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Access and benefit sharing for pathogens: An overview of the issues facing the 2021 World Health Assembly and WHO Executive Board

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Introduction

In the light of recent disease outbreaks, most obviously the COVID-19 pandemic but also epidemics of Ebola, Zika and other diseases, access to pathogens and the sharing of benefits from their use is a topic that will take a leading place on the World Health Assembly (WHA) agenda in 2021 and quite possibly thereafter. At its meeting in January 2021, the World Health Organization (WHO) Executive Board (EB) will discuss the issue under item 14.4, and the outcome of that discussion will proceed to the 74th WHA itself in May 2021. The WHA is WHO's top decision-making body.

The EB will consider implementation of WHA decision 72(13), "The public health implications of implementation of the Nagoya Protocol", which directed the creation of outputs that the WHA and EB will consider. WHA72(13) requested the WHO Director-General to provide information on current pathogen-sharing practices and arrangements, the implementation of access and benefit-sharing measures, as well as the potential public health outcomes and other implications.

The usual course of movement for pathogen samples that go into international research networks is that they are first characterized and sequenced for public health purposes, meaning that they are used to confirm diagnoses, to monitor genetic variations, and in other non-commercial research applications. Few, if any, object to the flow of pathogen samples around the world for such purposes.

But many of those same pathogens that are shared among public health labs, and information about them, are subsequently used for commercial, for-profit purposes. Viruses and their genetic sequences are used by companies to develop proprietary commercial products – vaccines, drugs and diagnostics. These products are typically patented and sold back to the rest of the world on a for-profit basis. Often an extremely for-profit basis, as developing-country public health systems have learned again and again as they confront unaffordable pricing of drugs to treat diseases like AIDS, hepatitis and, most recently, COVID-19.

Third World Network (TWN) is an independent non-profit international research and advocacy organisation involved in bringing about a greater articulation of the needs, aspirations and rights of the peoples in the South and in promoting just, equitable and ecological development.

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Fairness and equity in this commercial use of pathogens is at the root of the policy questions that the EB and WHA must confront. Though many pathogens are initially transferred for public health purposes, what frequently happens next is that the financial and sometimes health benefits from the use of those pathogens are disproportionately captured by proprietary economic interests and wealthy countries.

The core issue is fairness and equity

When the rhetoric is stripped away, and this paper seeks to clarify some of the more confusing issues, the core policy question for the EB to consider is how the "trade" in pathogens can be made fair. That is, how to create systems for international movement of pathogen samples which are reliable for necessary public health purposes, and which simultaneously respect the sovereign rights of WHO Member States in ways that promote fairness and equity in access to diagnostics, medicines and vaccines.

The latter problem – inequity in access to medical products – is one that has been strongly underlined in the course of the response to the COVID-19 pandemic. Many developing countries have freely shared pathogen samples and sequence information, and these have been used to develop diagnostics, vaccines and other treatments. Yet developed countries have locked up a very large share of vaccine production, with many rich countries securing more COVID-19 vaccine doses than they have citizens, while biopharmaceutical firms reap huge profits. At the same time, many developing countries, including the many that have contributed to the global effort to collect and analyze pathogen samples and to test therapeutics developed with those samples, have been unable to secure sufficient vaccines, treatments and diagnostics for their citizens, due to both scarcity and high cost.

The global issue of access and benefit sharing

Discussions at WHO on movement of human pathogens are one important part of a broader international issue called "access and benefit sharing" (ABS). Nearly all WHO Member States are also Parties to the Convention on Biological Diversity (CBD), which is the central international agreement on ABS. The CBD's objectives include the fair and equitable sharing of benefits arising from the use of biodiversity. And biodiversity has been affirmed in the CBD's Nagoya Protocol – a sub-agreement specifically directed to the subject of ABS – to include pathogens.

Because nearly all WHO Member States are Parties to the CBD, this enables application of the CBD and its Nagoya Protocol to transfers of pathogens in a way that helps to rectify the imbalances in the realization of benefits from their use.

