e.g. field) settings, and play a role in detecting outbreaks earlier;\(^8\)

10. Facilitating post emergency research and improving the evidence base of “lessons learned.” This in turn aids preparedness for the next outbreak, wherever it takes place. Epidemics are not bound by national borders, and sharing GSD from one country allows collaborative exchanges of ideas, products, and expertise which may be beneficial for a similar epidemic in a different country;

11. Monitoring resistance to therapeutics such as antivirals;

12. Allowing the self-correcting nature of science to progress. Initial interpretations of data can be mistaken, and data availability allows replication and peer review. For

---

translational research that leads to public health decisions, a wrong conclusion without prompt correction can slow progress significantly.

The participants highlighted that not all use cases can be predefined as unpredictable and new ideas can only occur through wide access to data. It was agreed that certain applications and utilities will only become manifest if broad pathogen GSD sharing is enabled. Some noted an increasing interest in phylogenetics as part of outbreak investigations and epidemiological studies that take place during outbreaks of emerging and re-emerging pathogens.

**Benefit sharing: capacity building and collaboration**

It was agreed that increased collaboration and coordination between research institutions, country authorities, and funders can improve preparedness to outbreaks and indeed outbreak response within affected countries.

13. Local researcher engagement and country involvement in current and future outbreak response is a key outcome of successful collaboration. Past collaborations have demonstrated a “clear enthusiasm” for sequencing in affected countries, and in some cases have led to the establishment of “legacy labs” which provide ongoing opportunities for early career researchers from low and middle income countries (LMICs);

14. These partnerships will also enable technological development and transfer between countries, for example the provision of portable sequencing technology that remains in the affected country for use in local labs and any future outbreaks;

15. Improved coordination will also limit duplication of efforts and contribute to a global network that encourages sharing of GSD. Both the Global Initiative on Sharing All Influenza Data (GISAID)⁹ and the Global Influenza Surveillance and Response System (GISRS) were discussed as examples of the positive impact of collaboration on global capacity for preparedness to outbreaks;

16. The Pandemic Influenza Preparedness (PIP) Framework was presented as an example for linking equitable sharing of influenza viruses and access to vaccines and other benefits;

---

17. Sequencing pathogens on a local scale also reduces the urgency of the need to ship samples outside the country, which can be a barrier to generating timely information;

18. Encouraging better data quality and management from researchers across the globe by promoting increased interoperability and prompt data cleaning.

The GSD sharing landscape

The participants believe that the sequencing community is moving “towards an assumption of sharing” data where the norm is becoming to share data rather than not share, with past experience suggesting that pathogen GSD is indeed rapidly and openly shared at the start of an outbreak, in many cases before official publication (via preprint servers or online platforms). For the participants, it was clear that pathogen GSD should be made accessible and easily discoverable (searchable) in a consistent way, with access to accompanying metadata in order to be a useful link to epidemiological data.

One gap in GSD sharing, based on participant experiences, occurs after an epidemic is concluded as samples and data are analyzed post-outbreak and publications are written, research groups apply for grants, and other forms of academic competition. This is where they perceived pathogen GSD could be generated but not shared. Participants felt that it is at this stage that funders and research institutions should articulate implementable policies to encourage prompt data sharing that ensures data providers are rewarded for this practice. Importantly, academic journals have a crucial role in developing incentives to share data, for example by requiring that all pathogen genomes during a public health emergency must be shared at the time of submission.

Several models for GSD sharing were discussed, including the GISAID model used in the context of influenza.\(^\text{10}\) There was agreement that effective models for GSD sharing require building trust between providers and users. While many participants were in favour of open access to data, they noted that where agreements are required (e.g. Data Access Agreements, or Material Transfer Agreements) pre-existing agreements (before outbreaks) were crucial to rapid and effective response, and network models were favoured over bilateral agreements. Additionally, participants noted that models applicable to multiple pathogens are needed.

