GLOBAL HEALTH CENTRE WORKING PAPER NO. 23 | 2020

"EVERYBODY KNOWS THIS NEEDS TO BE DONE, BUT NOBODY REALLY WANTS TO DO IT":

GOVERNING PATHOGEN- AND BENEFIT-SHARING (PBS)

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Abbreviations	
ABS	Access- and Benefit- Sharing
AUTM	Association of University Technology Managers
CBD	United Nations Convention on Biological Diversity
CDC	Centers for Disease Control and Prevention
CGEN	Genetic Heritage Management Council
CIOMS	Council for International Organizations of Medical Sciences
CITES	The Convention on International Trade in Endangered Species of Wild Fauna and Flora
CONEP	National Commission for Research Ethics in Brazil
DoD	Department of Defense
EPA	Environmental Protection Agency
ERL	Essential Regulatory Laboratories
EVD	Ebola Virus Disease
GISAID	Global Initiative on Sharing Avian Influenza Data
GISRS	Global Influenza Surveillance and Response System
GSD	Genomic Sequence Data
HIC	High Income Countries
ICMJE	International Committee of Medical Journal Editors
IHEID	Graduate Institute of International and Development Studies, Geneva
IHR	International Health Regulations
IVPP	Influenza Viruses of Pandemic Potential
IVTM	Influenza Virus Traceability Mechanism
LIBR	Liberia Institute of Biomedical Research
LMIC	Low- and Middle- Income Countries

Abbreviations	
MAT	Mutually Agreed Terms
MERS	Middle East Respiratory Syndrome
MoH	Ministry of Health
MTA	Material Transfer Agreement
NIC	National Influenza Centres
NIH	National Institute of Health
NPHIL	National Public Health Institute of Liberia
NREB	National Research Ethics Board
NRL	National Reference Laboratory
PBS	Pathogen- and Benefit- Sharing
PHEIC	Public Health Emergency of International Concern
PIC	Prior Informed Consent
PIP Framework	Pandemic Influenza Preparedness Framework
R&D	Research and Development
SARS-CoV-2	Severe Acute Respiratory Syndrome Coronavirus 2
SII	Specialized International ABS Instruments
SisGen	National System of Genetic Resource Management
SME	Small- and Medium Sized Enterprises
SMTA2s	Standard Material Agreements 2
UL-PIRE	University of Liberia – Pacific Institute for Research & Evaluation
WHA	World Health Assembly
WHO CC	WHO Collaborating Centres
WHO	World Health Organization

EXECUTIVE SUMMARY

Background: A perennially thorny issue hampering the global community's ability to manage infectious disease outbreaks is the fair, reliable, and rapid international sharing of pathogens and related benefits, which we refer to here as pathogen- and benefit- sharing (PBS). Access to pathogen samples and related data is critical for researchers seeking to identify and understand pathogens or to develop medical countermeasures (e.g. diagnostics, drugs, vaccines). At the same time, ensuring fair and equitable benefit sharing has proven difficult. Although there has been some progress in addressing challenges related to PBS, we remain far from a well-functioning international system to do so. This research project was motivated by the need to increase understanding of 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 arrangements.

Methods: This study sought to fill gaps in the literature by investigating current practices of PBS and their drivers, at both the international level and through two outbreak-specific case studies. We conducted 86 total interviews between November 2018 and October 2020. Of these, 53 were with experts involved in international policymaking or scientific practice around PBS, 20 were with experts involved in Ebola Virus PBS in Liberia during the 2014–16 Ebola epidemic, and 13 were with experts involved in Zika Virus PBS in Brazil during the 2015–16 Zika epidemic. We also reviewed the literature on PBS, analyzed data from the Influenza Virus Traceability Mechanism (IVTM), and solicited documents from interviewees, including 26 Material Transfer Agreements (MTAs). We triangulated among these data sources to generate the findings and conclusions presented in this Working Paper. There is a need for much more research on this subject, but we believe this study represents the largest collection of empirical data to date on PBS practices for emerging infectious diseases that is available in the public domain.

Findings: Respondents expressed significant concern that PBS was becoming increasingly complex and uncertain. Particularly in light of the coming into force of the Nagoya Protocol on Access and Benefit- Sharing in 2014, respondents noted a need for coherence across international and national principles, guidelines, rules, and regulations. Given a lack of global tracking mechanisms, it is unclear how many countries are actively engaged in PBS; however, analysis of international sharing of Influenza Viruses of Pandemic Potential (IVPPs) found that, in the past two decades, a relatively

small number of countries – about 15 – have been actively engaged in their international sharing. Drivers for pathogen sharing are multi-faceted and encompass instrumental, political, economic, and legal reasons. Trust, personal relationships, and long-term collaborations were identified as playing a defining role in the success or failure of effective PBS. The absence of trusted collaborations has often led to slow, inefficient, and potentially detrimental barriers to access pathogens or benefits, which may be difficult to overcome quickly in times of crisis. Overall, there appears to be growing recognition among interview respondents of the need for benefit sharing on equal footing with pathogen sharing. However, there is little consensus on what constitutes fair, equitable and reasonable benefits and we found large variations in practices and views among different groups and across global divides.

Interviewees pointed to areas in which current PBS arrangements are working, as well as ways in which they are falling short. In general, researchers reported being able to get desired pathogens under certain conditions and in normal (non-outbreak) situations. However, timely sharing during outbreaks was more problematic and numerous barriers to PBS were described, including those related to biosecurity concerns and the involvement of commercial interests. We found broad consensus that clarifying and improving the coherence of national and international normative frameworks around PBS was a priority, with strengthening the governance of benefit sharing needing particular attention. Respondents identified many options to address PBS governance, including less formal principles or codes of conduct, binding or non-binding formal rules, and expanded use of standardized MTAs. Each of these normative instruments could vary in terms of the scope of included countries, pathogens, uses and benefits. While each of these options have their proponents, there was no clear policy direction that was strongly supported or advocated by a critical mass of respondents.

Conclusions: Though policy options are many, the way forward is unclear. Additional research into PBS is needed. For example, further case studies are needed on PBS in specific outbreaks, the kinds of benefit sharing arrangements that have been implemented, as well as studies on PBS practices in plant and animal health. Nevertheless, a few conclusions about possible next steps can be advanced based on this research. **1.** The development of a traceability mechanism for PBS is both needed, in and of itself, and may be a useful first step that could contribute to the building of a comprehensive negotiated framework. **2.** Given preliminary findings on the relatively small number of countries actively involved in PBS, a small albeit representative group of stakeholders could start the process of clarifying and making more coherent international normative frameworks for PBS

governance. Leadership from a few countries, therefore, is urgently needed. **3.** It appears there is substantial agreement to build on, with widespread acceptance of the importance of benefit sharing being on equal footing with pathogen sharing. **4.** 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. **5.** 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. Any solution will need to address the governance of genomic sequence data (GSD) derived from pathogens, alongside or integrated into rules for physical pathogen samples. While there was considerable political hesitance among respondents to address the governance of PBS head-on, COVID-19 reminds us that nature does not wait. It is time to push for new international rules tailor-made for PBS.