In fact, the WHA has already done so for a small set of pathogens. In the Pandemic Influenza Preparedness (PIP) Framework of 2011, the WHA adopted a resolution setting forth a system for collecting and characterizing potentially pandemic influenza viruses, and sharing benefits on an equal footing. The PIP Framework has resulted in the reliable sharing of potentially pandemic influenza viruses and, among other benefits, has netted hundreds of millions of dollars of benefit-sharing payments from vaccine and other companies. These payments have been used to support developing-country public health labs and to prepare future influenza pandemic response.

Adapting the PIP Framework approach to other pathogens

The PIP Framework is a clear and successful example of the WHA applying the CBD and Nagoya Protocol's principles in public health in order to create greater fairness for pandemic influenza preparedness. However, when the EB meets in January 2021, it can be expected that many developed countries, and industry, will argue against using a PIP Framework-type approach for other pathogens. Why? It's very simple. They don't want to pay for something that they might be able to cajole and convince the WHA to give them for free.

But taking the positive example of the PIP Framework and adapting it for application to other pathogens is precisely the approach that WHO Member States should take. Industry can be expected to make arguments

suggesting that the Nagoya Protocol harms public health because it (allegedly) requires lengthy and complex negotiations for every transfer of every virus. This is simply untrue. As the PIP Framework demonstrates, standard terms of transfer of pathogens can be used to facilitate rapid and simple transfers of materials.

But it won't be easy. In tackling ABS for pathogens, like international organizations in environment and agriculture, WHO will have to grapple with what is the most difficult and pressing issue in ABS today, that of ensuring benefit sharing for the use of digital sequence information (DSI) – the genetic sequences and other information related to pathogens that are used for both public health and commercial purposes (see below).

The backstory

This is not a new issue. While ABS for pathogens may seem to be relatively new to public health policymakers, the topic is not novel. ABS has been discussed in international bodies since the late 1980s. And nearly all WHO Member States, which are also Parties to the CBD, have joined in a long record of decisions and precedents on sharing of biodiversity samples. Those past decisions already apply to pathogens, even if implementation of those decisions has, in some countries, lagged in the health sector.

A treaty with nearly universal membership,[1] the CBD and its Nagoya Protocol have enshrined national sovereignty over biodiversity in international law. These agreements have created an obligation on countries that collect and use biodiversity from other places to share the benefits of that use, especially when it is commercial (e.g., in a vaccine or therapeutic). These internationally agreed approaches to sharing biodiversity samples are typically implemented under national laws and are applicable to human pathogens unless national law or regulation establishes otherwise.

The adoption of the Nagoya Protocol in 2010 was the culmination of a lengthy struggle by developing countries to overcome the resistance of wealthy countries and the biotechnology industry to more strongly implementing the CBD's benefit-sharing obligations. The South's aim in concluding the Protocol was to ensure that when biodiversity, including pathogens, is shared between countries and then used to generate profits, the providing countries receive some of the benefits that result.

Thus, in a health-related example, if a developing country provides foreign industry with a soil microbe that yields an antibiotic drug that is patented and commercialized, the providing country has a right to expect to receive some of the benefits, such as access to the drug at low or no cost, or to receive a portion of the profits. These obligations are typically contained in a material transfer agreement (MTA) associated with the biodiversity transfer. When a single set of MTA terms is applied to many transfers, it is often called a standard material transfer agreement, or SMTA.

The PIP Framework is an established and successful WHO approach to pathogen sharing that is consistent with the CBD and Nagoya Protocol and that uses intergovernmentally negotiated SMTAs. It is of direct relevance to the discussions of the EB and WHA in 2021.

The PIP Framework came about because, in the mid-2000s, as fears of a new influenza pandemic mounted, Indonesia and other Asian countries, and countries in other regions, came under intense pressure to share samples of H5N1 influenza viruses. Despite the aggressive demands to share viruses, many of those countries were told that no vaccine was available, or that it was too expensive, for them to purchase. The situation was unfair, and Indonesia and other countries reacted.