Major differences between existing pathogen GSD sharing frameworks for tuberculosis, malaria, food safety and influenza and the R&D Blueprint pathogens were discussed, including the relative lack of commercial incentives for developing countermeasures for

\(^{10}\) [http://www.gisaid.org/](http://www.gisaid.org/)
Blueprint pathogens, and furthermore the limited commercial profit to be made from such countermeasures. WHO reiterated that the scope of the Blueprint is limited to pathogens with the potential to become epidemics, where there are few or no medical countermeasures in place.\textsuperscript{11} WHO noted that the Blueprint has examined several approaches to GSD sharing that have been developed or are used within different diseases at WHO (particularly influenza, HIV, tuberculosis, malaria, the WHO Health Emergencies Programme and the Food Safety Department) in order to further delineate elements of a common model that could be developed as a next step.

The work of the COMPARE project to scope incentives and perceived barriers for those working with pathogen GSD from research, public health and industry perspectives was presented.

There is a significant gap between know-how and resource availability for genetic sequencing in high-income versus low and middle income countries.\textsuperscript{12} WHO encourages that partnerships between high income countries and LMIC researchers and authorities are further established in the inter-emergency period with ongoing provision for capacity development (both human and infrastructure). Beyond legacy labs, true capacity building and governance structures that support the rights and needs of low-income countries are critical. This will be increasingly possible as mobile sequencing technology becomes more widely available, and more researchers can access it. This may also create challenges where groups completely separate from public health or government agencies can sequence genomes without guidelines in place. This further reinforces the need of developing appropriate guidance now. In time, it is hoped that the need for high income country mobilised support will decline as affected countries incrementally become independent.

**Remaining barriers to pathogen GSD sharing**

This meeting has highlighted issues around pathogen GSD and equitable benefit sharing that should be examined in future consultations. These issues include authorship/attribution for publications, results dissemination, access to products, commercialisation, ethical considerations, data ownership, and access to samples, for example. Developing principles underlying GSD sharing in consultation with the broader stakeholder community will form an important part of the way forward to a shared vision and framework for maximising pathogen GSD sharing with equitable benefit sharing in future.

\textsuperscript{11} [http://www.who.int/blueprint/en/](http://www.who.int/blueprint/en/)
It was noted that sequencing in outbreak response may be delayed and, even with permissions in place, samples and access to equipment and expertise, it might take several months to overcome technical hurdles to sequence novel emerging pathogens. Another barrier to rapid response the participants noted was the timeline of ethics approval, where expedited timeframes for ethics review are needed for the emergency context.

**Key outcomes of the meeting**

As the role of pathogen GSD in public health increases and as the technology becomes more widely available, it is timely to reflect on the applications of pathogen GSD in the outbreak area. Frameworks, norms and standards in this area need to take into account the different implications of south to north shipping with sequencing in laboratories in high income settings and in situ sequencing, through either mobile laboratories as was seen in Ebola or through increasing capacity in some LMIC settings.

There is a need to put in place mechanisms to ensure pathogen GSD sharing leads to benefits for data providers and data users through products, new skills and technology, and better preparedness for future outbreaks. This meeting has demonstrated that there is a need to develop further guidance to clarify principles for sharing GSD and the benefits derived from their use.

**Next steps**

Further consultation with other stakeholders will follow. Outbreak responders, epidemiologists, public health agencies, ethical and legal perspectives will be included in any development of guidance.

There were requests to better understand how pathogen GSD is reported or not within International Health Regulations channels and in general participants recommended that pathogen GSD could be included in IHR reporting going forwards as a useful addition for outbreak response. If this occurs with appropriate linkages to other epidemiological data, it is likely to provide greater power to detect and assess threats as they emerge, a major public health and health security related benefit for all WHO member states. This is already consistent with the 2016 WHO policy statement on data sharing in emergencies: “the sharing of genetic sequence data / information is as important as the sharing of other event-related information under the conditions laid out in Article 11 of the IHR ... sharing data allows the better tracking of epidemics, and aids the development of diagnostic tests, therapeutics and vaccines.”

http://www.who.int/ihr/procedures/SPG_data_sharing.pdf?ua=1
The applicability of GSD to outbreak response demonstrates a clear benefit to the rapid and equitable sharing of pathogen GSD. It would be beneficial to further elaborate on the specific uses of pathogen GSD during outbreaks bridging scientific and public health perspectives. As described above, these data can be helpful to emergency responders such as epidemiologists and public health officials making decisions during outbreaks, including identifying the pathogen, pinpointing the source and transmission patterns, and targeting interventions. Data availability, including GSD, also helps ensure that they are able to respond with confidence to other policymakers who may also be engaged in the response.