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DRIVERS AND BARRIERS TO PATHOGEN- AND BENEFIT-SHARING (PBS): AN EMPIRICAL STUDY OF GLOBAL PERCEPTIONS AND PRACTICES AND CASE STUDIES FROM EBOLA IN LIBERIA AND ZIKA IN BRAZIL

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Though ensuring the fair, reliable, and rapid international sharing of pathogen samples and related benefits is necessary to control infectious disease outbreaks, it has proven difficult. We gathered data from two country cases, influenza sample movements, interviews, and contracts to understand current practices and perceptions. We found that countries shared pathogens for instrumental, political, security, economic and scientific reasons; and that benefits were sought for the global public interest, academic recognition, strengthening national capacities, and economic returns. During outbreaks, barriers arose due to disparities in technology and capacity, biosecurity concerns, commercial interests, and the absence of clear rules. We found consensus on the urgency of improving the global governance of PBS, but not on how to do so. We discuss the options proposed for PBS governance and the need for more focused political leadership to achieve global health security, with equity.

INTRODUCTION

A perennially thorny issue hampering the global health community's ability to manage infectious disease outbreaks is the fair, reliable and rapid international sharing of pathogen samples and related benefits – what we refer to here as pathogen- and benefit-sharing (PBS). When outbreaks of infectious diseases occur, healthcare workers and researchers often take samples of biological materials, such as blood, saliva, and/or tissue, from infected persons for both medical and research purposes. Access to pathogen samples and related genomic sequencing data (GSD) is critical for identifying and understanding pathogens, enhancing the epidemiological response, and for the development of medical countermeasures, including diagnostics, drugs, and vaccines. In the early days of the emergence of SARS-CoV-2 in January 2020, Chinese researchers publicly shared GSD on the novel pathogen, but physical samples were difficult to obtain for researchers internationally.[1] Delays in sharing samples soon became moot as the virus itself spread worldwide. And as the outbreak became a pandemic, researchers voluntarily shared large volumes of GSD on publicly-accessible platforms like GISAID, making it possible to track and understand novel variants such as Delta and Omicron. Nevertheless, the absence of clear international rules and agreements on sample and GSD-sharing leaves the world vulnerable in future outbreaks.

At the same time, the ability of pathogen-sending countries to access countermeasures – including but not limited to those developed from shared samples – is critical for outbreak control and prevention. For many countries, securing access to countermeasures in pandemics is often an uphill battle, especially when governments compete over scarce supply, as demonstrated by the highly unequal rollout of Covid-19 vaccines globally. In the meantime, pathogen-sending countries are also increasingly

concerned about access to other benefits in return for granting access to their resources. Furthermore, pathogens and the countermeasures developed from their use are often controlled by different parties, in different countries, with different degrees of scientific, industrial, and economic resources. Ensuring the fair and equitable sharing of such resources and other benefits has proven difficult and remains far from a well-functioning international system.

The literature on PBS has focused on a relatively small number of cases in which pathogen sharing was controversial, such as the 2007 H5N1 influenza or 2013 Middle East Respiratory Syndrome (MERS) outbreaks.[2] At present, there remains little clarity on PBS practices for other pathogens of pandemic potential, or pathogens more broadly. In terms of the governance of pathogen sharing, the literature has largely focused on the relevant international legal norms,[3] namely the 2005 International Health Regulations (IHR),[4] the 2011 Pandemic Influenza Preparedness (PIP) Framework,[5] and the 2010 Nagoya Protocol on Access to Genetic Resources and the Fair and Equitable Sharing of Benefits (hereafter, the Nagoya Protocol) to the Convention on Biological Diversity (CBD).[6] Presently, there is no publicly available and centralized data source tracking the international movement of pathogen samples or related benefits – with the important exception of influenza viruses of pandemic potential (IVPP) – and, as such, we do not have a clear picture of who shares which pathogens with whom, how quickly, under what terms and conditions, what benefits (if any) apply to those exchanges, or which are the most frequent hurdles preventing or delaying PBS. The research reported here was, therefore, motivated by the need to clarify current practices in PBS and identify workable solutions for their improvement, especially in light of the scarcity of empirical data to inform the negotiation of such solutions.

We reviewed the literature on PBS and interviewed a range of respondents across low-, middle- and high-income countries and professional backgrounds, including experts involved in PBS policy or practice across laboratories, research organizations, universities, governments, the World Health Organization (WHO), civil society, and industry. In total, we conducted 86 in-depth interviews between November 2018 and October 2020, including with 53 individuals involved in international policymaking or scientific practice around PBS, 20 individuals engaged with Ebola PBS in Liberia during the 2014-16 Ebola Virus Disease (EVD) epidemic and 13 individuals engaged with Zika PBS in Brazil during 2015-16. Throughout this article, each interview is assigned a number and is cited parenthetically (e.g., #1, 2, 3, etc.) where appropriate. We also searched for publicly available documents and solicited documents from interviewees, particularly material transfer agreements (MTAs), applicable legislation, and organizational policy documents, collecting 26 MTAs throughout the study period. Altogether, we triangulated among these data sources to generate the findings and conclusions presented in this paper. Ethical approval was granted by the Institutional Review Boards of the Graduate Institute of Geneva (IHEID), the University of Liberia (UL-PIRE) and the National Commission for Research Ethics (CONEP) in Brazil. More information on research methodology can be found in a comprehensive report on the project, which was published as Global Health Centre Working Paper #23.[7]

This study has a number of limitations. There is little quantitative or qualitative data in the public domain on the sharing of pathogens or related benefits. Additionally, key documents such as executed MTAs – the contractual documents that are commonly used between providers and receivers of biological resources – and other contracts are

usually confidential. Therefore, we sought to reconstruct from interviews a necessarily impressionistic picture of current practices and drivers. Despite our efforts to cover a broad range of interlocutors, the number and breadth of interviewees does not capture all countries or stakeholder groups. Moreover, while interviewees generously shared their time and knowledge, the political sensitivity of the topic is likely to have limited the kinds of information and documents shared with us. Finally, two important issues were outside the scope of our research: PBS for animal, environmental and plant pathogens where practices may differ from those for human pathogens, and the sharing of genomic sequence data (GSD) that is sometimes replacing the sharing of physical samples. Both PBS for non-human pathogens and the governance of GSD merit further in-depth research. The results should be interpreted with these limitations in mind. Despite these limitations, we believe this study represents the largest collection of publicly-available empirical data to date on PBS for emerging infectious diseases and has important implications for global health policy.

A BRIEF OVERVIEW OF GLOBAL HEALTH POLICY AROUND PBS

Over the past two decades, health emergencies have been accompanied by high-profile cases of countries refusing or delaying the sharing of pathogen samples important for rapid and effective global health preparedness and response. Most prominent was Indonesia's decision, in 2007, to withhold international sharing of samples of human H5N1 influenza, citing sovereignty over genetic resources and concerns that it would not get access to vaccines developed from sample-sharing. Since then, pathogen sharing controversies have routinely emerged along with new outbreaks, including with MERS sample-sharing between Saudi Arabia and Erasmus University in the Netherlands in 2013,[8] delayed sharing of Zika samples from Brazil during the Zika outbreak of 2015-6,[9] and reports of the mass exodus of Ebola samples during West Africa's outbreak of EVD 2014-6.[10]

In response to Indonesia's position in 2007, WHO, its Member States and related non-state actors (e.g. vaccine developers, manufacturers, and non-governmental organizations) participated in negotiations that culminated in the adoption by the World Health Assembly (WHA) of the PIP Framework in 2011. The PIP Framework established a system based on reciprocity: countries with pandemic influenza samples would share them with the laboratory network coordinated by WHO as well as research institutions and pharmaceutical companies outside the network; in exchange, companies producing medical countermeasures (e.g. vaccines, drugs and diagnostics) from these samples would commit to provide WHO with a range of benefits negotiated case by case with WHO to contribute to national capacities for preparedness or outbreak response. The PIP Framework has been hailed as a "milestone in global health governance."[11] It remains, however, the only multilateral framework designed to govern PBS to date. Periodic calls have been made by global health experts to strengthen the governance of PBS,[12] but it remains an under-governed area of global health.

PBS falls within the realms of two global regimes that have previously operated quite separately from each other: the IHR (2005),[13] the purpose of which is to govern global preparedness and response to outbreaks of infectious disease (among other hazards); and the CBD (1992)[14] and its associated Nagoya Protocol (2011), which aim at conservation and sustainable use of biodiversity and ensure both access to genetic

resources as well as fair allocation of benefits deriving from their utilization. The CBD confirmed the principle of national sovereignty over genetic resources and that sharing of such resources must be based on the prior informed consent (PIC) of the source country and under mutually agreed terms (MAT). The CBD provisions on benefit sharing are general and relatively vague, however, and the Nagoya Protocol was negotiated to articulate them more precisely and render their implementation easier. In 2011, the Nagoya Protocol was adopted as a supplementary protocol to the CBD, expanding its existing provisions on access and benefit sharing (ABS) with the objective of promoting "fair and equitable sharing of the benefits arising from the utilization of genetic resources."[15] PBS can be seen as relevant to the goals of both regimes, but also falling into an under-governed gap between them. Although the PIP Framework (2011)[16] reflects the objectives of both sets of rules, it remains exclusive to pandemic influenza. As such, a climate of uncertainty continues to surround PBS.