1 | INTRODUCTION

A perennially thorny issue hampering the global community's ability to manage infectious disease outbreaks is the fair, reliable and rapid international sharing of pathogens and related benefits – what we refer to as pathogen- and benefit- sharing (PBS)[1] throughout this Working Paper. When outbreaks of infectious diseases occur, healthcare workers and researchers often take samples of biological materials (e.g. blood, saliva, tissue) from infected persons for both medical and research purposes. Access to pathogen samples and related data is critical for researchers seeking to identify and understand pathogens or to develop medical countermeasures (e.g. diagnostics, drugs, vaccines). At the same time, the ability for pathogen-sending countries to access the medical countermeasures developed from the use of pathogens is critical for outbreak control and prevention. Pathogens and the countermeasures developed from their use are, however, often controlled by different parties (public and private), often in different countries, with different degrees of scientific, industrial, and economic resources. Ensuring the fair and equitable exchange of such resources has proven difficult. The past two decades have witnessed some progress in addressing challenges related to PBS, but we remain far from a well-functioning international system to do so.

This research project was 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. Presently, there is no publicly available and centralized data source tracking the international movement of pathogens or related benefits – with the important exception of one type of pathogen, 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. Furthermore, while the literature on PBS has focused on a relatively small number of cases in which pathogen sharing was controversial (e.g. 2007 H5N1 influenza, 2013 Middle-East Respiratory Syndrome (MERS)) [1]–[5], there remains little clarity on PBS practices for other pathogens of pandemic potential, or pathogens more broadly. In terms of

1 Pathogen- and benefit-sharing (PBS) is used here to designate access- and benefit-sharing (ABS) of pathogens.

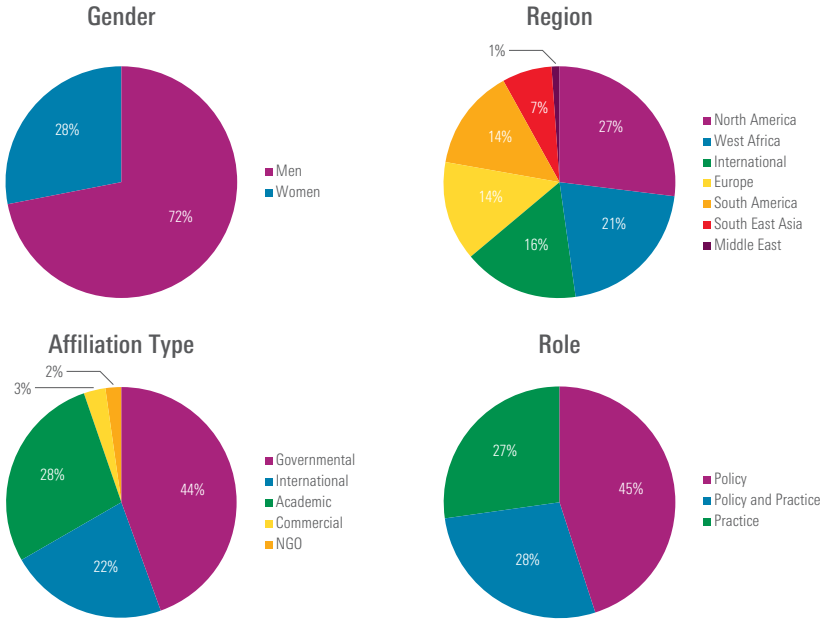
the governance of pathogen sharing, the literature [6]–[9] has largely focused on the relevant international legal norms, namely the 2005 International Health Regulations (IHR) [10], the 2011 Pandemic Influenza Preparedness (PIP) Framework [11], and the 2010 Nagoya Protocol on Access to Genetic Resources and the Fair and Equitable Sharing of Benefits (hereafter, the Nagoya Protocol) to the Convention on Biological Diversity (CBD) [12]. Important gaps remain in understanding the role of other factors relevant to PBS, including the conditions under which PBS is likely to become problematic, informal norms governing PBS, such as those between scientists or networks of research institutions, and agreements between organizations, such as material transfer agreements (MTAs) or research contracts.

We reviewed the literature on PBS, including known cases of contested PBS and broader analyses of relevant international norms, rules, and political economy. We also searched for any publicly available data on the actual international movement of pathogens and related benefits, and found only one source – the Influenza Virus Traceability Mechanism (IVTM), established as part of the PIP Framework [11]. We identified an initial list of interviewees based on published experts on the topic, inputs from our advisors and project partners, and our knowledge of the field and relied on snowball sampling to expand the list until thematic saturation. We sought to interview 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 interviews between November 2018 and October 2020 across two phases of research. Phase 1, between November 2018 and December 2019, focused on interviewing 53 experts involved in international policymaking or scientific practice around PBS. Phase 2 focused on two in-depth case studies, one on Ebola PBS in Liberia during the 2014–2016 Ebola Virus Disease (EVD) epidemic, for which we conducted 20 interviews (mostly in-person in Liberia) in November 2019, and another on Zika PBS in Brazil during the 2015–2016 Zika epidemic, for which we conducted 13 online interviews from July 2020 to October 2020. For a summary of interviewee characteristics, see **Figure 1**. We also searched for publicly available documents and solicited documents from interviewees, particularly 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 Working Paper. Interviews were recorded with the consent of respondents, or otherwise detailed hand-written notes were taken, and transcripts were analyzed thematically by

the research team. Transcripts were coded using themes developed deductively from the interview guide and inductively for emerging themes, and results were developed iteratively. 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.

Figure 1: Interviewee characteristics



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. Therefore, we sought to reconstruct from interviews a necessarily impressionistic picture of current practices and drivers. In addition to the near total absence of quantitative data, key documents such as executed MTAs or other contracts are usually confidential. Despite our efforts to cover a broad range of interlocutors, the number and breadth of interviewees does not capture all countries or stakeholder groups. In Phase 1, 16 persons did not accept our request for an interview, including 4 from the commercial sector and 9 from Low- and Middle-Income Countries (LMICs). Furthermore, interviews for the case study on Zika PBS in

Brazil were conducted as the COVID-19 pandemic was in full swing, contributing to a low response rate in Brazil (37%) as opposed to the Liberia case study (83%) and Phase 1 interviews (77%). For a detailed summary of interview characteristics across the different phases of research, see **Annex 1**. The results should be interpreted with these limitations in mind. 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), which we examined in relation to the sharing of physical samples (see **Box 1**) but did not analyze in-depth. Both PBS for non-human pathogens and the governance of GSD merit further in-depth research.