The result, after years of negotiation, was the PIP Framework, a system to ensure consistent international shipment of potentially pandemic influenza viruses among networks of WHO-affiliated labs and, on an equal footing, benefit sharing through annual payments by vaccine companies and other benefit-sharing commitments, such as setting aside a portion of production, in the event of a new influenza pandemic. Since

[1] The United States is one of the only, and by far the largest, country that has not ratified the CBD.

2012, the PIP Framework has collected over $200 million in annual payments, called "partnership contributions", from industry and it has secured product commitments from many vaccine and other manufacturers.[2]

The PIP Framework's access and benefit-sharing structure is a multilateral system that is consistent with the Nagoya Protocol and the CBD, and it has been a remarkable success for WHO. The PIP Framework shows that by implementing the Nagoya Protocol – as opposed to working against or around it – the ends of global public health are well-served. As a result of the Framework, influenza pandemic preparedness has not only been improved globally, but the network of public health laboratories supported by the Framework, with expertise in respiratory pathogens, has played an important role in responding to COVID-19.

For example, according to WHO, the PIP-supported influenza laboratory network has "proved instrumental" in COVID-19 testing in Africa. Funding and capacity building to national laboratories from PIP has also bolstered COVID-19 testing and surveillance in developing countries across the globe, including the Philippines, Costa Rica, Bhutan and Sri Lanka. And the system developed by WHO, with PIP support, to assess the quality of influenza testing at national labs has also been used in COVID-19 testing, in order to support good laboratory practices and accurate SARS-CoV-2 identification in samples.[3]

Thus, the first agreement that WHO developed for pathogen ABS implements and is consistent with the Nagoya Protocol, and has been a strong success for WHO and developing-country Member States. Now, it may be time to expand such approaches to additional pathogens, especially seasonal influenza viruses and potentially pandemic pathogens.

Dispelling two key misperceptions about pathogens and ABS

In the context of ABS, there are two important misperceptions that Northern countries and companies often seek to perpetuate about human pathogens and their use in science and industry. These misperceptions aid the maintenance of wealthy countries' policies that seek to reduce or eliminate benefit sharing, especially financial benefit-sharing obligations for the use of pathogens by industry. They are rooted in subtly, and sometimes not so subtly, promoting an antiquated understanding of legal and economic realities about genetic resources, and rely upon not squarely acknowledging realities apparent for a generation or more.

The need to acknowledge and respect sovereign rights

The first misperception is created by many Northern countries and industry's reluctance to squarely recognize the legal reality of sovereign rights. When Northern countries and companies avoid explicit acknowledgement of national sovereignty over pathogens, and the rights that go with it, a false perception is generated that countries may not be acting properly – and may somehow be in contravention of commitments – if they were to reduce or restrict sharing of pathogens in the absence of a benefit-sharing agreement.

This perception is, of course, untrue. The PIP Framework, adopted by consensus by the WHA, recognizes national sovereignty over pathogens (and other genetic resources) in its Article 1, paragraph 11. And apart from the PIP Framework, there are no agreements under WHO, or any international instrument, that require sharing of pathogens, with or without a benefit-sharing agreement. This includes the International Health Regulations, which require neither sharing of pathogens nor of sequence information. In fact, with respect to other agreements such as the CBD, the IHR expressly states in its Article 57 (paragraph 1) that "The

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2 The PIP Framework website contains an accounting of benefit-sharing payments as well as commitments for other benefits in the event of a pandemic. Information on the partnership contributions, including a listing of payments received to date, may be found here: https://www.who.int/influenza/pip/partnership_contribution/en/ Information on other benefit sharing, including commitments to donate or provide reduced pricing for vaccines and antivirals, is here: https://www.who.int/influenza/pip/smta2/en/

3 For more information on these and other examples of how benefit sharing under the PIP Framework has helped the COVID-19 response, see the WHO Influenza Newsletter archive, at https://www.who.int/influenza/publications/newsletter_influenza/en/

provisions of the IHR shall not affect the rights and obligations of any State Party deriving from other international agreements."