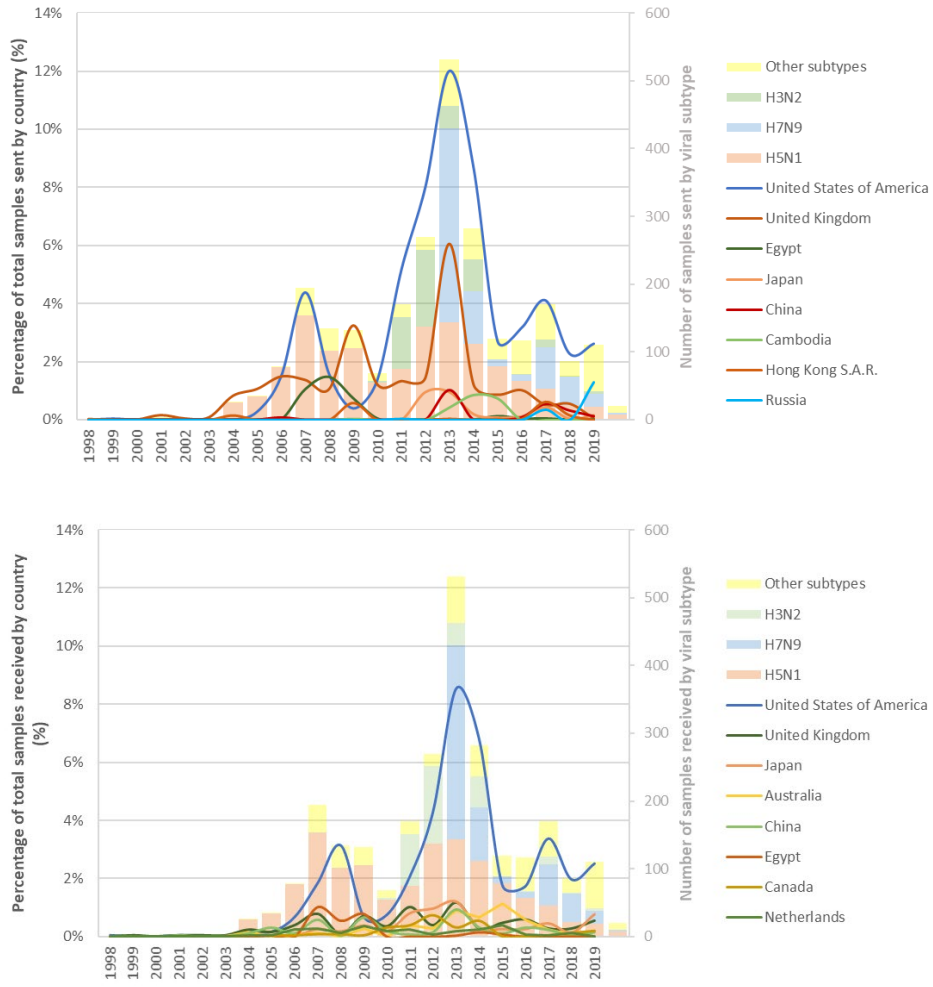
The interviews we conducted with policymakers and practitioners working on PBS reflected this uncertainty, revealing a shifting and uncertain policy and legal landscape for PBS. In Europe, changes in privacy and data protection laws and the implementation of the Nagoya Protocol are expected to have a "tremendous effect on what we can and cannot do (#45)," including anticipated difficulties in linking pathogen samples to clinical data and, for viruses other than influenza, impacting long-standing collaborations. In pathogen-sending countries, an interview respondent from a government-affiliated laboratory described situations where "nobody knows exactly what to do … whether they have a right to share, with whom, and which framework (#39)." Industry representatives have expressed concern that the growing difficulties with pathogen sharing is "generat[ing] instability in commercial practice," such that small- and medium-sized pharmaceutical companies may find themselves at a comparative disadvantage to large companies when attempting to navigate an emerging "mosaic" of international and national legal regimes (#46). Perceptions of the changing landscape varied from viewing it as "a threat" to long-standing and established systems of sharing (#20), to "business as usual" for those who routinely navigate complex legal systems in their everyday practice (#18), to an opportunity to redress historical inequalities between countries through PBS (#38). Left unattended, such a climate of uncertainty is expected to continue to grow, and there are calls to move towards increased coherence and clarity in the governance of PBS.

WHAT DO WE (NOT) KNOW ABOUT PATHOGEN-SHARING?

Presently, publicly available and centralized information on global movements of pathogen-samples and the benefits associated with their sharing are scarce, with the important exception of influenza viruses of pandemic potential (IVPPs). As such, we do not have a clear global picture of which countries are most centrally involved in sending and receiving pathogens, under what terms and conditions, what benefits (if any) apply to those exchanges, and which are the most frequent hurdles preventing rapid, reliable, and fair PBS. To develop some granularity on these questions, we first examine what is and is not publicly known about pathogen sharing through existing data on the global movement of IVPPs and our respondents' identification of drivers and barriers to pathogen sharing.

The WHO's Influenza Virus Tracking Mechanism (IVTM) is the only publicly-available data repository we found that tracks global pathogen movement—in this case the global sharing of IVPPs. We analyzed data on the global movement of IVPP samples from the IVTM,[17] studying patterns in a total of 2,601 IVPPs recorded between January 1998 and 2019 (latest data retrieval date: May 7th 2020). While this data source only covers IVPPs and therefore cannot be taken as representative of the sharing of pathogens more broadly, it does offer a significant level of otherwise unavailable detail regarding sending and receiving countries, participating organizations, and key developments across time in the actual international sharing of influenza pathogens.

Figure 1: Top 8 IVPP-sending (top) and IVPP-receiving (bottom) countries by time and frequency of IVPP subtypes shared



Note: The line graph represents percentage of total samples sent by country (left y-axis) and the bar graph represents number of samples sent by viral subtype (right y-axis).

Throughout the recorded period, a relatively small number of countries – about 15 – have been actively engaged in IVPP-sharing, with the United States and the United Kingdom acting as central hubs (Figure 1). Between 1998 and 2019, the United States

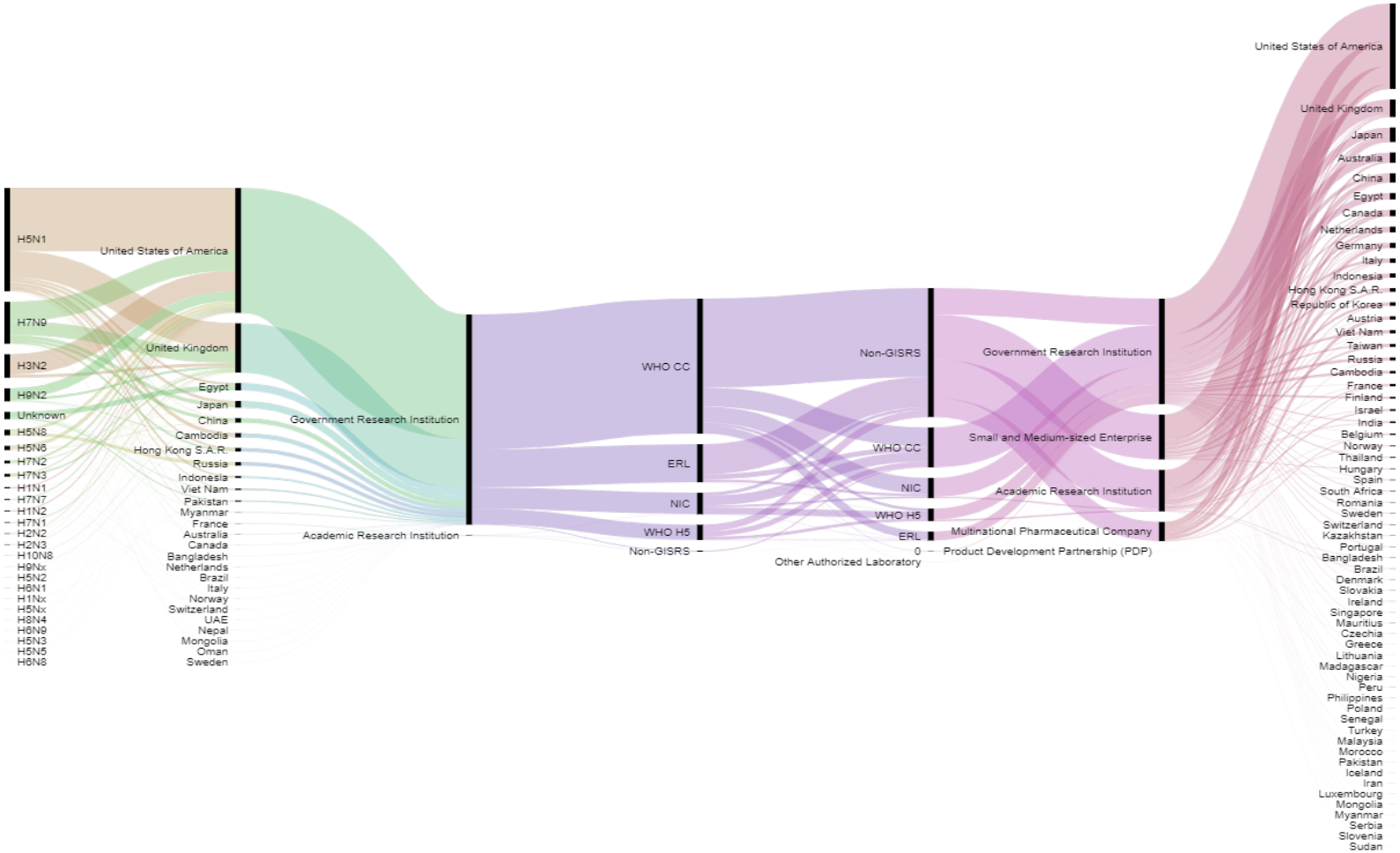
alone sent 59% and received 41% of all IVPP samples logged by the IVTM, followed by the United Kingdom (24% sent and 8% received) and, to a far lesser extent, Japan, Egypt and China (each sending between 2-4% and receiving between 3-7%). Whereas IVPP-sending institutions have almost exclusively been government-affiliated (99%) and part of the Global Influenza Surveillance and Response System (GISRS) (99%), IVPP-receiving institutions have been more variable, including both GISRS (39%) and non-GISRS (61%) affiliated institutions, indicating that samples are shared widely beyond the WHO network of GISRS-affiliated laboratories alone. IVPP-receiving non-GISRS institutions included, by order of density, small- and medium-sized enterprises (SMEs) (21%), academic institutions (20%) and multinational pharmaceutical companies (9%) (Figure 2). SMEs were the main recipients of the GISRS network from 2005-2009 and again from 2010-2015; however, from 2016-2019, there was decreased sharing with SMEs and increased sharing with academic institutions. In terms of bilateral sharing relationships, IVPP-sharing from the US and the UK has largely been with other high-income countries (HICs) – with the exception of high sharing density between the UK and China.

Our interviews with study participants across scientific and policy spheres focused on two areas of interest: drivers for sharing pathogens and the differences in practice between "ordinary" and "outbreak" contexts. While the picture is necessarily incomplete, the interview data begins to lay the groundwork for understanding drivers and barriers.

For the most part, respondents agreed that pathogen sharing practices differ between outbreaks and ordinary circumstances. In ordinary circumstances, the ability to access pathogens seems to be contingent on a number of factors, including: participation in international collaborative pathogen sharing networks, an institution's size and geographic location – with a few major institutions having a far wider reach than most others – and an institution's capacity to navigate a mosaic of national and international laws, regulations, and permit requirements. Outbreak contexts, however, are characterized by panic and confusion, where normal processes for pathogen sharing, if regulated, are often suspended in favor of expedited processes. Participants from many countries report that their ability to negotiate favorable terms and conditions are inhibited by the immediacy of needing access to collaborations and medical countermeasures during outbreaks. In emerging infectious disease outbreaks, pathogens "become hot items to acquire" (#17) and highly valued internationally, which may either lead to more flexible and unrestricted sharing for the rapid development of medical countermeasures or to reservations around sample-sharing, often to retain negotiating power over potential benefits. When the latter has occurred, it can be rendered ineffective by wide cross-border disease spread, where "over a very short span of time, they become accessible to the rest of the research community, so it was a matter of just waiting" (#18). Regardless, ensuring access to pathogen samples—rapidly, in adequate volumes and at acceptable quality—also remains instrumental for epidemic response, particularly, but not only, in the earliest period of an outbreak (#28).

With the absence of clear, coherent international frameworks and regulations, trust in international collaboration plays a defining role in the success or failure of effective PBS. The absence of trusted long-term collaborations has often led to slow, inefficient, and potentially detrimental barriers to access to pathogens or benefits, which may be difficult to overcome quickly in times of crisis. As PBS practices seem to be qualitatively different between ordinary and outbreak contexts, different approaches to their governance may need to be considered.