Despite these limitations, we believe this study represents the largest collection of empirical data on PBS practices for emerging infectious diseases that is available in the public domain. This Working Paper is divided into five sections. Section 2, "*Growing Uncertainty in Pathogen- and Benefit-Sharing*" analyzes current challenges in PBS resulting from changes in international law and the complex interplay of competing formal and informal norms. Section 3, "*PBS in Practice: What do we (not) know?*", presents the current state of PBS practice as found by our research. Section 4, "*Pathogen- and Benefit- Sharing: What are the issues?*", identifies the main aspects of PBS that we found to be well-functioning or problematic. Section 5, "*Case Studies: Pathogen- and Benefit- Sharing in Outbreak Response*" presents findings on the politics and practice of PBS during two health emergencies, namely Liberia's EVD epidemic (2014–2016) and Brazil's Zika epidemic (2015–2016). Section 6, "*Governing Pathogen- and Benefit- Sharing: What are the options?*", presents and discusses the spectrum of policy options that respondents have considered in governing PBS. Lastly, we offer conclusions on what is necessary to improve the governance of PBS and highlight several areas for further research.

2 | GROWING UNCERTAINTY IN PATHOGEN- AND BENEFIT- SHARING

"You know, if I share my influenza virus, what's happening? Do I lose ownership or not? And this is the uncertainty, I think, which makes things more difficult (#39[2])."

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 samples of H5N1 influenza, citing sovereignty rights over genetic resources and concerns that it would not get access to vaccines developed from sharing its pandemic influenza samples. Since then, pathogen sharing controversies have routinely emerged along with new outbreaks, including with MERS-sharing between Saudi Arabia and Erasmus University in the Netherlands in 2013 [13], delayed sharing of Zika samples from Brazil during the Zika outbreak of 2015–6 [14], and reports of the mass exodus of Ebola samples during West Africa's outbreak of EVD 2014–6 [15].

In response to Indonesia's position in 2007, WHO, its Member States and related non-state actors, such as vaccine developers, manufacturers, and non-governmental organizations participated in negotiations that culminated in the PIP Framework, which was adopted by the World Health Assembly (WHA) in 2011. The PIP Framework established a system based on reciprocity: countries with pandemic influenza samples would share them with the WHO's laboratory network as well as research institutions and pharmaceutical companies outside the network; in exchange, companies producing medical countermeasures from these samples, such as vaccines, medicines and diagnostics, committed to provide WHO with benefits for affected countries in the event of an outbreak. The PIP Framework has been hailed as a "milestone in global health governance" [8]. The PIP Framework remains, however, the only multilateral framework designed to govern PBS to date. Throughout, periodic calls have been made by global health experts to strengthen the governance of PBS during outbreaks [16]–[18], but it has remained an under-governed area of global health.

2 Throughout the Working Paper, interview transcripts are cited as (#1,2,3, etc.) where #1–53 are transcripts from Phase 1 interviews, #54–73 designate transcripts from Phase 2 interviews for the Liberia case study and #74–86 designate transcripts from Phase 2 interviews for the Brazil case study.

In this study, respondents described a general climate of uncertainty around PBS. This state of uncertainty has reportedly been exacerbated by the coming into force in 2014 of the Nagoya Protocol [12] and the beginning of its implementation in national laws. In 2011, the Nagoya Protocol was adopted as a supplementary protocol to the UN CBD [19], 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" [12]. Despite some disagreement on the inclusion of pathogens within the remit of the Nagoya Protocol [20], its implications for pathogens has drawn growing attention.

What does this uncertainty look like? In pathogen-sending countries, a respondent from a government-affiliated laboratory described situations where "nobody knows exactly what to do … whoever holds the samples doesn't know whether they have a right to share, with whom, and which framework (#39)." 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 pathogens to clinical data and, for viruses other than influenza, impacting long-standing collaborations. Industry representatives have expressed concern that the growing difficulties with pathogen sharing is "generat[ing] instability in commercial practice", where large pharmaceutical companies may be better able to navigate an emerging "mosaic" of international and national legal regimes than their small- and medium-sized counterparts (#46). For others, such as researchers already routinely involved in systems that adhere to the Convention on International Trade in Endangered Species of Wild Fauna and Flora (CITES)[3], impending changes are expected to be "just another legal process…[that] will just add time and delays depending on how these countries structure these processes (#15)." One respondent, part of a global funding agency, explained how contending with this growing uncertainty is becoming increasingly unavoidable:

> *"We see this as a continuation of a number of countries' specific laws that we have to deal with, and Nagoya will be one of them. Every country has its own requirements of what you can and you can't do, what they allow certain institutions to do; we have to just deal with it (#18)."*

Overall, this shift has elicited a number of responses, ranging from perceiving the changing landscape 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). While respondents largely agreed that timely sharing of pathogens is important, there is a recognition that rapid pathogen sharing may only be realizable once "uncertainties [around benefits] are reduced to a minimum (#39)." 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. Respondents have reported, however, that the formal and informal norms that govern PBS – the principles, guidelines, laws, and regulations – are becoming increasingly complex.[4]

2.1 Formal norms for PBS

Respondents expressed significant concern over the need for coherence across international and national regimes (See **Table 1** for examples). Two regimes have previously operated quite separately from each other: the IHR (2005) [10], the purpose of which is to govern global preparedness and response to outbreaks of infectious disease (among other hazards) and the CBD (1993) [19] and its associated Nagoya Protocol (2011) [12], which seek to protect biodiversity and ensure countries benefit from their genetic resources. The PIP Framework (2011) [11] reflects the objectives of both sets of rules. More broadly, PBS can be seen as relevant to the goals of both regimes, but also falling into an under-governed gap between them.

4 By formal norms, we mean the norms that have been accepted by a formally legitimized body (be it governments or intergovernmental organizations) and, by informal norms, we mean the norms that inform everyday social organization, often based on shared beliefs or social conventions [21].

Table 1: Examples of formal norms relevant to PBS

International Formal Norms	
Binding legal instruments	• International Health Regulations (IHR) (2005) • Convention on Biological Diversity (CBD) (1993) • Nagoya Protocol on Access and Benefit Sharing (2014)
Non-binding frameworks	• Pandemic Influenza Preparedness (PIP) Framework (2011)
National Formal Norms	
National laws	• Brazil's new Biodiversity Law (Law 13,123/15 and Decree 8772/16) (2015) • India's Biodiversity Act (2002) and Guidelines on Access to Biological Resources and Associated Knowledge and Benefits Sharing Regulations (2014) • Malaysia's Access to Biological Resources and Benefit Sharing Act (2017)
Governmental policies	• Varied US government policy across the National Institutes of Health (US NIH), • Centers for Disease Control and Prevention (US CDC) and the US State Department • Ministerial policies across sectors (health, environment, trade, etc.)
National Research Ethics Guidelines	• Binding national research ethics guidelines, when enforced by national research committees, for example

The CBD is based on a number of driving principles, including conservation and sustainable use of biodiversity as well as fair and equitable sharing of benefits deriving from its utilization. CBD reinforced the principle of national sovereignty over genetic resources and that sharing of such resources must be based on the prior informed consent (PIC) and mutually agreed terms (MAT) with the source country. 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. 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 [22], [23], 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.