It is important to place recognition of sovereign rights at the centre of the WHA debate, as it is through developing countries asserting those rights that a fair and equitable solution may be reached. Exercising those rights, including to limit sharing of pathogens, could be a necessary step to create conditions that will advance benefit-sharing agreements.

The need to acknowledge and address the economic value of pathogens

The second misperception perpetuated by Northern countries stems from their reluctance to acknowledge the immense commercial value of shared pathogens and their digital sequence information. By only referring to the public health use of shared pathogens, or by conflating public health uses and proprietary economic uses, enemies of benefit sharing seek to keep access to pathogens free, even while the vaccines, diagnostics and therapeutics developed with shared pathogens are monopolized by patents and too expensive or simply unavailable for developing countries, with devastating consequences for their peoples. Simultaneously, they are the source of immense profits for the pharmaceutical industry.

Pathogens aren't just the cause of disease, they are a source of treatments. Treatments made from or made using pathogen genetic resources include influenza and many other vaccines. The critical components of a seasonal and pandemic influenza vaccine are typically two gene segments that usually have been recently isolated from a "wild type" strain. Many vaccines for other diseases also incorporate pieces of a wild type strain, including COVID-19 vaccine candidates, or are composed of such a strain – perhaps modified, e.g., to attenuate virulence – adapted to grow in cell culture.

Similarly, to produce monoclonal antibody drugs, therapeutic antibodies are generated using wild type viruses (or pieces thereof), and the characteristics of the monoclonal antibody drugs are directly linked to the specific genetic composition of the wild type virus. Even in the development of small molecule drugs, that is, synthesized chemicals, access to and use of wild type strains is an absolute requirement for drug development and regulatory approval.

Seasonal influenza virus sharing: Not part of the PIP Framework

Another issue that requires enhanced clarity in the WHO discussions is the question of sharing of seasonal influenza strains. Industry cites difficulties that it has allegedly encountered in accessing seasonal influenza viruses to cast aspersion on the Nagoya Protocol and the PIP Framework. These complaints are misleading, however, as a careful examination reveals.

The critical piece that needs understanding and clarity in order to begin a useful discussion of access to seasonal influenza viruses is that the PIP Framework does not cover sharing of seasonal strains. Rather, the Framework's virus transfer obligations apply only to potentially pandemic influenza strains, such as new H5N1 and H7N9 isolates.

Because seasonal influenza virus transfers are not part of the PIP Framework, the ABS status of seasonal viruses is just like that of other pathogens: They are not required to be shared by any WHO agreement and they are covered by the CBD and Nagoya Protocol and national implementing legislation. As such, Member States are presently able to adopt what laws and policies they see fit with respect to sharing seasonal influenza viruses consistent with the CBD and Nagoya Protocol, which includes not shipping seasonal influenza samples in the absence of an acceptable benefit-sharing agreement.

Thus, industry's complaints about access to seasonal influenza strains do not reflect anything awry with the PIP Framework nor any other WHO agreement.

Yet many countries are sharing seasonal influenza strains with the WHO laboratory network, and some of those strains are used in seasonal vaccines sold globally. So it does make sense to have a multilateral framework of access and benefit sharing along the lines of the PIP Framework to cover access to seasonal influenza viruses and benefit sharing.

This reveals how industry's complaints about access to seasonal flu viruses are disingenuous, given that it has consistently objected to the development of a framework for seasonal strains. This may be because industry believes that advancing confusing complaints about seasonal virus access might result in it being given access to seasonal viruses for free.

In any event, should Member States deem a multilateral WHO agreement for benefit sharing for seasonal flu viruses to be desirable, it should be a newly negotiated approach. While taking the PIP Framework's approach as a starting point, it should be a new agreement separate from the PIP Framework, given that the PIP Framework is functioning well. New benefit sharing for seasonal viruses from industry should be part of that agreement, especially given the industry's growth and rising global seasonal flu vaccine sales.