Figure 2: Global flow of IVPP samples from sending countries (far left) to receiving countries (far right) (1998-2019, n=2,601)



Notes: Sending countries (left) are not necessarily the originating countries of IVPP samples. IVTM-classified designations for laboratories are WHO Collaborating Centres (WHO CC), National Influenza Centres (NICs), Essential Regulatory Laboratories (ERLs), WHO H5 Reference Laboratories (WHO H5) for GISRS-affiliated laboratories and non-GISRS for all other laboratories. Affiliations were manually designated by the research team as either: Government institutions, academic institutions, SMEs, or multinational pharmaceutical companies. Websites of sending and receiving institutions were consulted in designating affiliations. Government-funded academic research centers (such as those in public universities) were considered academic institutions.

WHAT DO WE (NOT) KNOW ABOUT BENEFIT-SHARING?

Outside of benefit sharing as it is codified in the PIP Framework, there is little clarity or agreement about what constitutes a benefit in relation to pathogen sharing, how benefits are negotiated and implemented in practice, or how such decisions are made. To this end, this section explores what "benefits" can mean in two ways. First, we show the breadth of understandings of "benefits" as discussed with interview respondents and, second, we explore how benefits have been codified in everyday scientific practice through a collection of both publicly available and privately shared MTAs.

There appears to be growing recognition among interviewees, from both the policy and scientific spheres, of the need for reasonable, fair, and equitable benefits to be on equal footing with pathogen sharing. However, there is little consensus on what constitutes fair, equitable and reasonable benefits and there is large variation in views and practices among different groups and across global divides. Respondents' perspectives on benefit sharing appear to be organized around four non-mutually exclusive understandings of benefits, each with certain implications for developing governance systems for PBS. First, that pathogen sharing generates benefits as a *global good* for global public health (as in the PIP Framework). Second, benefits understood as *access to countermeasures* and *increasing local preparedness and response capacities* envision PBS as a vehicle through which local capacities increase, future dependency on external parties decreases, and disparities may be reduced. Third, benefits may be understood as *scientific and intellectual recognition* in academic spheres (e.g., credit, authorship, acknowledgement, impact rating for academic publications), where the International Committee of Medical Journal Editors (ICMJE) guidelines[18] may provide normative clarity. And fourthly, benefits may be defined as *economic and financial benefits* – such as intellectual property rights or royalties – for pathogen-sending countries or specific institutions within them.

Furthermore, two main areas of contention appear when discussing benefit-sharing for pathogen samples. The first area is in a *bifurcation between academic and economic benefits* in understandings of benefit-sharing. Some respondents argued that academic benefits are becoming disproportionately represented in benefit sharing discussions, at the expense of economic benefits (#32). Others, however, believed that benefits cannot be seen in purely economic terms, as "a pot of gold at the end of the pathogen rainbow" (#27) or as "something in the bank account" where "information itself is a benefit" (#30). Though financial benefits for developing countries are encouraged in general terms under the CBD, there is an absence of clear norms on what constitutes equitable distribution of economic benefits, especially with respect to IP ownership or distribution of royalties. The second key area of contention revolves around *valuation of pathogen samples*. With little to no international guidance, respondents noted that it is difficult to "value" pathogens and identify what is a reasonable and fair associated benefit when their future value is uncertain at the time of sharing (#26). Some responded that pathogens are only valuable in aggregate, especially in the development of diagnostic tests, or in relation to thousands of other pathogens, such as with the selection of candidates for the influenza vaccine. The explicit monetization of pathogens, whether by sending or receiving entities such as pharmaceutical companies, however, seems to be disapproved of by many, with one respondent noting that: "benefit sharing, if that equals to money … I think it's only greediness and it's not really respecting even the principles of the CBD" (#35). Overall, it

is not straightforward to reach common understandings of benefit sharing or, more concretely, to assign clear values to pathogen samples.

To gain some insight on how benefit sharing is codified in everyday scientific agreements, we collected 26 Material Transfer Agreements (MTAs). MTAs are legal contracts that govern the transfer of research materials and associated data between parties and are regularly used to set out the terms and conditions for PBS. There are numerous standardized or model MTAs that have been prepared by organizations to handle PBS, with variations by pathogen, organization, and country, a main example of which is the Standard Material Agreements 2 (SMTA2s)[1] of the PIP Framework.[19,20] Only four of the collected MTAs were executed MTAs; 22 were model or template agreements. Most of the MTAs collected from interviewees were from organizations and governments of HICs, and only 8 of the 26 (including 3 of the 4 executed MTAs) originated in or involved parties based in LMICs.

The majority of MTAs studied include provisions on ownership of samples and associated IP rights as well as limitations on third party transfers of materials, with 14 stating that ownership and associated rights rest with the provider of the material. All examined MTAs contained at least one benefit; however, there were significant variations in benefit provisions. The benefit provisions included: *acknowledgement in publications,* (17/26 MTAs) where acknowledging providers of samples was required, with 4 MTAs explicitly including co-authorship as a possibility, and *cost recovery,* (11/26 MTAs) where provisions were included on the costs of transfer, with 10 MTAs stating coverage or possible coverage of costs of transfer by the receiving party. *Capacity building and training* (2/26 MTAs) was rarely included through specific provisions, despite anecdotal evidence of capacity building and training as benefits associated with pathogen sharing. *Access to research outcomes* was present in 15/26 MTAs to pathogen providers, including informational outcomes and material benefits, where 11 MTAs were primarily concerned with the sharing of a scientific report on research outcomes. Four MTAs incorporated more complex arrangements regarding access to research outcomes, including access to more material benefits such as the payment of a fixed percentage of sales to third parties, that products be made available to providers for internal research purposes, and provisions on the donation of products or their sale at affordable prices. In 14 SMTA2s between WHO and commercial entities examined, all companies selected the benefits that involved donations of products and reserving products for pandemics to be sold at affordable prices to WHO, rather than benefits involving granting licenses to or ownership of intellectual property rights.

While MTAs provide a way to codify benefit-sharing into pathogen sharing arrangements, it is worth noting that enforcing an MTA in case of suspected violation of the terms is not straightforward, automatic, or easy. The likelihood of judicial enforcement can be remote, especially when the parties are separated by geographical distance, technological capacity, or other power disparities.

[1] SMTA2s have been developed as part of the PIP Framework. The SMTA2s examined were identical except for the choice of benefits companies selected from a list of preset options, which can be found on the WHO's webpage on the SMTA2: https://www.who.int/initiatives/pandemic-influenza-preparedness-framework/standard-material-transfer-agreement-2-(smta2)

WHAT IS (NOT) WORKING WITH PBS?

What did respondents identify as working and not working well in current PBS practices? As empirical evidence remains scarce, preliminary findings were collected here from the perspectives of stakeholders involved in both the policy and practice of PBS.

What is working? Respondents, especially scientists and researchers, described a system that works in many ways. Some researchers reported that "people tend to get what they want" (#12) – that is, that researchers are generally able to get desired pathogens under certain conditions and in normal (non-emergency) situations. When significant challenges or unsuccessful attempts were reported, they tended to be singular events rather than ongoing problems. However, respondents reported that they often do not try to acquire pathogens from certain countries or institutions that are outside the scope of existing partnerships or where they expect challenges. Networks of trusted collaborators and longstanding relationships and projects between researchers were described by multiple respondents as determinative (#18,19), over and above other policy-level considerations, and as embedded in scientific conventions. Several noted a positive feedback loop: collaborations that result in shared benefits are more likely to build further trust and willingness to share. For example, one respondent noted that over time, "the partnerships have, if anything, strengthened and become more fruitful" because the collaborating partners are "able to look retrospectively and see tangible benefits in terms of skills and capabilities and knowledge that they've accrued" (#19). However, when trust has been violated between collaborators, several interviewees noted that more restrictive policies tend to be put in place (#21, 36).

Another area that appears to be a bright spot in PBS is the evolution of informal norms of scientific collaboration to include recognition of all partners. This recognition takes the form of formal acknowledgement in, or co-authorship of, scientific publications. As one interviewee expressed it: "There is much, much more sharing, not only of microbes themselves, but a realization that you really have to share credit, you have to share intellectual academic credit" (#10). Through the interviews, acknowledgement was repeatedly mentioned as the right thing to do and as a necessary (if insufficient) component of benefit sharing. It was also identified as something that has now become more or less routine. While some research organizations struggle with navigating new legal terrain, others, especially those with long-standing international collaborations, have reported established practices of "putting ethics first" above and beyond international and national legal requirements in regard to sharing benefits for access to pathogens. Such measures have been enshrined in organizational policies, many of which are now codifying provisions on PBS, with publicly available sample MTAs and draft MTAs used for opening negotiations around PBS becoming more frequent, especially among institutions in HICs.

What is not working? Respondents identified numerous areas where PBS arrangements fall short; the reasons for these shortcomings can be grouped into five main categories:

Disparities in technology and capacity: Respondents described a wide range of disparities across income levels in technology and capacity, including a lack of access to equipment needed for laboratory isolation of pathogens from samples (#13), lack of in-country diagnostic capacity (#53), lack of robust surveillance systems in humans and animals for many pathogens (#7,13), a relatively higher cost of conducting scientific

research in low-resource environments (#38), and insufficient national infrastructure (e.g. electricity) for laboratory capacities (#67). These disparities shape the benefits that are sought in PBS arrangements. Many respondents agreed that capacity building and technology transfer should be part of PBS. Respondents mentioned a range of ways this could occur, including capacity building arrangements; sharing of laboratory equipment and technology, including genomic sequencing technology (#2); sharing of laboratory material, including reagents to perform tests (#20,40); and education (via targeted trainings or degree programs) (#53,67). In addition, providing back up laboratory capacity during emergencies was also identified as a valuable benefit for countries (#73).

Complications due to biosecurity and biosafety concerns: Where biosecurity is concerned, sharing may be restricted (such as with Ebola, for example) or pathogen samples may be destroyed if countries lack the laboratory capacity necessary for their safe storage and upkeep. As such, countries with limited laboratory capacity that experience outbreaks of pathogens requiring high-level containment, such as Liberia's experience with Ebola, may be requested to share such pathogens with better-equipped countries due to biosafety and biosecurity concerns. Respondents discussed this as a politically charged process, where sending countries may feel considerable pressure to share such pathogens for biosecurity reasons. Some respondents argued that samples have and can be kept in-country when secure laboratory capacity is available (#40) or can be created (#39).

Complications due to commercial interests: Complications due to the involvement of commercial interests include diverging views on balancing commercial interests against other interests, challenges in assigning value to pathogens, and mutual distrust. Several respondents argued that commercial interests negatively affected both the speed at which pathogens were shared and the potential for benefits to be secured, albeit in two conflicting ways. On the one hand, some interviewees were concerned that once IP issues entered the conversation, the sharing of pathogens critical to an effective outbreak response would be significantly slowed. One interviewee noted that, when it comes to addressing IP, "it's one thing to work it out over a year or something and it's another to begin a process like that in an emergency" (#23). In contrast, other respondents were concerned that when tangible commercial benefits were at stake, particularly during wide scale emergencies, pathogen sharing would hasten, but attempts to secure adequate benefits would be steamrolled.