Two main concerns were raised by interviewees related to the implementation of the Nagoya Protocol. First, that its implementation may impact the everyday functioning of global pathogen sharing networks, such as the Global Influenza Surveillance and Response system (GISRS) and, secondly, that the emergence of a "mosaic" of national legislation around PBS may complicate timely and effective PBS more broadly. One respondent attributed this to the Nagoya Protocol allowing "too much space for countries to implement" where "if you receive different samples from India, Brazil, China and Bangladesh, you have four different legal frameworks you have to deal with (#25)." Variation among countries was noted, with some having a clear system for managing PBS, while others are characterized by competing norms and policies across different governmental sectors (such as health, environment, and trade), as explained by the following respondents:

"In terms of sharing viruses, if it's an international body, WHO or even CDC, usually there's not much of a hurdle and part of our commitment for global health…In case we have some novel viruses that is unknown…I think the arrangement of getting the Ministry of Health approval to send out, we can do that … [if it is] important to identify quickly and if we don't have the local expertise to do that…If you are thinking about commercializing… I think the kind of mechanism is slightly different because now it's going to have a commercial value to that…that will go under the [national law on access and benefit sharing] and have to get the consent of the Ministry of Health (#40, scientist involved in national policy)."

"We're a governmental agency, which means we can only do things that we're authorized to do [by law]. So, sometimes we come upon terms that perhaps a private university or other kind of organization would be able to accept but because of our limitations, by law and regulation, we cannot always accept everything everyone else can (#17)."

"There is a statute for [granting licenses in MTAs], you can't just give it up to people because you feel like, so there are these different laws that intersect in these agreements…so there's different legal authorities, different policy requirements that come into play in each of these agreements (#18, policy expert affiliated with a national government)."

2.2 Informal norms for PBS

Informal norms (see **Table 2**) also play an important role in governing PBS. Respondents pointed to the informal norms of demonstrating an open "collaborative spirit" and "sense of duty" to global public health (#29) in scientific practice, as well as a push for more equity and transparency in current PBS arrangements. Trust, personal relationships, long-term collaborations, and the desire to behave ethically or promote equity emerged as key factors that impact the way PBS takes place in scientific practice. Personal relationships were particularly emphasized and were reported to precede legal arrangements, where invariably "a disconnect [takes place] between the way projects begin, which is often very personal, with the way these things need to be dealt with, which is institutional and legal (#16)." This disconnect leads to a wide variety of case-by-case agreements, negotiations, and the absence of clear standards for PBS. Reliance on informal norms for PBS has its limitations, however, where "trust-based personal relations might work well in a sunny climate, but as soon as the weather gets stormy, as soon as there is a pressure on resources, a need for benefits in terms of countermeasures…trust-based personal relationships can't be carried on in the same way that formal understandings [would be], with expectations, obligations and rights, clearly set out (#27)."

Table 2: Examples of factors impacting informal norms relevant to PBS

Personal relationships	"For many years there was just an informal understanding…and these collaborations and willingness to share reagents really grew out of just individual collaborations and building trust and partnerships (#20)." "We trust a lot [with non-commercial organizations]…we trust that they're bound by the same ethos that we are governed by in terms of sharing, we obviously don't have the mechanism with which to police that (#46)."
Trust	A "sense of duty" to global public health (#29). "We've always been driven by the ethics of this rather than law, so…we've always gone beyond what the law requires because we want to make sure the ethics of benefit sharing and IP and all of those things are in place. So, we don't anticipate any problems… (#15)."
Desire to behave ethically	Binding national research ethics guidelines, when enforced by national research committees, for example
Desire to promote equity and transparency	"[PBS principles] provide good academic reward for African scientists… [instead of] a model where people say 'in the name of data sharing' just bring your samples across the Atlantic and then they get lost…[we are] pushing for equity in science and more transparency in the way science is being done (#38)."

Respondents anticipated tensions between the informal norms shaping previous PBS practices, on one hand, and emerging formal norms for the governance of PBS, on the other. Respondents who belong to long-established networks have pointed to how PBS practices that have organically emerged from years of collaboration and negotiation may be upended as informal relationships become formalized (#20), while other international collaborations anticipate little friction or change, citing that they have "always worked under the principle [of ABS], so now the thing about Nagoya is it's more about the paperwork, it's not about the concept (#15)." In some instances, however, established ways of pathogen sharing may be impacted by new laws introduced to govern it, as noted by a respondent involved in global health policy:

> *"I spoke to people operating a GISRS national influenza centre and they were not concerned about national legislation and I said, look, you have to take a look at the law because you might be breaking it. Because, you know, GISRS has been running around for more than 60 years so people just kept doing what they did. People who come to the job just asked what should we do and were told, every night we send a box of samples to [redacted: locations] and that's what we do, this is the form, this is the PIP resolution, so then people just kept doing what they did… I told the person; you have to look into this paper called the law because you might be held responsible…People were not aware of the final use of the material (#25)."*

Calls for increased coherence in governing PBS are not only about reconciling formal laws, but also about bridging formal and informal norms.

3 | PATHOGEN- AND BENEFIT-SHARING IN PRACTICE: WHAT DO WE (NOT) KNOW?

Presently, publicly available, and centralized information on global pathogen movements and the benefits associated with their sharing are scarce, with the important exception of 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, fair PBS. To develop some intuition on these questions, we first examined 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, and then examined what is and is not publicly-known about benefit sharing in both scientific and legal practice.

3.1 What do we (not) know about 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 first present an analysis of data from the IVTM and then focus on respondents' characterizations of key drivers and barriers for current pathogen sharing practices.