In sum, ABS for seasonal influenza is distinct from that for the potentially pandemic influenza viruses under the PIP Framework, and seasonal flu viruses are among the pathogens which are subject to the Nagoya Protocol and for which no WHO-negotiated access agreement exists. Seasonal viruses are then part of the wider universe of pathogens, including haemorrhagic fever viruses, respiratory viruses, etc., for which the WHA may consider developing a PIP Framework-like ABS approach harmonized with the Nagoya Protocol.

Potentially pandemic virus transfers: Reliable under the PIP Framework

An important lesson about access and benefit sharing for pathogens is that since the implementation of the PIP Framework, transfers of potentially pandemic viruses have generally been reliable. According to WHO, potentially pandemic viruses are being shared without any problems associated with the Nagoya Protocol.[4] The relative reliability of transfers of potentially pandemic strains today is an improvement over conditions that existed prior to the PIP Framework.

It is claimed by industry and some others that Nagoya Protocol-related delays in sharing of seasonal viruses are a significant problem. (Here it should again be noted that seasonal viruses are not covered by the PIP Framework and that Member States may be acting within their rights to withhold or delay sharing of seasonal strains until benefit sharing is agreed upon.)

But WHO research casts doubt on the extent of Nagoya Protocol-related delays in access to seasonal strains. A WHO survey found that less than half of responding labs – both WHO-affiliated and unaffiliated – reported any delays accessing seasonal influenza vaccine strains. Some of the minority of labs that reported problems did cite the Nagoya Protocol as a reason (the proportion of such labs was not given), but the Protocol was only one among a number of reasons labs identified as being the source of delays. Other reasons included the cost of courier services, the process to obtain import/export permits (not Protocol-related), policies on data protection, and other issues.[5]

To the extent that problems of access to seasonal viruses actually exist, the issue could be addressed by a multilateral benefit-sharing framework for seasonal viruses. Since there is no framework for seasonal viruses, to facilitate their transfer under standard mutually agreed terms, some countries are, as is their right, requiring the execution of material transfer agreements for seasonal viruses. In many cases, this is in accordance with their national ABS laws. Such requirements likely seek to ensure that if transferred viruses are used for commercial purposes, benefit sharing will take place.

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4 WHO (2020). Pandemic Influenza Preparedness Framework for the sharing of influenza viruses and access to vaccines and other benefits (DRAFT). February.

5 Ibid.

A move that undermines benefit sharing for seasonal influenza?

It was recently revealed, at the Member States Information Session on the Health Implications of the Nagoya Protocol (20 November 2020), that WHO staff have drafted and begun using, in at least some circumstances, a standard material transfer agreement for seasonal influenza viruses. The decision to write and use this agreement has bypassed the WHO governance structure and has taken place without any request by or the supervision of the WHA.

Our requests to review a copy of this agreement have yet to be honoured by WHO staff. What are the terms of this agreement and who drafted it? How does it treat commercial interests? What benefits are shared? None of these questions can be answered until this agreement is made available.

Any initiative to establish a new access and benefit system under the WHO aegis should be undertaken by Member States and approved by the WHA. The development of an agreement for seasonal flu by WHO staff may not reflect Member State interests and may undermine efforts to create a PIP-like system for seasonal influenza viruses.

The lesson that can be learned from this is that the PIP Framework, with its multilaterally negotiated standard access and benefit-sharing terms, has improved and made reliable transfers of the pathogens that it covers.[6] If, as industry and some governments say, the situation for seasonal viruses should be improved, then the logical next step to take would be the negotiation of multilateral access and benefit-sharing terms for seasonal viruses.

Digital sequence information and access and benefit sharing for pathogens

Digital sequence information, or DSI, is a term used by the CBD to refer to information about genetic resources. While the term has yet to be formally defined, and may be replaced by an alternative, DSI is widely understood to include the genetic sequences of an organism (DNA and RNA), as well as amino acid sequences and other information, and may include but not be limited to protein structures, epigenetic information, such as DNA methylation, genome assembly information, and other types of what is sometimes termed "natural information".