Limited awareness of changing rules and their usability for researchers: Institutions and researchers report varying ability to respond to growing and changing legislation around PBS, often contingent on the availability of experienced legal offices and a sensitization of researchers to changing rules. International scientific institutions and collaborative networks report needing significant legal resources to "follow protocols…[we] have been able to request the appropriate permissions and we've gone through all the steps to get letters of authorization, MTAs, and export permits for every sample that does leave the country" (#31). The increasing complexity of rules surrounding PBS raises challenges for researchers. There is a recognition that significant steps need to be taken to sensitize researchers to emerging legislation, with some institutions needing to strengthen legal offices within their universities to ensure that researchers comply with policies, (#48) which is sometimes perceived as "one more administrative step" (#49).

Lack of clear or responsive arrangements or regulations: With the coming into force of the Nagoya Protocol in 2014, many respondents expected that the involvement of national bureaucracies and multiple agencies would run the risk of complicating pathogen

sharing on both practical and normative levels, incurring delays and/or reductions in sharing. Many respondents expressed concerns that governing PBS through the Nagoya Protocol would potentially introduce too much red tape into the sharing process and lead to an increased need for researchers to convince government officials of the importance of pathogen sharing. Importantly, an increase in bureaucratic red tape combined with a decreased prioritization of sharing was noted as having not only the potential to lead to a decline in overall sharing of pathogens, but as creating a particular risk during outbreaks, where timely and widespread sharing is of critical importance. While respondents expressed a desire for greater regulation of PBS, many also expressed concern that Nagoya was being inadequately implemented or weakened during implementation, limiting its ability to produce more equitable benefit sharing. Others advanced a related criticism: that the Nagoya Protocol was too flexible in how it could be implemented by countries and, therefore, that the resultant patchwork of laws and approaches was itself daunting for researchers and companies looking to access pathogens.

Generally, revisiting normative frameworks around PBS was largely considered to be a priority issue, especially in terms of the governance of benefit sharing. One respondent explained that "there's a great deal of importance in having an international norm and having something in writing" because that can provide countries with enough certainty and confidence to share (#7). Despite this desire, there was a reticence expressed by many of the same respondents for entering into the lengthy negotiations necessary to develop that type of framework; in short, that "everybody knows this needs to be done, but nobody really wants to do it" (#7).

CASE STUDIES: PBS IN OUTBREAK RESPONSE

There has been little empirical research on how PBS occurs in practice during outbreaks. We conducted two case studies to better understand these practices, the first on PBS during Liberia's EVD epidemic (2014-2016) and the second on PBS during Brazil's Zika epidemic (2015-2016). While the two countries and their related outbreaks differ substantially (Table 2), they both experienced outbreaks that escalated to public health emergencies of international concern (PHEICs) under the IHR (2005) after the coming into force of the Nagoya Protocol in 2014. Each case offers distinct insights, with additional analytical value arising by considering them side by side.

Table 2: Development and health indicators for Brazil and Liberia (2018)[21]

Indicators	Liberia	Brazil
GDP (current US$) (billions)	3.3	1,885.5
GNI per capita, PPP (current international $)	1,330.0	14,520.0
Current health expenditure (%GDP)[2]	8.2	9.5
Life expectancy at birth, total (years)	63.7	75.7
Mortality rate, infant (per 1,000 live births)	63.3	12.8
Mortality rate, under-5 (per 1,000 live births)	86.4	14.4

[2] Data only available for 2017.

Case studies were conducted using in-depth key informant interviews with scientists, policymakers, and government officials at national and international levels, including at relevant ministries, laboratories, research programs and non-governmental organizations in both Liberia and Brazil. Fieldwork in Liberia was conducted in-person between November 11-17, 2019 and included 20 in-depth interviews (83% response rate, total interview requests = 24), while, due to the COVID-19 pandemic, interviews in Brazil were conducted virtually between July and October 2020 and included 11 in-depth interviews and 2 informal discussions (37% response rate, total interview requests = 43) (**Annex 1**). External factors contributed to the low response rate for interviews in Brazil: many respondents were occupied with the COVID-19 pandemic, respondents who had previously agreed to an in-person interview declined to participate in an online interview, and the topic itself was sensitive for Brazilian scientists, made more-so by the political climate in Brazil.

Case Study 1: PBS during Liberia's EVD Epidemic (2014-2016)

On August 8, 2014, the WHO officially declared an outbreak of EVD in Liberia, Sierra Leone, and Guinea a PHEIC under the IHR (2005). At the onset of the outbreak earlier that year, Liberia's healthcare system was still recovering from over 15 years of civil war. Although Liberia's economy was one of the fastest growing prior to the epidemic, there remained high levels of poverty with an average per capita income of 690 USD in 2014, poor road infrastructure, unreliable power and communications networks, and limited access to safe water supply. Liberia's healthcare system was beset with severe shortages in health workers, health facilities, pharmaceuticals, funding for health, and other necessary materials.[22] The EVD response deployed more than 40 organizations and 58 foreign medical teams, including from China, Cuba, the UK and the USA, and thousands of international and national staff.[23] In total, the epidemic caused an estimated 28,600 cases and 11,325 deaths.[24] While the response to the West African epidemic attracted criticism for being late and expensive,[25] the combination of community, national and international efforts succeeded in averting the US CDC's projection of 550,000 cases in both Liberia and Sierra Leone.[26] Table 3 details a timeline of PBS practices during the EVD outbreak and the next section details the key findings of the case study.

Table 3: Timeline of Ebola pathogen- and benefit- sharing during Liberia's EVD epidemic

***Before March 28, 2014*: Pre-EVD outbreak**		
Outbreak Context	*Governing framework*	*Pathogen- and Benefit- Sharing*
EVD outbreak declared in southeastern Guinea on March 23, 2014. No cases yet identified in Liberia.	No governing frameworks in place for PBS. UL-PIRE's IRB procedures and MTAs are in place for sample-sharing in collaborative research studies (#66).	In-country diagnostic and research capacity are limited. Priority samples for yellow fever, measles and cholera are tested at the newly established National Reference Laboratory (NRL) with the support of the Global Fund while samples for Lassa

		fever and polio are routinely sent abroad with limited traceability (#62). MTAs for research samples are standard inter-laboratory agreements without benefit sharing stipulations (#66).
***March 28-April 2014*: Emergency mode**		
Outbreak Context	*Governing framework*	*Pathogen- and Benefit- Sharing*
Two cases reported in the Foya District of Lofa County in Liberia, bordering Guinea, on March 28th, 2014, one of whom passes through Monrovia and dies in Margibi County on April 7, 2014. Total of six cases reported across Liberia by April 12th, 2014, with a case fatality rate of 100%.	No policy framework existed for PBS and no legally binding contracts were signed between the Government of Liberia and regional or international testing centers for Ebola.	The initial response was "confused (#55)" and a "crisis mode" prevailed for EVD testing (#57); samples were sent to Guinea, Senegal, France, among others (#54,57,62,68). Negotiating benefits was not a priority at the outset of the outbreak (#57). Sample movement was not tracked or regulated and Liberians "did not have much control at the time" (#56).
***May-August 2014*: The scramble for Ebola samples**		
Outbreak Context	*Governing framework*	*Pathogen- and Benefit- Sharing*
EVD reaches Monrovia. By August 2014, monthly case incidence is 1,049 in Liberia and a PHEIC is declared by the WHO.	Beginning of case-by-case negotiation of MTAs (#54). The National Research Ethics Board (NREB) released 14 provisions for MTAs (#66).	Proliferation of mobile laboratories and testing centers in collaboration with international partners. Samples were also being tested at the Liberia Institute of Biomedical Research (LIBR) through a joint effort with the US NIH and the US Department of Defense (DoD). The Liberian government responds to the exodus of samples by empowering the NREB (#66) and a proposed HIV/AIDS lab at the NRL, funded by Global Fund, is converted to the Ebola testing laboratory. A blanket MTA is signed between the governments of the US and Liberia where "samples belong to the Government of Liberia who

		retained ownership by default" (#54).
***September 2014-December 2015*: Samples centralized at the National Reference Laboratory**		
Outbreak Context	*Governing framework*	*Pathogen- and Benefit- Sharing*
EVD cases peak in September and October 2014 and begin to decline by late October to November 2014. Liberia first declared Ebola-free on May 9th, 2015 and a second declaration is made in September 2015.	Though no national policy framework is introduced, sample movement is more strongly regulated, and MTAs begin to be negotiated and signed for diagnostic samples.	All EVD sample testing and storage was centralized at the newly established NRL in Monrovia (#62,69). Riders for Health became operational in April 2015 to establish secure sample transportation (#60,61). A batch of EVD samples leave Liberia for the US due to biosecurity concerns (#63): "[it was] a political decision, high-level, signed on the grounds that we did not have storage capacity" (#68). Liberian scientists begin discussing the need for a national biobank to keep EVD samples in-country.
***January 2016 onwards*: Building capacity for the future**		
Outbreak Context	*Regulatory System*	*Pathogen- and Benefit- Sharing*
Liberia declared Ebola-free in January 2016 and for the final time in June 2016.	The National Public Health Institute of Liberia (NPHIL) is established. It is mandated with establishing national guidelines for PBS and undertaking case-by-case negotiations of MTAs with international partners (#55).	Laboratory capacity in-country remains limited due to absence of genomic sequencing equipment and expertise (#56,70) and EVD samples kept in Liberia are considered a biosecurity risk (#54,57). All remaining EVD samples are sent to the US with a signed MTA that retains Liberian ownership of samples alongside continued capacity-building and infrastructure-development support to Liberia (#54,56,57). Liberian scientists continue to explore options for a national or regional biobank (#68).

PBS under the pressure of the EVD epidemic. International actors played a major role in supporting the outbreak response, with US government agencies and mobile laboratories supported by international scientific collaborators playing a particularly

prominent role. With the absence of clear rules governing PBS, there was a large exodus of EVD samples from Liberia during the outbreak[27]:

> *"When you are in crisis, when you're drowning, even if someone gave you a hot iron you will hold it before you burn. In 2014, the crisis, we were looking for anything…the goal was, get the things under control. As it subsided, everybody checked back and said look, we have to do things differently (#73)."*

While the WHO played a key role in providing technical assistance during the outbreak, WHO was not actively involved in providing substantive guidance to Liberian scientists and officials on negotiating PBS agreements (#64). Liberian scientists and the Liberian Ministry of Health (MoH) were involved in negotiating MTAs for the international movement of EVD samples with some negotiating leverage (#64) due to biosecurity concerns (#58), resulting in retaining Liberian ownership of EVD samples sent to the United States.