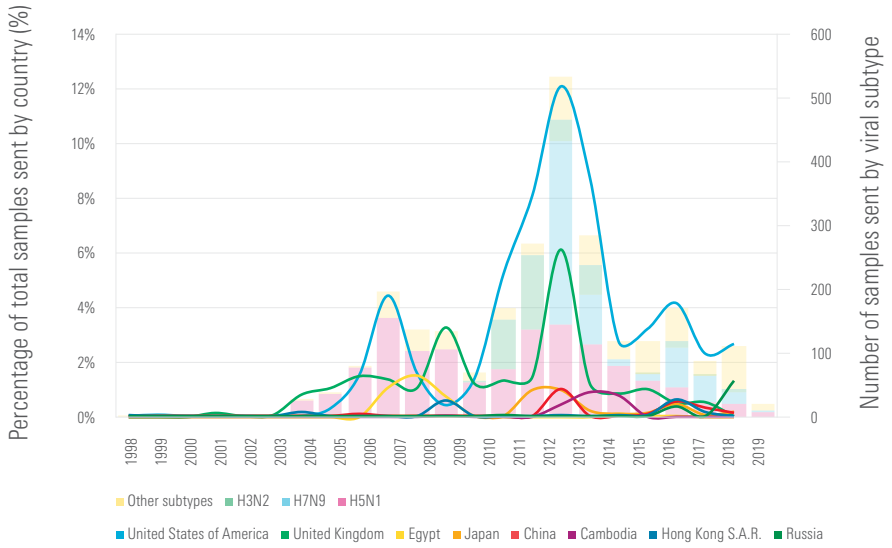
A global flow of pathogen sharing: Influenza viruses of pandemic potential (IVPPs)

We analyzed data on the global movement of IVPP samples from the IVTM [24], studying patterns in a total of 2,601 IVPPs recorded between January 1998 and 2019.[5] Data extracted from the IVTM

5 IVPP data using the "Shipments and Materials" option were downloaded from the IVTM database (https://extranet.who.int/ivtm/Search.aspx), date of retrieval: 7 May 2020.

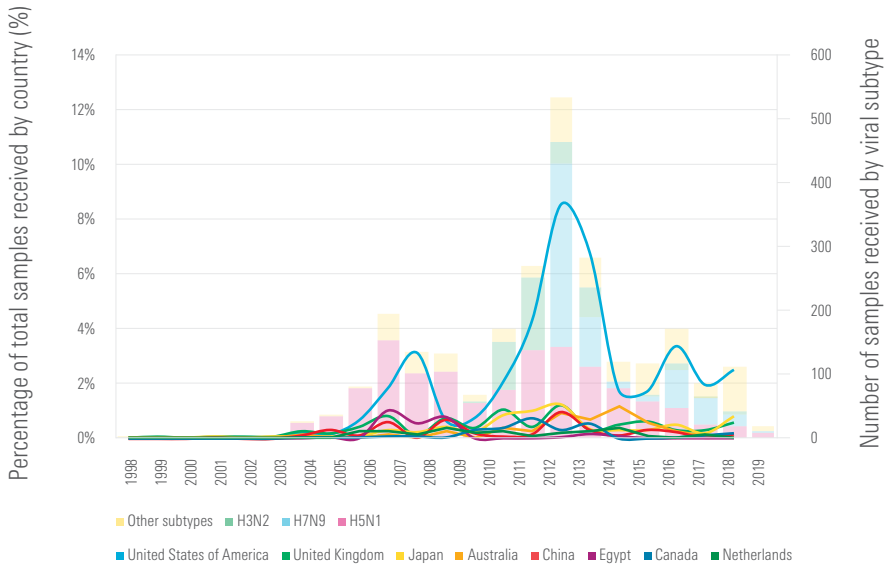
include shipment numbers, data on sending and receiving laboratories (their location and designation[6]), the date of shipment (if available) and influenza subtypes. While this data source only covers IVPPs and therefore cannot be taken as representative of the sharing of pathogens more broadly, it does 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. Throughout the recorded period, a relatively small group of countries has been actively engaged in IVPP-sharing, with the United States and the United Kingdom acting as central hubs (**Annex 2**). 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%). **Figure 2** shows trends in IVPP-sharing by time for the 8 top sample-sharing countries, with IVPP-sharing peaking in 2007 (of which 79% were H5N1), 2013 (of which 59% were H7N9) and 2017 (of which 36% were H7N9 and 26% were H5N8).[7]

Figure 2: Top 8 IVPP-sending (top) and IVPP-receiving (bottom) countries by time and frequency of IVPP subtypes shared



6 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.

7 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).



The global flow of IVPP samples is illustrated from sending countries (far left) to receiving countries (far right) in **Figure 3**, with the columns characterizing the institutions by affiliation[8] and GISRS-related designations. With the exception of Egypt and China, bilateral sharing between high-income countries (HICs) has accounted for a disproportionate share of IVPP-sharing density. Overall, IVPP-sending institutions have almost exclusively been government-affiliated (99%), part of the GISRS network (99%) and include WHO Collaborating Centres (WHO CCs) (64%), Essential Regulatory Laboratories (ERLs) (18%), National Influenza Centres (NICs) (10%) and WHO H5 Laboratories (7%).[9] IVPP-receiving institutions have been more variable, including both GISRS (39%) and non-GISRS (61%) affiliated institutions. While sharing between GISRS-affiliated institutions has almost exclusively been inter-governmental, receiving non-GISRS institutions include, by order of density, small- and medium-sized enterprises (SMEs) (21%), academic institutions (20%) and multinational pharmaceutical companies (9%).[10]