How to deal with benefit sharing for DSI is perhaps the most important and difficult topic in access and benefit sharing today. It has been an ongoing subject of work by the CBD and UN Food and Agriculture Organization (FAO) for several years and will inexorably be central to any future WHA work on access and benefit sharing for pathogens.

In the DSI debate, the vast majority of developing countries contend that given the rise in sequencing and gene synthesis technologies, DSI and physical genetic resources should be treated as being effectively the same in the context of benefit sharing. That's because, for example, sequence information can be downloaded, a gene synthesized from that information, and that gene "brought back to life" in an organism. There is no rational basis, then, developing countries argue, to differentiate between a "hardware" copy of an organism (a physical sample) and a "software" version (its DSI).

Also important is that in addition to moving into digital and back to physical form, through developments in bioinformatics and artificial intelligence, DSI itself has taken on substantial commercial value. Databases of gene sequences and other DSI can be and are being "mined" for valuable commercial purposes, and most observers expect this trend to continue to rise in importance as more biodiversity is sequenced and advances in bioinformatics and artificial intelligence continue.

[6] National security-related laws – export controls and anti-terrorism laws – appear to be causing the majority of what delays do exist for potentially pandemic strains. Another source of delays is manufacturers not obtaining required permits (unrelated to the Nagoya Protocol).

Probably less than a handful of countries, all developed-country holdouts, still argue that DSI is not part of the CBD or Nagoya Protocol at all. These countries say that the "hardware" copy and the "software" copy of an organism are completely distinct. They do not want substantive benefit sharing for DSI and therefore resist efforts to develop an approach to DSI under the CBD by claiming that DSI is not part of that agreement.[7]

More developed countries, however, appear – sometimes reluctantly – willing to concede that DSI is at least a "benefit arising from the use of biodiversity" and that Parties to the CBD must share such benefits. These countries are more prepared to engage in discussions about how to structure benefit sharing for DSI, which will be an unavoidable topic for WHO in relation to pathogens.

Indeed, with the growth of bioinformatics and synthesis, most observers today understand that if commercial use of DSI is allowed in an unrestrained fashion – without benefit sharing – then the CBD's third objective, "the fair and equitable sharing of the benefits arising out of the utilization of genetic resources", will be undermined and the entire treaty's future threatened.

In the case of pathogens, the DSI issue has both simplifying and complicating effects. These can mostly be linked to the small genome size of pathogens which contrasts to that of higher organisms.

Pathogens are small. On the one hand, because pathogens are relatively simple and small organisms, defining what is most important about pathogen DSI is relatively easy compared with organisms with much larger genomes. Since viruses, for example, borrow other organisms' cellular machinery to reproduce, the pathogens themselves simply don't have the organismal complexity that has so far confounded a definition for DSI for biodiversity more broadly.

But pathogens are most easily synthesized from DSI. But on the other hand, the comparative genomic simplicity of pathogens means that, more than any other kind of organism, a living pathogen can be recreated in its entirety from a gene sequence through techniques like reverse genetics. This means that, more easily than for any other type of organism, pathogens can move between existing "in silico", that is, in informational form, and "in vitro", meaning existing in a physical, naturally reproducing form.

Pathogens very quickly yield commercially valuable information. For similar reasons – the small genome – a pathogen sequence can be "mined" for commercially valuable information in a period of hours, enabling nearly immediate commercial use of pathogen DSI when it becomes available to companies. This can be contrasted, for the time being, with many other types of DSI, such as sequences of crop plants, which are not as immediately commercially exploitable.

For example, the time necessary for a specialized lab to recreate a complete influenza virus in cell culture from an internet sequence is measured in hours. And multiple vaccine companies boasted of designing COVID-19 vaccines from sequence data within days of the first SARS-CoV-2 sequences being posted online,[8] with one company claiming that it used the first available CoV-2 sequence information to design a COVID-19 vaccine *in only three hours*.[9]

Thus, if the EB and WHA are to expand and advance work on access and benefit sharing for pathogens, it will be impossible to make progress if this work does not include consideration of pathogen DSI from the very beginning. Concluding any sort of benefit-sharing agreement on pathogens that does not address DSI

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7 The negotiating history of the CBD as well as national (and regional) implementation laws dating back to the 1990s, such as that in Andean countries, clearly does include DSI within the scope of the CBD and access and benefit-sharing rules. And, in any event, through material transfer agreements, providers of biodiversity, including pathogens, have the right to place limits on the use of DSI generated from the materials they provide.