Benefit sharing in practice for Ebola samples. The interviews reflected a broad understanding of benefits. Interviewees discussed benefits as including education and training for students in the US (#58), technical capacity building for Liberian scientists and healthcare workers and technology transfer to Liberian laboratories (#63), among others. Authorship and scientific credit were mentioned as necessary, but insufficient, benefits from pathogen sharing. Intellectual property (IP) rights were reportedly a "rare benefit (#70)" that often was not explicitly codified in legal agreements (#70), and at least one agreement with a commercial enterprise reportedly fell through due to disagreement about IP (#58). Access to countermeasures was highlighted as a key benefit arising from the utilization of samples, more desirable than financial benefits – with one interviewee stating that: "I'm not thinking in terms of financial benefit, it's more of mitigating action for prevention and control (#69)." This has become particularly relevant in light of the recent regulatory approval of an Ebola vaccine (#62). Although the large Phase-2 clinical trial for this vaccine was first initiated in Liberia, legal provisions for access to the vaccine were not included in existing PBS or other arrangements (#64). Liberia is engaging in the processes to be included in an in-country or regional stockpile (#58, 66). Previous experiences with access to countermeasures have not been encouraging, and have raised doubts among Liberian scientists about whether fair agreements are possible between host countries and commercial firms, especially given that access to countermeasures is often left to goodwill rather than legally binding agreements (#70).

Effect of PBS on Liberian laboratory and scientific capacities. Liberian laboratory capacities experienced rapid growth during and after the outbreak, especially through the strengthening of the national reference laboratory. Laboratory infrastructure, however, remained inadequate (#66), reportedly both a precipitating factor and an outcome of the decision to move EVD samples out of the country due to biosecurity concerns (#58). Liberian scientists expressed a deep interest in the need to retain EVD samples in-country. Scientists explained that samples retained in-country draw researchers and funding and would contribute to the growth of Liberian science (#56), especially with diagnostic samples routinely repurposed for research (#62). Another explained:

> *"If you compare to other countries that did not send their samples, they still have a lot of bargaining chips regarding research collaboration, funding, because they*

> *still have the samples stored in-country and some have biobanks. […] Some capacity will be held back from the country [if we don't have the samples]. Why shouldn't we have the sequencing capacity here in order to sequence our samples? […] When you have the pathogen that you want to study, it should provide for all of those resources and capacity (#67)."*

Keeping the EVD samples in-country, however, was contingent on building the needed capacity for their safe and secure storage. Liberian scientists stressed the need to leverage access to pathogens for laboratory capacity building and infrastructure development projects in Liberia, in order to build sustainability and reduce dependency on external capacities going forward (#63,67):

> *"We were giving the samples when we had the Ebola outbreak at its peak and then we had a change in leadership and…there was time now, because the outbreak was also over, to actually sit down and discuss and negotiate things better. So, the negotiation was that we wanted to have our own biobank, we wanted to do our own research, we wanted improvement in our laboratories (#64)."*

To this end, the possibility of a Liberian or a jointly governed West African biobank has been repeatedly discussed as a possibility (#58,63), but concrete steps towards this end have yet to be taken.

The need for PBS governance. Clearer and stronger governing frameworks for PBS were identified as an imperative by interviewees. With the EVD outbreak experience, PBS governance in Liberia has rapidly transitioned from a situation of no governing framework to a case-by-case system under the purview of the National Public Health Institute of Liberia (NPHIL). Liberia is a party to the CBD and Nagoya Protocol. As elsewhere, a disconnect exists between governmental bodies focused on the implementation of Nagoya (mainly the Environmental Protection Agency, EPA) and health agencies (such as the MoH, and NPHIL) (#54). A draft law on Access and Benefit-Sharing has been developed but had not yet been finalized as of this writing[28] and amendments to address biosafety and biosecurity in Liberia's Title 33 Public Health Law are before the national legislature. Up to the time of our study, there were no policies or regulations specific to PBS, and legal resources were unequal when negotiating contracts with larger, more experienced, international research institutions. As has been seen in other countries, sharing of pathogen samples and related benefits depends heavily on personal relationships and long-term collaborations that engender trust (#58). Nevertheless, the use of contractual agreements such as MTAs has become established practice since the outbreak, and some benefits are included in these agreements. There are also substantial, multi-year scientific collaborations, aid flows, and political relationships between the Liberian and the US governments, which are important contextual factors in the background of any specific MTA negotiation. There is a growing and concrete interest in developing normative frameworks and governance mechanisms for PBS, both nationally and regionally, and among both scientists and policymakers.

Case Study 2: PBS during Brazil's Zika Outbreak (2015-2016)

In October 2015, the Brazilian MoH was notified of a sudden increase in cases of newborns with microcephaly and other neurological impairments in Northern Brazil. Soon linked to the spread of the Zika virus by Brazilian scientists in Recife, the Zika epidemic was officially announced an Emergency in Public Health of National Importance on November 11th 2015 and a WHO PHEIC declaration followed on the 1st of February 2016 as the Zika virus spread across the Americas and beyond. By the time the Zika outbreak subsided in 2016, there were more than 500,000 suspected and 173,000 confirmed cases, including more than 3,474 cases of confirmed congenital syndrome associated with Zika virus infection.[29] Zika exposed the social and health inequalities in accessing specialized healthcare in Brazil as, until the end of 2019, only 33% of children received early intervention and 50% had access to financial aid from the Brazilian Government.[28] As efforts to respond to the Zika epidemic were rapidly launched, international researchers faced difficulties securing samples of the Zika virus from Brazil, the epicenter of the outbreak. Table 4 details a timeline of PBS practices during the Zika outbreak and the next section details the key findings of the case study.

Table 4: Timeline of Zika pathogen- and benefit- sharing during the Zika epidemic (2015-2016)

***Before November 2015:* Pre-Zika Outbreak**		
Outbreak Context	*Governing framework*	*Pathogen- and Benefit- Sharing*
In March 2015, the Brazilian MoH identified Zika infections in Brazil. By October 2015, the MoH was notified of unusual increases in cases of microcephaly in infants.	The Provisional Act 2, 186-16, of August 2001 regulated access to genetic resources, not including pathogens. The new Biodiversity Law (Law 13, 123) is adopted in May 2015, which includes "microbial species" within the remit of its definition of genetic heritage (Art 1, IV).	Before Law 13, 123, sharing of pathogen samples was less restricted and primarily at the discretion of scientists without the need for prior approval or reporting: • "The rules existed but weren't so strong (#74)." • "We sent [dengue] samples abroad without any problems (#75)." • "[10-15 years ago] we were just sharing samples and not having any kind of benefit at all (#76)."
***November 2015-July 2016:* Zika-sharing interrupted**		
Outbreak Context	*Governing framework*	*Pathogen- and Benefit- Sharing*
In November 2015, the MoH recognized the link between Zika infection and microcephaly and declared an	On November 17th, 2015, the Biodiversity Law came into force, establishing the rules for access to genetic resources and benefit	"The whole world wanted Zika samples (#77)," but international sharing of Zika samples was officially halted (#75,76,77) until an online registration system was established

Emergency in Public Health of National Importance. The WHO announced a PHEIC on February 1st, 2016. Zika outbreak response efforts were underway until the closure of the Public Health Emergence of National Importance in July 2016.	sharing. The regulatory system to enforce the law was delayed. In July 2016, the executive secretariat of the Genetic Heritage Management Council (CGen) was established.	that allows scientists to comply with the law (#79): • "With Zika, we started to have a different behavior. If the government knew that we had shipped samples to other countries without following all the rules, we could be prosecuted. So, we decided not to ship samples (#75)." • "It was in the heart of the Zika epidemic that we were delayed one or two months until we cleared internally with our legal teams (#76)." • "There was lots of discussion, they [governmental officials] were trying to find alternatives for sharing despite the fact that we were not officially allowed, I think that everyone really agreed that things should be done differently, but at the same time with the urgency of Zika it was just taking too long… (#77)."
***July 2016 onwards:* Post-Zika, a New Normal**		
Outbreak Context	*Governing framework*	*Pathogen- and Benefit- Sharing*
Zika outbreak had ended.	The National System of Genetic Resource Management (SisGen) became available in November 2017. The use of MTAs was formalized.	Regulation of international sample-sharing was clarified and regularized once the SisGen was in place. The system for compliance with the Biodiversity Law has reportedly improved to accommodate the needs of scientists (#79) and negotiating benefit sharing agreements through MTAs has become a common practice: • "We started to share samples from the end of 2016 … it just took time at the beginning but nowadays is very quick because I think everyone is more mature in terms of understanding that we are protecting our institutions and

		the receiving institution (#78)." • "I think that scientists in Brazil have learned that we have some power in terms of determining what our terms are, what changed is the fact that we can tell them what is interesting for us and then officially we can go through all the bureaucracy of sample sharing…it's still not that easy…the process takes too long [sometimes] so the international groups tend to look for other options and not really wait for us (#77)."

The new Biodiversity Law. The Zika outbreak coincided with a period of changes to Brazil's biodiversity laws. The Provisional Act 2, 186-16, of August 2001 was the first legal framework in Brazil to regulate access to genetic resources and associated traditional knowledge for purposes of scientific research, bioprospecting, and technological development. Fourteen years later, the new Biodiversity Law (Law 13, 123 of May 20th, 2015) was adopted, establishing new rules for access to genetic resources and benefit sharing. Brazil was not a party to the Nagoya Protocol during the Zika outbreak, but ratified it in 2021. Nevertheless, Brazil has long been an active voice in international debates on sovereignty over natural resources and the importance of fair benefit sharing. Benefit sharing in the Brazilian legislation includes both monetary and non-monetary benefits, either of which will only become applicable once a product derived from the use of genetic resources is marketed.[30] While the new Biodiversity Law entered into force on November 17, 2015, only weeks before the Zika epidemic was announced in Brazil, its online registration system, the National System of Genetic Resource Management and Associated Traditional Knowledge (SisGen) (under Decree No. 8772 of May 11, 2016), was unavailable until November 2017, months after the Brazilian government had declared the Zika epidemic to have subsided (#79). As a result, throughout the Zika epidemic, PBS was strongly influenced by this legislative change. Although the new Biodiversity law posed barriers the during Zika outbreak, it is important to mention that until 2016 there was no clear regulation on biodiversity, including genetic materials and benefits sharing, and how to improve equity and protect Brazilian scientists and research institutions against predatorial agreements.[31]

Motivations for Zika sample sharing and non-sharing. The coming into force of Law 13,123 marked the beginning of a period of transformation in Brazilian scientific practice that coincided with the urgency of the Zika epidemic, reportedly impacting Brazilian scientists' ability to share Zika samples and related benefits throughout the outbreak. While previous legislation exempted basic research, such as microbiology, from the Provisional Act 2, 186-16 (August 2001), the new definition of "genetic heritage" in Law 13, 123 included pathogens within its scope (#79). One key improvement of the law was allowing Brazilian scientists prior authorization to use genetic resources, with the

main obligation being reporting to relevant authorities before publication, commercialization, patenting, or international sharing (#79). The law, however, created a regulatory vacuum between the time of its coming into force on November 17th, 2015 and the creation of the online registration system to enforce it, the SisGen, in November 2017 (#79). This vacuum coincided with the entire period of the Zika outbreak:

> *"The problem was that our previous legislation was revoked and then only in November 2017 we had the SISGEN…we had one year without regulation…and we had two years without the instruments we needed to comply with the legislation. So, during this period, we were forbidden from doing any shipment of biological material (#79)."*

The Biodiversity Law was, however, not the only reason for hesitancy in Zika sample-sharing. At a time when "the whole world wanted Zika samples (#77)" hesitancy to share Zika samples was also informed by previous experiences of inadequate benefit sharing (#75,76,77,79,80) and a belief in the importance of using national capacities, fostering equitable international collaborations and securing official benefit sharing arrangements (#76,77,80,86). As one Brazilian scientist put it, "we don't have to be just sample providers [anymore], we can do a lot more than that nowadays (#77)." At the time of the Zika outbreak, Brazil had the technological capacities and materials to isolate the Zika virus, develop and validate diagnostic tests, conduct cohort and case-control studies and clinical trials, and begin vaccine development (#76). Zika sample-sharing was, therefore, motivated either by studies that required expertise or technologies that exceeded Brazil's existing capacities or when in-country studies would be prohibitively expensive (#76,77). While many Brazilian scientists interviewed believed in scientific collaboration and partnership as fundamental to knowledge production (#74), difficulties with Zika sample-sharing were jointly attributed to regulatory delay as well as the desire to have legal protections in place for PBS. "On one hand, the law introduced complexities to pathogen sharing for the global health response to the Zika epidemic (#75-77). On the other hand, scientists interviewed in Brazil foregrounded the need for "legal instruments that would guarantee that if we share samples, we will have benefits from diagnostic tests and vaccines (#75)" and for strengthening national capacities, arguing that "it's important for a developing country like Brazil … to put our feet in there and say, okay, we can do some of it, let us take care of what we can do and let us do other things in collaboration (#77)."

Benefit sharing in practice for Zika samples. Though the Biodiversity Law stipulates that benefits only kick in once a product developed through the use of pathogens reaches commercialization, Brazilian scientists interviewed had a wider understanding of benefit sharing in practice. These included both monetary benefits, in the form of sharing grants that fund laboratory activities (#77), and non-monetary benefits in the form of co-authorship in high-impact publications, capacity building through scholarships, trainee-ships and scientific exchanges, and the transfer of equipment and technologies (#76). Benefits to patients were also emphasized, with one participant noting, "I was pissed off with this because everyone wanted to have access to our biorepository and no one wanted to help the mothers…I told them, 'look, I will lock the biorepository if you won't help these mothers' (#74)." Long-term collaboration had a significant impact beyond the sharing of samples:

> *"[In international collaborations], we share much more than the sample, we share knowledge, databases, people that come in and go abroad. Zika, it was amazing, the number of researchers and students that came in from the United States, from Europe, to stay with us … now we are doing COVID studies with the same people with whom we were doing the Zika studies (#78)."*

At the height of the outbreak, significant delays were incurred as Brazilian institutions set up legal instruments to ensure compliance with new legislation (#74-77,79,80). These delays impacted, at the time, the ability of scientists to share in the benefits of research on Zika:

> *"[I was asked] if I can send samples of Zika and they offered me equipment…they proposed to pay for some fellowships because I explained that I was in the middle of a big outbreak…they also sent a document that says that any publication, we will have an important position in the paper, so on … it was just in the moment that [we] couldn't ship samples abroad because there was a law that prohibits it… I could not send the samples and it was really terrible, a very difficult situation… (#75)."*

Adaptations to the Biodiversity Law. As the Zika epidemic in Brazil subsided, the SisGen became available to Brazilian scientists and researchers in November 2017 the online registration system for the Biodiversity Law under the auspices of the CGen. Throughout this period, scientists adapted to new regulations and shifts in standard scientific practice. It is unclear, from our interviews, when Zika sample-sharing became authorized under the new Biodiversity Law, in what form, and to what extent Zika samples were sent abroad during this period. We received conflicting information in the interviews as to whether any samples had been exported at all prior to the establishment of SisGen; it is possible that some sample-sharing did take place, either via an exception for Zika samples under the new Biodiversity Law or outside of a clear regulatory framework.

These adaptations included an increased focus on data-sharing in lieu of sample-sharing (#81,83,85) and the formalization and standardization of the use of MTAs (#76,78). In addition, scientists reported a shift in conventional scientific practice from sending samples out—which remains a difficult process—to receiving test kits, equipment and researchers for in-country diagnostic testing and research studies (#74-77,81). The online registration system has also undergone revisions to better accommodate scientists in basic research. One example is changes to the standardized MTA to allow umbrella MTAs for several sample shipments valid over a 10-year period in lieu of individual MTAs per shipment. (#79) Interviewees also reported that the online registration system of the SISGEN was not designed with basic research scientists in mind (#76,80); such scientists are currently exempt from registering samples, pending a new version of the system (#79). Nevertheless, many scientists reported that sample sharing was "not yet ideal (#77)"; it remains a slow process and requires a wide range of institutional authorizations and government permissions for shipping (#74,75,85). Presently, the main barriers reported are continued dysfunctions in the regulatory system for PBS (#74,75,77), "enormous paperwork" and long bureaucratic delays with shipments, sometimes leading

to the spoiling of samples stuck in ports (#75,79) and a lack of funding and capacity to store and curate pathogen collections in-country in Brazil (#78). Some scientists expressed concern that opportunities for knowledge generation, publishing and grant-raising had been lost due to these continuing barriers (#78).

PBS in Outbreak Response

Despite stark differences between Liberia's EVD and Brazil's Zika outbreaks – including different national research capacities and governance frameworks – our case studies found a number of characteristics common to both cases of PBS: First, outbreak pathogens became highly sought-after and valuable resources at the outset of the epidemics. Second, previous experiences with benefit sharing perceived as unfair informed the decisions of governments and scientists in these specific outbreaks. Third, the absence of previously negotiated benefit sharing arrangements resulted in intense negotiations around PBS, some of which impacted either rapid pathogen sharing or fair and equitable benefit-sharing. Fourth, access to pathogens has been leveraged for certain benefits in both outbreaks. Last, both countries experienced post-outbreak formalization of PBS processes through the institutionalization of standardized MTAs and legislative or regulatory change – in other words, crises drove change.

Findings show that outbreak pathogens became valuable resources in both contexts, both nationally and internationally. The benefits that outbreak pathogens were leveraged for were, for the most part, focused on building local and national capacity for outbreak response, present and future. EVD samples in Liberia, though ultimately shared internationally, were instrumental in capacity-building negotiations, underscoring the need for strengthening national laboratory capacity and precipitating interest in national or regional biobanks for their safe and secure storage. Zika samples in Brazil – the sharing of which was delayed and partially restricted by the new Biodiversity Law – led to some benefits flowing into Brazil (e.g. access to testing kits, reagents, visiting scientists) but could also have limited the possibility of other benefits that might have been negotiated in relation to exported samples (e.g. co-authorship of publications, grants, collaborations). It is unclear, from our findings, what impact these restrictions had on the development or deployment of countermeasures to control Zika. Although no vaccine or treatment for Zika has been developed to date in Brazil and abroad, so access to countermeasures has been perhaps of limited relevance, there is some evidence that restrictions on Zika sample sharing has weakened diagnostic capacity for Zika and contributed to barriers in the global response to the Zika epidemic.[32]

Evidence from these case studies support the conclusion that national governance of PBS is an emerging reality that global health actors will have to contend with. Though progress on national governance of PBS has been made in both Brazil and Liberia, national governing frameworks for PBS that are consistent with both global health need and Nagoya-related considerations have yet to be fully developed. In Liberia, PBS is still negotiated on a case-by-case basis by a public agency—the NPHIL—and, in Brazil, the system in place does not yet guarantee rapid pathogen sharing when needed for outbreak response. It is not certain, as a result, that PBS will be timely or equitable in either country in future epidemics, leaving many of the original problems unresolved.

Furthermore, it is likely that such situations will recur in future infectious disease outbreaks in countries beyond Liberia and Brazil. This is especially the case as many

countries remain either without clear national governing frameworks for PBS—as with Liberia before the EVD pandemic—or with ABS governance that affects pathogen sharing—as with Brazil during the Zika pandemic. With growing ABS legislation worldwide, rapid, unregulated, and unfettered pathogen sharing may be slowly becoming a thing of the past. Fair and equitable PBS systems should be in place ahead of outbreaks of pathogens of pandemic potential at both national and international levels, to ensure more reliable sharing of both pathogen samples and benefits in the future. This remains a significant policy challenge, as the next section discusses. Real-world experiences and perspectives from Liberia and Brazil can and should inform debates and negotiations that aim to develop global frameworks for PBS that are fair, acceptable, and functional.

GOVERNING PBS: WHAT ARE THE OPTIONS?

What do the data suggest regarding workable solutions for the key issues identified in PBS? Overall, we found that even though there are many policy options, each with their proponents, there was no one clear policy direction that was strongly supported or advocated by a critical mass of respondents. As such, there is little consensus on a clear direction going forward. We first present the many options that have been raised for governing PBS, placing them within a spectrum of approaches that cut across different levels of formality and scope, and then identify key debates in the interaction of existing rules for PBS.

Many interviewees highlighted as problematic the absence of clear international rules to govern PBS, notwithstanding the increased participation in the Nagoya Protocol. At the same time, several respondents recalled the four years required to reach agreement on a set of rules for pandemic influenza alone (the PIP Framework) and expressed reservations about the time required and difficulty of reaching agreement on a broader framework covering multiple pathogens. For this reason, it may be useful to consider a broad set of normative instruments, ranging from less to more formal, from few countries to all, and from select pathogens to all:

Informal rules, or Codified non-binding rules: At one end of the spectrum are codified non-binding rules, such as a set of principles agreed upon by a group of stakeholders for the governance of an issue of common concern. Such rules would not have binding force but would establish some norms in this under-governed area. Potential examples for PBS include developing non-binding though codified PBS principles, codes of conducts or guidelines, similar to their use in related fields such as the Declaration of Helsinki on ethical principles for medical research involving human subjects[33] and the Council for International Organizations of Medical Sciences' (CIOMS) "International Ethical Guidelines for Health-Related Research Involving Human Subjects" (2017).[34]

Non-binding formal rules backed by an inter-governmental entity: One step towards more formal rules would be non-binding formal rules that are backed by an intergovernmental authority such as WHO. By "formal" we mean that they are negotiated and agreed upon by governments through a structured process. Examples of non-binding formal rules include the PIP Framework and the WHO Codes of Conduct on health worker recruitment and the marketing of breastmilk substitute. Nagoya parties may also adopt codes of conduct specific to PBS, though this has not been actively discussed at this point by the parties. Non-binding formal rules are likely to require more time to negotiate, but, in principle, would have greater normative weight than informal rules alone, and could

generate buy-in from key stakeholders. Potential examples for PBS could include, for example, the expanded use of standardized MTAs or the use of a traceability mechanism for PBS (fulfilling the role of the IVTM for pandemic influenza sharing, for example).