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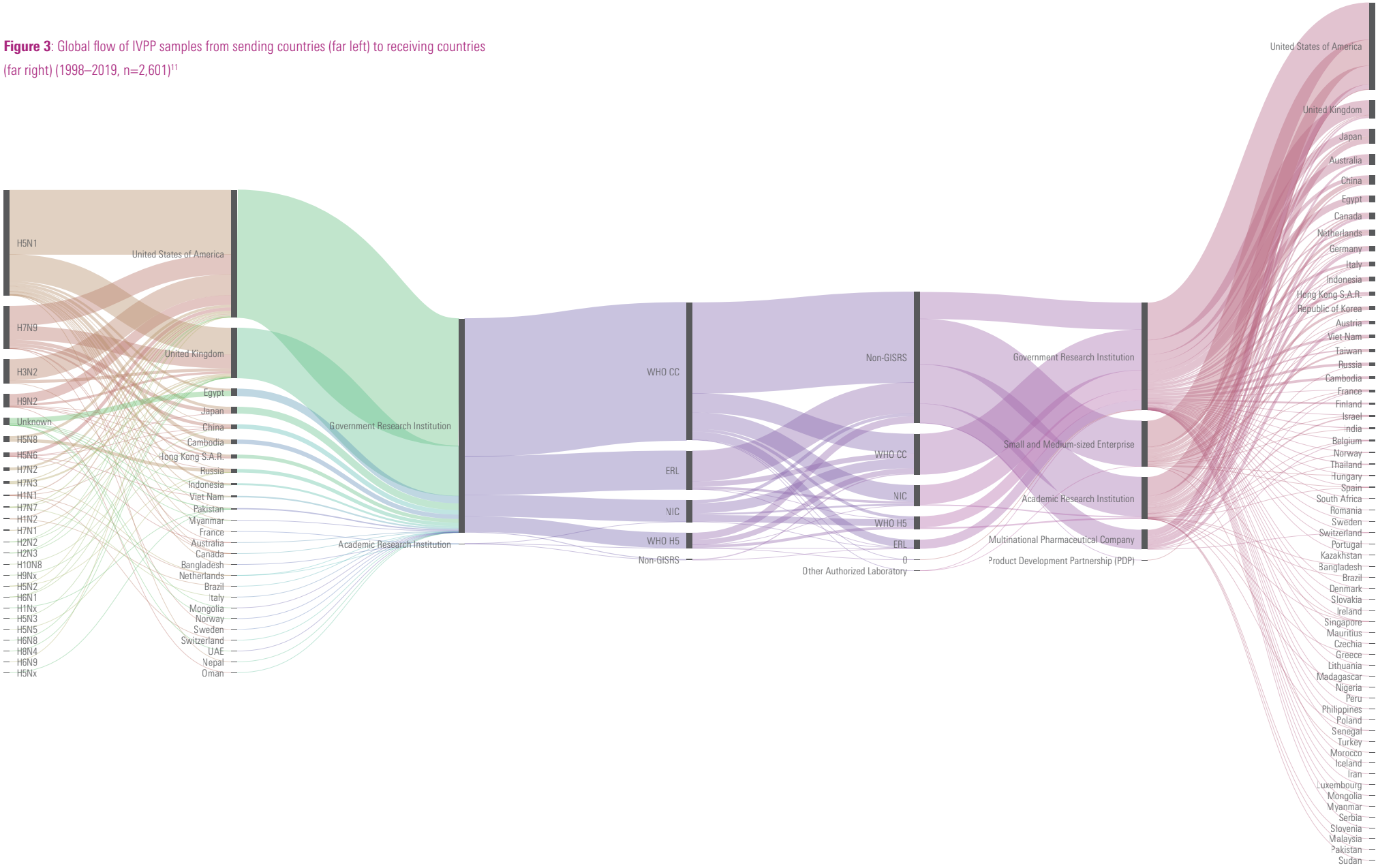
8 Affiliations were manually designated by the research team as either: Government institutions, academic institutions, SMEs, or multinational pharmaceutical companies. Websites of sending and receiving institutions were consulted in designating affiliations. Government-funded academic research centers (such as those in public universities) were considered academic institutions.

9 Laboratories characterized by IVTM can have multiple designations (e.g. US CDC is a WHO CC, WHO H5 and a NIC), however the IVTM exportable database treats WHO CC as a principle designation. The distribution of WHO H5s, NICs and ERLs are therefore under-represented in the current preliminary analysis and will be rectified in the final version.

10 An ad-hoc examination of sharing patterns during the three peak periods (2005–2009, 2010–2015 and 2015–2019) identified the following trends: While UK institutions shared the most IVPP samples in 2005–2009, US institutions had shared more than triple the amount of IVPP samples than their UK counterparts by 2016–2019. The largest number of countries receiving IVPP samples occurred in 2010–2015 and dwindled to less than half that peak amount by 2016–2019. While SMEs were the main beneficiaries of the GISRS network in the first two time periods, there is indication of decreased sharing with SMEs and increased sharing with academic institutions by 2016–2019. In terms of bilateral sharing relationships, IVPP-sharing from the US and the UK has largely been between HICs, with the exception of high sharing density between the UK and China, and sharing from the US being more densely internal than external.

Figure 3: Global flow of IVPP samples from sending countries (far left) to receiving countries (far right) (1998–2019, n=2,601)[11]



PBS Practices: Drivers in and outside of outbreaks

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. Drivers for pathogen sharing, as shared by respondents, are multi-faceted, from instrumental to political, economic, and legal (**Table 3**).

Table 3: Drivers of pathogen sharing

Instrumental	**To respond effectively to outbreaks**: "We share because pathogens have no borders, if you want to functionally respond and save lives everywhere, then you need to be able to share information to do that (#7)." **To receive benefits from participation in pathogen sharing networks**: such as access to reagents when participating in GISRS
Scientific Obligation	**Open sharing conventions among scientists**: "a lot of journals, when you publish something there, have a little contract you sign that says you have to share any materials, resources, strings, with the scientific community (#9)."
Political	**Political standing**: "you're showing the world community that you're a leader, you are shown to be a leader in global public health (#34)."
Security	**National security**: "there are national security interests of a number of developed countries that are at play in this and if they really want these pathogens, they'll steal them (#32)." **Biosecurity**: "We had to make a decision about keeping samples in-country with the biosecurity risk involved; those tensions go into making a decision (#53)."
Economic	**Commercial**: "There is money in some of them…[there] is only one of two companies that have contracts to do Ebola drugs for the US biodefense stockpile, so there is money there (#32)."
Legal	When PBS are on equal footing in participation in international legal agreements such as the PIP Framework or the enforcement of the Nagoya Protocol (#32).

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, seem to share the following characteristics that affect pathogen sharing practices:

Outbreak contexts 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, as explained by a respondent involved in global health policy:

> *"Developing countries are in general the weaker link of the chain when it comes to bilateral negotiations. So, if you're having an outbreak and you need a medicine or some kind of therapeutic, the device, and your population is rioting in the streets against you, you just say 'take it away, please, help me', and you go to France and to the US and to China and say 'please, I need something', and then people say, 'Okay, I'll help you, but you will not have access, you will not have royalties, you will not have that, etc.'. You say okay (#25)."*

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 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 (#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 a respondent from an international organization explained:

> *"A lot happens when you're trying to share pathogens in an outbreak, and you do not have that trusted system, nor the governance to underpin how to do it. I think that came to the fore with Ebola…We know people wanted to get that data out there… [and] some people withheld the data for publication purposes and other purposes. And I think that leads to mistrust (#26)."*

As PBS practices seem to be qualitatively different between ordinary and outbreak contexts, different approaches to their governance may need to be considered. Clear arrangements for governing PBS are needed before, rather than during, crises.

3.2 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 publicly available and privately shared MTAs.

What does benefit sharing mean in everyday practice?

Overall, there appears to be growing recognition among interviews, 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 large variation in views and practices among different groups and across global divides. **Table 4** demonstrates the wide breadth of respondents' attitudes and practices around benefit sharing, organized around four non-mutually exclusive understandings of benefits: 1) benefit as the "global good" that pathogen sharing generates for global public health, 2) benefits as access to countermeasures, and increasing local preparedness and response capacities, 3) benefits as scientific and intellectual recognition in academic spheres, 4) benefits as the realization of economic benefits for pathogen-sending countries.