8 LaFraniere S et al. (2020). Politics, Science and the Remarkable Race for a Coronavirus Vaccine. *New York Times*. 21 November. URL: https://www.nytimes.com/2020/11/21/us/politics/coronavirus-vaccine.html

9 CBS Channel 8 (San Diego, California) (2020). San Diego lab discovers COVID vaccine in three hours. 11 February. URL: https://www.cbs8.com/article/news/health/coronavirus/coronavirus-vaccine-san-diego/509-e18e37f6-347c-4b08-ad33-910968abb04f

will only result in that agreement being circumvented by pathogens being transferred and used in the form of DSI, which would completely thwart the fairness and equity aims of developing countries.

Indeed, the costly mistake of attempting to negotiate a multilateral ABS system without explicitly addressing DSI has already recently been made. In November 2019, a six-year effort to modify the International Treaty on Plant Genetic Resources for Food and Agriculture (ITPGRFA) collapsed.[10] The primary reason for the failure was that developed countries refused to allow the negotiating group to address DSI until the last moment. When a pressured compromise could not be reached, the lengthy effort on access and benefit sharing for crop seeds fell apart. Had the North assented to a negotiation that considered DSI earlier, and had the negotiators "baked in" an approach to ensuring DSI benefit sharing in the complex crop seed exchange system, things might have turned out very differently.

Two examples follow that describe how DSI relates to discussions on pathogen sharing by the WHA.

A drug for Ebola made with West African DSI[11]

Created using DSI from a West African gene sequence, Inmazeb (formerly REGN-EB3) is the first approved monoclonal antibody drug to treat Ebola disease. Made by the US company Regeneron, Inmazeb has attracted over $730 million in R&D support and product orders from the US government.[12] In addition, when Inmazeb was approved by the US Food and Drug Administration in October 2020, Regeneron collected a government incentive, called a priority review voucher, that allows for expedited regulatory review of a future drug candidate. Such vouchers – which are bought and sold between pharmaceutical companies – are worth about $100 million or more, bringing Regeneron's total take so far on the newly approved drug to well over $800 million. Additional US government purchases are expected in the future and there is a likelihood that some other wealthy countries will also stockpile Inmazeb doses.

Inmazeb was created by exposing humanized mice to synthesized pieces of an Ebola virus. The virus strain, called C15 or Makona, was isolated in 2014 from the clinical sample of a then 28-year-old woman from Guinea. While the woman survived the outbreak, two of her brothers did not. The woman did not consent, nor does the consent of the Guinean government appear to have been obtained, before her sample was exported to France and Germany.

After the sample arrived in Europe, researchers at the Bernhard Nocht Institute in Hamburg sequenced the strain found in the woman's sample and uploaded it to the GenBank database, part of the US-EU-Japanese government-funded "open access" International Nucleotide Sequence Database Collaboration (INSDC). Regeneron then downloaded the sequence information of the Makona strain and synthesized portions of the virus. These it used to create Inmazeb. Because Regeneron downloaded the viral sequence from an INSDC database, it has no obligations to share benefits with Africa and no benefit-sharing agreement is known to exist.

Ironically, because the Nocht Institute is based in Germany, which has ratified the Nagoya Protocol, if Regeneron had requested a physical sample of the virus from Nocht, it would have been required to sign a material transfer agreement obligating it to negotiate a benefit-sharing agreement with the Guinean authorities, but because Regeneron instead downloaded the sequence, it did not do so.

What the Inmazeb case shows very concretely is that any WHA-sponsored approach for access and benefit sharing for pathogens must address DSI and physical samples on an equal footing, because Regeneron was able to avoid any obligation to share benefits with Africa by using sequence information rather than a physical pathogen sample.