Binding formal norms backed by an inter-governmental entity: Binding formal norms include international legal instruments such as the WHO IHR (2005) and treaties such as the CBD and the Nagoya Protocol. While treaties have the advantage of carrying, in principle, greater normative weight than non-binding or less formal instruments, they may take longer to negotiate and enter into force, and are usually difficult to amend or adapt – posing challenges given that PBS is an issue area characterized by rapid technological change. Finally, formal treaties do not necessarily have a greater impact on policy or practice than less formal or non-binding rules. No interviewee suggested a formal treaty would be the appropriate instrument to improve PBS practices, although at least one interviewee noted that making the PIP Framework binding international law would have been preferable but was not supported by key stakeholders.

Table 1: Perspectives on Formality and Scope of Policy Options

Informal rules, or Codified non-binding rules	• "…if you have a long cumbersome process that could just have people run away from it, I think you can get some sort of norm, like an agreement… (#10)." • "It's very hard to find universal governance instruments and legal instruments that everyone will sign up to…[with] the pathogen community, you could get some global norms in terms of principles that people would adhere to and then you could create some rules and some implementation strategies…I think it's the right time to stand back and look where the self-regulation works and where it could be supported by other types of mechanisms…(#26)."
PBS Principles, Guidelines or Codes of Conduct	• "It's a very fine balance because you don't want to turn academics or product developers into [slowed down] bureaucratic enterprises, but if we can define timely sharing and what's a reasonable framework for negotiations around benefits [that would be good] (#23)." • "If it doesn't come out of WHO, I think there's a role for academics [and] think tanks to play and put forward templates—like Chatham House did with the data sharing—as models for potential ways of making sure that…sharing is on a common platform (#11)."
Non-binding formal rules, or Codified non-binding norms backed	• "There's a great deal of importance in having an international norm and something in writing…if you play by the rules, you also get the benefits…you have

by an inter-governmental entity	to believe that the system works well enough for your population not to be forgotten about (#7)." • "Then the question is, okay, if it's done bilaterally, then maybe that is not the best way to address in times of pandemic, so you might want something more internationally (#14)." • "We have treaties in other areas than public health to try and have some norms in place that keep us from going off the rails…the challenge is, it's one thing to work it out over a year and it's another to begin a process like that in an emergency…the time to be prepared is now (#23)."
Expanded use of Standardized MTAs	• "You can have standardized terms where the template would be adjustable for [specific] purposes…[and] have those pegged as part of the common approach…so you can make sure that the access and the benefit sharing remain somewhat on an equal footing (#11)." • "That's all about hav[ing] the right agreements and enforcing them, so you need good negotiating capacity, if you fail in drafting, then there is no way of doing it (#24)."
Traceability Mechanism	• "[A traceability mechanism is]…helps everyone understand at least part of that bargain, so we have reporting about what's been promised and the money that comes in on the benefit side, and …the traceability mechanism…lets us see what's being shared with who and on what basis so that we can look at the adequacy and the timeliness of the sharing and evaluate that (#11)."
"Netflix" model	• "Another possibility would be that all benefits are translated into a financial benefit, which goes into a fund and you can have therefore a subscription… and it goes into a fund (#39)."
Binding formal norms, or Codified binding norms backed by an inter-governmental entity	• "Worldwide, I think, you may have expected reluctance from some countries in particular developed countries to enter into a binding agreement. As you know in WHO there is only one binding agreement, tobacco. So, that's the only one. So, in WHO it is not a common practice to give binding agreement. And, I imagine, as far as I follow the process and that some countries were not prepared at all to enter into a binding scheme (#24)."

The above possibilities need to be understood in the context of existing rules and frameworks.

IHR (2005). The IHR (2005) does not explicitly require sharing pathogen samples, raising two questions: The first is whether state parties may nonetheless be under an obligation to share pathogens if this is necessary for surveillance and response, as arguably it is with influenza. An argument in this sense was made during the PIP Framework negotiations, but that obligation would be too inchoate to be of practical relevance and could create conflicts with the Nagoya Protocol. Secondly, Article 6 of the IHR (2005) requires parties to communicate to WHO a broad range of information on notifiable health events and it was argued that this could be interpreted to include at least GSD; this interpretation was never discussed in WHO and this was certainly not the intention of the negotiators of the IHR (2005). It is noteworthy that the IHR (2005) were hardly ever mentioned in our interviews and that their feasibility as a possible regulatory instrument for PBS was questioned in view of their perceived ineffectiveness despite their formal binding legal status.

PIP Framework (2011). Referred to by many interviewees as a successful model for PBS, the PIP Framework is an innovative instrument involving not only states but also industry, civil society, and scientific institutions. It was adopted by the WHA as a non-legally binding instrument under Article 23 of the WHO Constitution. It is credited for injecting principles of equity and distributive justice that are missing from the IHR (2005) (#11). The possibility of extending the PIP Framework to seasonal flu, which has been informally discussed in WHO, or to expand the PIP Framework into a broader framework applicable to non-flu pathogens did not receive much support from interviewees. Influenza is seen as a unique case both because of the existence of GISRS (on which the PIP Framework is built) and because the need to produce annual vaccines requires institutionalized cooperation. Some of the key principles agreed in the PIP Framework – especially putting access and benefit sharing on equal footing, and multilateral sharing of both samples and benefits – and the mechanisms to implement those principles (e.g., use of standardized MTAs, pre-negotiation of benefits, financing options) could be built upon or adapted for other pathogens.

CBD (1992) and Nagoya Protocol (2011). The CBD (adopted in 1992) and its Nagoya Protocol negotiated in parallel to the PIP Framework (adopted in 2011 and in force for 132 parties as of September 2021) dominated the interviews as the legal instruments that are changing the global outlook on PBS. At the same time, there is a limited awareness of the implications of the Nagoya Protocol and even of its existence among scientists, and it is creating confusion and uncertainties because of its lack of universality and the uneven way in which it is being implemented across and within countries. There were remarkably different positions on the implications for pathogen sharing and what could be done to improve the current situation. Pathogen sharing for public health purposes, with its arguably special needs, in particular with regard to disease outbreaks, was clearly not on the mind of the CBD's drafters. Several interviewees were adamant that the bilateral and transactional approach to ABS enshrined in the CBD and Nagoya Protocol were not fit for public health, which requires unfettered and quick multilateral sharing (#45). For some respondents, the CBD and Nagoya Protocol have formalized and politicized scientific cooperation unnecessarily and raised bureaucratic hurdles that create delays and make cooperation difficult and unpredictable. Even though most interviewees seemed to consider pathogens as falling within the scope of the

CBD/Nagoya as genetic resources, some interviewees still questioned this (#24). Other interviewees felt equally strongly that the CBD/Nagoya broke with "neo-colonialist" behavior by developed countries and their industries, gave more leverage to source countries and enshrined fundamental notions of equity in international law (#15).

The Nagoya Protocol took into account the concerns raised by the PIP Framework negotiation and introduced a number of flexibilities that have been referred to in the academic literature,[35] and are being discussed in WHO and CBD governance. There are three main flexibilities. First, the recognition in Article 4.4 that the Nagoya regime shall not apply to the parties to specialized international ABS instruments (SII) consistent with the Protocol. Second, the requirement in Article 8(b) that parties, in developing their ABS legislation, "pay due regard" to present or imminent emergencies and consider the need for quick access to genetic resources and related benefits, including access to countermeasures (e.g., drugs, diagnostics, vaccines). Third, Articles 19 and 20 encourage the development of model contractual clauses (Article 19) as well as voluntary codes of conduct, guidelines, and best practices (Article 20) to harmonize and smooth the terms of ABS. Despite some disagreement on the inclusion of pathogens within the remit of the Nagoya Protocol, its implications for pathogens have drawn growing attention.

Despite the uncertainties surrounding the implications of the Nagoya Protocol for pathogen sharing and the parallel discussions within WHO and the CBD governance to clarify the terms of pathogen sharing, some interviewees argued there is no inherent conflict between the Nagoya Protocol and public health needs; and that the Nagoya Protocol provides clarity as a general regime and more time should be given to its implementation (#32).

In addition to the form of any governing instrument and its relationship to existing law, the question of scope arises across three dimensions: which countries, which pathogens, and for what uses and benefits.

Geographical scope: "Club models" of governance have increasingly been used to address global governance challenges when global approaches seemed elusive. Regional models could also be explored. Smaller groups of states, and/or non-state actors such as research institutes, could agree on mutually acceptable norms, principles, and PBS arrangements. For the sake of both effectiveness and political acceptability, it would be critical that such groupings include key countries and/or institutions where emerging or re-emerging infectious diseases are likely to be found and key countries/institutions where scientific research and health technology research and development (R&D) capacity are concentrated. Our analysis of IVTM data found that influenza sample-sharing is highly concentrated among about 15 sending and receiving countries; to the extent this pattern holds for other pathogens, a small group of countries or research institutes could kick-start a negotiation process.

Scope of pathogens: The scope of rules could also vary, from a narrower list of priority pathogens to a broader set. Our research found that challenges with reliable PBS arose under two main conditions – when national security concerns or commercial interests were at stake. Otherwise, pathogen sharing and at least some benefit sharing appeared to be regular and reasonably reliable within research networks for non-commercial purposes. A key question is the feasibility of determining such a list of pathogens *ex ante*, and how to determine whether a novel pathogen would fall within scope, especially in the earliest days after such a pathogen is identified. It will also be critical to include consideration of GSD from the start, rather than physical samples alone.

Scope of use and benefits: Finally, the scope of any normative framework could vary with respect to types of use permitted with a shared pathogen, or types of benefits included. In particular, it may be easier to reach agreement on PBS for non-commercial use – e.g., for research and surveillance purposes – which could be governed under specific standardized terms, whereas economic benefits would remain to be negotiated on a case-by-case basis or within a broad set of principles.

In identifying potential solutions to the challenge of PBS, key variables include the choice of normative instrument, its relationship to existing international treaties, its degree of formality and the scope of actors negotiating it, the pathogens to be included, and scope of use and benefits. While keeping these options in mind, overall, it is critical to reach a minimum level of agreement on the ultimate purpose of such an instrument – that is, form should follow function. If key stakeholders agree that there is a shared global public interest in ensuring reliable, rapid pathogen sharing and fair, equitable benefit sharing, the question of form could be more easily addressed.

CONCLUSIONS: A WAY FORWARD?

The ongoing COVID-19 pandemic underscores the urgent need to find governance solutions for PBS, and the political appetite for multilateral instruments for PBS may be changing as a result. Although additional research into PBS is needed, a few conclusions can be advanced at this time. First, there is a need for traceability of PBS beyond pandemic influenza – and the development of a traceability mechanism could act as a first step in the development of a comprehensive negotiated framework. Second, given preliminary findings on the relatively small number of countries involved in PBS, a small albeit representative group of stakeholders could begin to create clearer international normative frameworks for PBS governance. Third, there is agreement to build upon, with widespread acceptance of the importance of benefit-sharing to be on equal footing with pathogen-sharing. However, ongoing disagreements about what benefits should entail will need to be addressed. Fourth, as the case studies of Ebola and Zika underscored, PBS arrangements need to be in place ahead of outbreaks, at both national and international levels, to ensure fair and reliable sharing of both pathogens and benefits in the future. Finally, while the interaction of existing rules for health and biodiversity are complex, it is possible to develop specific rules for PBS while remaining consistent with the objectives of both regimes. Given the general agreement about the need for clarity, predictability, and equity in PBS, there are many possibilities for a way forward – if political leadership emerges.