Table 4: Breadth of benefit sharing in practice

	Non-material benefits	Material benefits	Perspectives
Global Good	**Direct benefits** - "The advancement of public health everywhere (#39)" -The benefit of public use of associated data - Information as the primary benefit	No direct or indirect benefits recognized	- "Global benefit is a benefit to the country as well (#20)" - "The perception that information [needed to protect the population] itself is a benefit is missing, a lot of people only see benefits as something tangible, something in the bank account (#30)"
Preparedness & Response	**Direct benefits** - That knowledge, results and data flow back - Capacity building and training in sending or receiving countries **Indirect benefits** - Capacity to inform local policy and the public	**Direct benefits** - Access to countermeasures (vaccines, drugs, diagnostics, reagents, etc.) - Technology transfer - Building laboratory and health infrastructures - Provision of research grants **Indirect benefits** - Laboratory and healthcare system strengthening	- "For us, the benefit in the end is knowing that the samples that are collected are actually improving healthcare (#37)" - "We should be certain that if I share the pathogen, whatever they're developing, would be marketed here and at an affordable price (#47)" - "As we collect samples, we make an explicit investment in laboratory capacities to be able to ensure that this work can be carried out locally (#19)" - "I'm a strong advocate that everything must be done on the ground…we should stop shipping samples (#38)"
Academic	**Direct benefits** - Intellectual recognition, "being treated fairly (#26)", scientific credit, co-authorship in publications, and acknowledgement of the source of samples **Indirect benefits** - Stronger standing in the scientific field - Ability to inform policy and the public	**Direct benefits** None recognized **Indirect benefits** - Better capacity to attract funding - Promotions, salary increases	- "We benefit from the samples we collect by publishing papers, which then we raise money off the back of to fund our [non-profit] work (#16)" - "The direct benefits are intellectual and scientific recognition; we don't trade or sell biological agents. But we have to be honest there's a benefit that we accrue over time from that work, we use that expertise to apply for grants and funding from agencies (#15)"
Economic	**Direct benefits** - Intellectual property rights - Rights to royalties - Licensing and ownership of future inventions **Indirect benefits** - None recognized	**Direct benefits** - Monetary gain **Indirect benefits** - None recognized	- "If you share pathogens then you are entitled to financial benefit (#14)" - "Most of the benefits are indirect…[but] when we work out agreements with partners, we try and cover all intellectual property that could come out of those samples and we cast a wide net (#16)" - "In our agreements, the obligation to pay financial benefits is triggered when the first invoice is issued for a product put to market (#25)"

Though these are non-mutually exclusive understandings of benefits, each has certain implications for developing a governance system for PBS. Understanding benefits as a "global good" suggests that a benefit sharing system should arrange for benefits to be shared with any pathogen-sending country (as in the PIP Framework). Understanding benefits as being part and parcel of preparedness and response, moreover, is an equity argument for PBS—if pathogen sharing countries receive capacity-building as a primary benefit, then benefit sharing becomes a vehicle through which local capacities increase, future dependency on external parties decreases, and disparities may be reduced:

> *"Getting agreement of what it [benefit sharing] is or what it should be unleashes a whole can of worms because it's also about the inequity in the current system. I think you can't always right all the wrongs. It's not a reason not to attempt to right something, some of the wrongs, but realistically that's not always possible, so where you draw the line is really, really, complex (#26)"*

Understanding benefits as primarily "academic" or "economic/financial" was contentious, however. Some respondents argued that academic benefits are becoming disproportionately represented (#32) in benefit sharing discussions, at the expense of economic benefits. For example, one respondent suspected that offering academic acknowledgement on publications was "being somewhat cynically pushed forward by people that want to avoid having a real discussion" about monetary compensation (#32) and that the focus on non-monetary compensation was disadvantageous to sending countries. 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). This last point was particularly contentious, especially as financial benefits for developing countries are encouraged in general terms under the CBD but were considered inappropriate in the context of pathogen sharing by some respondents.

Some respondents favored distinguishing the benefit sharing arrangements of non-commercial (e.g. government, academic) from commercial actors. But others argued that the distinction between "academic" and "commercial" research may not be so clear:

> *"The problem is that…it's incredibly difficult…[to differentiate] between what is truly non-commercial research, particularly if you don't control sequence data, and what is commercial research…at the end of the day…there are enough non-commercial researchers whose research eventually becomes intellectual property, or is utilized commercially, that that distinction is only of marginal use (#32)."*

Another point of contention revolved around what is the value of pathogens, and how value should be ascertained. It is difficult to "value" pathogens and identify what is a reasonable, fair associated benefit when their future value is uncertain at the time of sharing: "there is something in the fact that some of what you're sharing, you just don't know what the ultimate benefit will be and how you build that into an agreement is really tricky (#26)." Respondents indicated that, in practice, parties often agree on general principles in contracts (see next section for PBS-related terms in contracts and MTAs) and return to the negotiating table once valuation becomes a necessary consideration (#29). Furthermore, 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 vaccine candidates for the influenza vaccine. Others argued that it is difficult to assign relative value to a pathogen sample in relation to a product, as many other investments were also necessary to develop that product.

When it comes to how valuation is done, little international guidance is available. In the distribution of academic benefits (e.g. credit, authorship, acknowledgement, impact rating for academic publications), the International Committee of Medical Journal Editors (ICMJE) guidelines provide normative clarity [25]. However, 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. Many international collaborative networks have already developed internal policies to this end, though concrete benefits appear to be negotiated case-by-case. The explicit monetization of pathogens, however, seems to be discouraged by some, 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 samples:

> *"When you come to the value piece of this and discussing what the value of particular pathogens are, I think that's when it gets really sticky and people shy away from it and don't want to have this conversation because it is extremely difficult to put a value on that… we can all agree but when you start hammering out the details that's when it gets very complicated…and communication starts to break down in this space (#33)."*

What does benefit sharing mean in legal practice?

Contracts are regularly used to set out the terms and conditions for PBS. These contracts mostly take the form of MTAs – legal contracts that govern the transfer of research materials and associ-

ated data between parties. 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) of the PIP Framework [26].[12] However, some respondents noted 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, time, technological capacity, or other power disparities. To gain some insight on how benefit sharing is codified in everyday scientific agreements, we collected 26 MTAs (four of which were executed and 22 of which are model agreements)[13] to study their benefit sharing provisions (see **Table 5** for MTA characteristics). 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 were agreed with parties based in LMICs.

Table 5: MTA characteristics

	Party A	Party B[14]
Executed MTAs	Government agency (3)	Government agency (1); International entity[15] (2); Academic institution (1)
	Academic institution (1)	Academic institution (1)
Sample MTAs	Government agency (12)	Unspecified (10); Commercial entity (1); Government Agency (1)
	Intergovernmental organization (2)	Unspecified (1); Commercial entity (1)
	Academic institution (4)	Unspecified (3); Commercial entity (1)
	Multi-government funded research organization (2)	Unspecified (2)
	Unspecified (2)	Unspecified (2)

12 For example, WHO has developed an MTA tool with options and explanations on potential provisions in MTAs [27].

13 For signed and executed agreements, we developed a Document Usage Agreement between the research team and the authorized sharing party that sets the terms and conditions for its use and its level of anonymity. Even then, high levels of confidentiality around signed agreements impeded access, and respondents were more willing to share model agreements. Model (or "sample") agreements are useful templates, though they have considerable limitations as they only set out the starting points of negotiations and may be missing key provisions in the final legal contract signed by sharing parties.