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10 For more information on the ITPGRFA, see: http://www.fao.org/plant-treaty/en/

11 This case is discussed in greater detail in: Hammond E (2019). Ebola: Company avoids benefit-sharing obligation by using sequences. TWN Briefing Paper #99. May. URL: https://twn.my/title2/health.info/2019/hi190506.htm (This paper was written before the latest US government contracts with Regeneron and hence reports a lower total in contract and other income.)

12 US Department of Health and Human Services Contract HHSO100201700016C.

Influenza vaccine made from DSI

Just as drugs can be made using sequence information, so can vaccines. The US government has contracted with Battelle, a private organization, to manufacture a vaccine against the potentially pandemic H7N9 influenza type. To do so, the key genes used were those of a recently isolated Chinese influenza strain named A/Gansu/23277/2019.

But neither the US government nor Battelle obtained a sample of A/Gansu/23277/2019 from China (which would have occurred under the PIP Framework, since it is a potentially pandemic strain). Instead, the US government and Battelle synthesized the genes necessary for the vaccine from sequence information.

The synthetic vaccine project was not publicized, nor was it reflected in the virus tracking mechanism of the PIP Framework (since no transfer of physical material occurred). The project only came to light in January 2020 when Battelle suffered a manufacturing accident that necessitated a report that was made public under the US Freedom of Information Act.[13]

This example, which is not unique, demonstrates that, for some pathogens, a vaccine may be manufactured without physical access to a sample, again underscoring the importance of the WHA placing ABS for DSI at the centre of any work on pathogen access.

What should the Executive Board do?

Access and benefit sharing is an issue which dates to the late 1980s, when the CBD was under negotiation, and which began to rise again on the international policy agenda while the Nagoya Protocol was under negotiation in the late 2000s. ABS issues also made their first appearance on the WHA agenda at that time, in the form of the virus transfer discussion that eventually led to the adoption of the PIP Framework. Since the Nagoya Protocol entered into force in 2014, ABS has stayed prominent in policy discussions and has now arrived in earnest at the WHA in its consideration of the Nagoya Protocol and pathogens beyond strains of potentially pandemic influenza.

Some of the forces pushing for an ABS discussion by the EB and WHA – including many in the vaccine industry – are hostile to the Nagoya Protocol. These groups believe that WHO can be steered to be the ally of proprietary economic interests that oppose substantive benefit sharing for pathogens, especially financial benefit sharing and ensuring sufficient allocation of vaccines, antivirals and diagnostics. These groups argue that pathogens, including DSI, should be freely shared for reasons of public health. But these groups, and their allies, conveniently ignore that they are the ones that take pathogens and DSI shared for "public health" and turn them into sometimes obscenely profitable proprietary products that are frequently unavailable, unaffordable and inequitably distributed in developing countries (as well as to many people of limited economic means in developed countries).

But the narrative of the Nagoya Protocol posing a threat to public health by complicating access to pathogens is a false one. The reality is that WHO's experience implementing the Nagoya Protocol has been positive. The ABS approach of the PIP Framework is harmonious with the Nagoya Protocol, and it has raised a considerable sum of money for public health. It has also promoted reliable virus transfers, and stabilized the previously faltering WHO Global Influenza Surveillance and Response System (GISRS). It has even helped the response to COVID-19. By WHO's own judgement, the investment in influenza pandemic preparedness enabled by the PIP Framework's Nagoya Protocol implementation has paid off in the present pandemic by bolstering the capabilities of respiratory virus labs in developing countries in ways useful for responding to SARS-CoV-2.

[13] Battelle Memorial Institute (2020). Incident report under the NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules, 9 January. Obtained under the US Freedom of Information Act.

Implementation of the Nagoya Protocol through the development of PIP Framework-type approaches for seasonal influenza and perhaps potentially pandemic pathogens can bolster public health by creating standardized systems for access and fair and equitable benefit sharing, and the EB and WHA should consider undertaking such an approach.

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