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[1] The Shanghai Public Health Clinical Center & School of Public Health, in collaboration with the Central Hospital of Wuhan, Huazhong University of Science and Technology, the Wuhan Center for Disease Control and Prevention, the National Institute for Communicable Disease Control and Prevention, Chinese Center for Disease Control, and the University of Sydney, Sydney, Australia, "Novel 2019 Coronavirus Genome - SARS-CoV-2 Coronavirus," Virological, January 10, 2020, https://virological.org/t/novel-2019-coronavirus-genome/319; Michelle Rourke et al., "Policy Opportunities to Enhance Sharing for Pandemic Research," *Science* 368, no. 6492 (May 15, 2020): 716–18, https://doi.org/10.1126/science.abb9342.

[2] David P. Fidler, "Indonesia's Decision to Withhold Influenza Virus Samples from the World Health Organization: Implications for International Law," *ASIL Insight* 11, no. 4 (2007); David P. Fidler, "Influenza Virus Samples, International Law, and Global Health Diplomacy," *Emerging Infectious Diseases* 14, no. 1 (January 2008): 88–94, https://doi.org/10.3201/eid1401.070700; David P. Fidler, "Who Owns MERS?," *Foreign Affairs*, June 6, 2013, https://www.foreignaffairs.com/articles/saudi-arabia/2013-06-06/who-owns-mers; Andrew E. Bollinger, "E-Mers-Gency: An Application and Evaluation of the Pandemic Influenza Preparedness Framework to the Outbreak of Mers-Cov," *Temple International & Comparative Law Journal* 29 (2015): 1, https://heinonline.org/HOL/Page?handle=hein.journals/tclj29&id=9&div=&collection=; Jeremy Youde, "MERS and Global Health Governance," *International Journal Canada's Journal of Global Policy Analysis* 71, no. 1 (March 1, 2015): 119–36, https://doi.org/10.1177/0020702014562594.

[3] Kenan Mullis, "Playing Chicken with Bird Flu: 'Viral Sovereignty,' the Right to Exploit Natural Genetic Resources, and the Potential Human Rights Ramifications," *American University International Law Review* 943 (2008); Jason Carter, "Who's Virus Is It Anyway - How the World Health Organization Can Protect against Claims of Viral Sovereignty," *Georgia Journal of International and Comparative Law* 38 (2010 2009): 717, https://heinonline.org/HOL/Page?handle=hein.journals/gjicl38&id=727&div=&collection=; David P. Fidler and Lawrence O. Gostin, "The WHO Pandemic Influenza Preparedness Framework: A Milestone in Global Governance for Health," *JAMA* 306, no. 2 (July 13, 2011): 200–201, https://doi.org/10.1001/jama.2011.960; Meena Krishnamurthy and Matthew Herder, "Justice in Global Pandemic Influenza Preparedness: An Analysis Based on the Values of Contribution, Ownership and Reciprocity," *Public Health Ethics* 6, no. 3 (November 1, 2013): 272–86, https://doi.org/10.1093/phe/pht027.

[4] World Health Organization, *International Health Regulations (2005)*, 2nd ed. (Geneva: WHO Press, 2008), https://www.who.int/ihr/publications/9789241596664/en/.

[5] World Health Organization, "Pandemic Influenza Preparedness Framework for the Sharing of Influenza Viruses and Access to Vaccines and Other Benefits," 2011, https://apps.who.int/iris/bitstream/handle/10665/44796/9789241503082_eng.pdf.

[6] Secretariat of the Convention on Biological Diversity, *The Nagoya Protocol on Access to Genetic Resources and the Fair and Equitable Sharing of Benefits Arising from Their Utilization to the Convention on Biological Diversity* (Convention on Biological Diversity, 2011), https://www.cbd.int/abs/.

[7] Anthony Rizk et al., "'Everybody Knows This Needs to Be Done, but Nobody Really Wants to Do It': Governing Pathogen- and Benefit-Sharing" (Global Health Center, Graduate Institute of International and Development Studies, Geneva, July 2020).

[8] Declan Butler, "Tensions Linger over Discovery of Coronavirus," *Nature News*, January 14, 2013, https://doi.org/10.1038/nature.2012.12108.

[9] Maria Cheng et al., "Brazil Not Giving Enough Zika Samples, World Health Officials Complain | CBC News," CBC, February 4, 2016, https://www.cbc.ca/news/health/zika-virus-brazil-1.3433339.

[10] Emmanuel Freudenthal, "Ebola's Lost Blood: Row over Samples Flown out of Africa as 'big Pharma' Set to Cash In," *The Telegraph*, June 26, 2019, https://www.telegraph.co.uk/global-health/science-and-disease/ebolas-lost-blood-row-samples-flown-africa-big-pharma-set-cash/.

[11] Fidler and Gostin, "The WHO Pandemic Influenza Preparedness Framework."

[12] Endang R Sedyaningsih et al., "Towards Mutual Trust, Transparency and Equity in Virus Sharing Mechanism: The Avian Influenza Case of Indonesia," *Annals Academy of Medicine Singapore* 37, no. 6 (2008).

[13] World Health Organization, *International Health Regulations (2005)*.
[14] United Nations, *Convention on Biological Diversity* (United Nations, 1992), https://www.cbd.int/doc/legal/cbd-en.pdf.
[15] Secretariat of the Convention on Biological Diversity, *The Nagoya Protocol on Access to Genetic Resources and the Fair and Equitable Sharing of Benefits Arising from Their Utilization to the Convention on Biological Diversity*.
[16] World Health Organization, "Pandemic Influenza Preparedness Framework for the Sharing of Influenza Viruses and Access to Vaccines and Other Benefits."
[17] World Health Organization, "Influenza Virus Traceability Mechanism (IVTM)," 2020, https://www.who.int/influenza/pip/ivtm/en/.
[18] International Committee of Medical Journal Editors (ICMJE), "Defining the Role of Authors and Contributors," accessed May 19, 2020, http://www.icmje.org/recommendations/browse/roles-and-responsibilities/defining-the-role-of-authors-and-contributors.html.
[19] World Health Organization, "Standard Material Transfer Agreements 2 (SMTA2)," World Health Organization (World Health Organization, 2020), http://www.who.int/influenza/pip/smta2/en/.
[20] For example, WHO has developed an MTA tool with options and explanations on potential provisions in MTAs World Health Organization, "Draft R&D Blueprint MTA Tool," n.d., https://apps.who.int/blueprint/mta-tool/..
[21] World Bank, "World Development Indicators | DataBank," accessed November 17, 2020, https://databank.worldbank.org/source/world-development-indicators.
[22] Maureen Quinn and ed., "Governance and Health in Post-Conflict Countries: The Ebola Outbreak in Liberia and Sierra Leone," *International Peace Institute* (blog), June 6, 2016, https://www.ipinst.org/2016/06/ebola-outbreak-liberia-sierra-leone.
[23] World Health Organization, *2015 WHO Strategic Response Plan: West Africa Ebola Outbreak*. (Geneva: World Health Organization, 2015), http://apps.who.int/iris/bitstream/10665/163360/1/9789241508698_eng.pdf.
[24] CDC, "2014-2016 Ebola Outbreak in West Africa | History | Ebola (Ebola Virus Disease) | CDC," March 17, 2020, https://www.cdc.gov/vhf/ebola/history/2014-2016-outbreak/index.html; Adelaida Sarukhan, "Ebola: Two Years and 11,300 Deaths Later," ISGlobal, March 17, 2016, https://www.isglobal.org/en/ebola.
[25] Suerie Moon et al., "Will Ebola Change the Game? Ten Essential Reforms before the next Pandemic. The Report of the Harvard-LSHTM Independent Panel on the Global Response to Ebola," *The Lancet* 386, no. 10009 (November 28, 2015): 2204–21, https://doi.org/10.1016/S0140-6736(15)00946-0.
[26] Martin I. Meltzer et al., "Estimating the Future Number of Cases in the Ebola Epidemic -- Liberia and Sierra Leone, 2014–2015," ed. Centers for Disease Control and Prevention (U.S.), National Center for Emerging and Zoonotic Infectious Diseases (U.S.). Division of Preparedness and Emerging Infections., and National Center for Emerging and Zoonotic Infectious Diseases (U.S.). Division of High Consequence Pathogens and Pathology., *MMWR. Morbidity and Mortality Weekly Report ; v. 63, Suppl. 3*, September 26, 2014, https://stacks.cdc.gov/view/cdc/24901.
[27] World Health Organization, "World Health Organization Report on Ebola Samples," March 18, 2016.
[28] CBD Secretariat, "Libera - Main Details" (Secretariat of the Convention on Biological Diversity, n.d.), https://www.cbd.int/countries/profile/?country=lr#measures.
[29] Ministério da Saúde, Secretaria de Vigilância em Saúde, "Síndrome Congênita Associada à Infecção Pelo Vírus Zika: Situação Epidemiológica, Ações Desenvolvidas e Desafios, 2015 a 2019," November 2019, https://portalarquivos2.saude.gov.br/images/pdf/2019/dezembro/05/be-sindrome-congenita-vfinal.pdf.
[30] Access and Benefit-Sharing Clearing House, "Brazil Country Profile," n.d., https://absch.cbd.int/countries/BR.
[31] MD Silva, DR Oliveira. The new Brazilian legislation on access to the biodiversity (Law 13,123/15 and Decree 8772/16). Braz J Microbiol. 2018 Jan-Mar;49(1):1-4. doi: 10.1016/j.bjm.2017.12.001. PMID: 29348034; PMCID: PMC6112059.
[32] Marion Koopmans et al., "Familiar Barriers Still Unresolved—a Perspective on the Zika Virus Outbreak Research Response," *The Lancet Infectious Diseases* 19, no. 2 (February 1, 2019): e59–62, https://doi.org/10.1016/S1473-3099(18)30497-3.

[33] World Medical Association (WMA), "Declaration of Helsinki – Ethical Principles for Medical Research Involving Human Subjects," 2018, https://www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-medical-research-involving-human-subjects/.
[34] World Health Organization and Council for International Organizations of Medical Sciences, *International Ethical Guidelines for Health-Related Research Involving Humans* (Geneva: CIOMS, 2017).
[35] Marie Wilke, "Chapter 4. A Healthy Look at the Nagoya Protocol—Implications for Global Health Governance," in *The 2010 Nagoya Protocol on Access and Benefit-Sharing in Perspective* (Brill Nijhoff, 2013), 123–48, https://brill.com/view/book/edcoll/9789004217201/B9789004217201_006.xml; Stephanie Switzer et al., "Biodiversity, Pathogen Sharing and International Law," in *Environmental Health in International and EU Law*, ed. Stefania Negri (London: Giappichelli-Routledge Studies in Law, 2019), 253–71, https://strathprints.strath.ac.uk/68600/.