14 There are more Party B entities than Party A entities because some MTAs are tripartite MTAs.

15 Includes international scientific networks and partnerships acting as a single entity.

A summary of the benefits provided in the collected MTAs is presented in **Annex 3**. The majority of MTAs 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 MTAs contained at least one benefit; however, there were significant variations in benefit provisions among the MTAs examined:

1. **Acknowledgement in Publications**: A majority (17/26) required acknowledgement of providers of the samples, with 4 explicitly including co-authorship as a possibility. This is in keeping with the interviews, where acknowledgement in publications was perceived by many as standard conduct.
2. **Cost Recovery**: Under half (11/26) included provisions on the costs of transfer, with 10 stating coverage or possible coverage of costs of transfer for sample providers by the recipient party. One stated that the recipient will not be charged for the costs of transfer.
3. **Capacity Building and Training**: Only two MTAs included specific provisions related to capacity building or training. We heard anecdotal evidence of capacity building and training as benefits associated with pathogen sharing; it is possible these are negotiated under separate contracts and not necessarily included in MTAs.
4. **Access to Research Outcomes**: Over half of MTAs (15/26) included a provision for providers of samples to have access to the research outcomes, whether informational outcomes or material benefits. Of these, 11 were primarily concerned with the sharing of a scientific report on research outcomes (informational outcomes) and 4 MTAs incorporated more complex arrangements, 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 addition, we also collected 14 executed SMTA2s between WHO and commercial entities from the PIP Framework. These SMTA2s were identical except for the choice of benefits companies selected from a list of preset options. In the 14 SMTA2s 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. For a full list of benefit sharing options itemized in SMTA2s, please see **Annex 4**.

4 | GOVERNING PATHOGEN- AND BENEFIT- SHARING: WHAT ARE THE ISSUES?

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.

4.1 What is working?

Respondents, especially scientists and researchers, described a system that works in many ways. Researchers reported being able to get desired pathogens under certain conditions and in normal (non-emergency) situations, with one respondent stating that "people tend to get what they want (#12)." 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 locales 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:

> *"I think long-term relationships and collaboration is how science works and legal agreements are like, you know, the dressing on the cake. But without the scientists willing to work with each other, none of this would happen (#18)."*

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 collabo-

rating 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, as one scientist involved in long-term collaborations noted:

> *"Samples were indeed transferred without consent and with the explicit non-allowance … from here to another country ... I was a bit shocked that this can happen under trustful collaboration of partners. I would say nothing really bad happened out of this, but it changed a bit our practices (#21)."*

> *"Countries were really reluctant to share their own data ... because a lot of data were taken [in the past] by other third parties and used by third parties ... mainly without permission, which created a lot of mistrust between countries (#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.

The availability of new technologies such as genomic sequencing capabilities have introduced new opportunities and challenges (see **Box 1**).

Box 1: PBS and Genomic Sequence Data (GSD)—A Closer Look

In recent years, technological advances have raised the possibility that access to data about pathogens –namely, nucleic acid, genomic, and proteomic data, which we refer to here collectively as genomic sequence data (GSD for brevity) – may diminish the need for access to physical samples for certain types of pathogens (particularly for viruses) and for certain research purposes (such as phylogenetic analysis). As a result, while the availability of genetic sequencing does not eliminate the need to access physical samples, sharing of physical samples has become less important for certain, specific types of research. This technological development has raised concerns among some that leverage to negotiate benefits could be weakened (#14,24). The increased relevance of GSD has also raised the risk of upsetting the delicate balance between the interests of sample source and recipient countries that was struck in the PIP Framework.

Respondents have noted that in countries where capacity to generate GSD exists, this may facilitate conducting research in-country and reduce the need to export samples for analysis, confirmatory testing, and/or product development. Nevertheless, many experts interviewed noted that access to physical samples is still needed for many types of research, and that the need for access to physical samples will likely remain the case for the foreseeable future, due to: limitations on the accuracy and utility of sequencing data, different technological capacities and possibilities, and different regulatory requirements by country, product, and purpose. As such, the need for access to physical pathogen samples varies depending on the purpose and the pathogen.

Data sharing arrangements for GSD are governed differently than physical samples. GSD may be shared via bilateral sharing agreements, including MTAs, though there are also numerous public databases that serve as data-sharing platforms. Such databases allow the rapid sharing of critical information about pathogens, particularly during outbreaks and can be broadly grouped as open access databases (e.g., GenBank and the European Nucleotide Archive) or controlled open access databases (e.g., the Global Initiative on Sharing Avian Influenza Data, GISAID):

Open access databases provide a platform for contributors to upload sequence data that the general public may use or distribute without restrictions [28], [29]. Controlled open access databases are also publicly available but require registration for access and can impose restrictions on use and distribution. For example, GISAID, which compiles GSD on influenza viruses (as well as on SARS-CoV-2), is a controlled open access database. Access to GISAID is limited to registered individuals; among other terms, contributors retain ownership of their data but grant access to it for a wide range of uses; users agree to not distribute to third parties, to acknowledge sources of data, and to make best efforts to collaborate with originating laboratories [30]. It is unclear what kinds of benefits data contributors may have sought or obtained, beyond those explicitly provided for in the terms of use (e.g. acknowledgment in publications), and this is an area where further research is needed.

To the extent that benefit sharing concerns may impede the rapid sharing of data, a GISAID-type model has been considered by many respondents to facilitate sharing. Notably, Chinese researchers shared GSD on SARS-CoV-2 in early January 2020 on the GISAID platform, whereas it remains unclear whether or when physical samples were exported and to whom; in subsequent months, researchers in 96 countries have shared SARS-CoV-2 GSD on GISAID, in comparison to researchers in 50 countries on GenBank. As of June 18, 2020, the total number of SARS-CoV-2 sequences shared on GISAID was 48,031, the majority from the UK (21,432), the US (9,308), Australia (1,959), the Netherlands (1,603), and Spain (1,506).

However, once GSD is published – even within a controlled open access database – it is more difficult to trace who uses it and how. Questions have been raised about the feasibility of negotiating benefits based on data user agreements. Whether GSD derived from pathogens – in addition to the physical sample itself – qualifies as a genetic resource under Nagoya is a hotly-debated question.

Though the issues are complex, it is clear that GSD (and likely, future technological developments to come) raises critical questions for PBS that must be addressed and clarified in the elaboration of any national and international governance framework.

4.2 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; complications due to biosecurity and biosafety concerns; complications due to commercial interests; limited awareness of changing rules and their usability for researchers; and a lack of clear or responsive arrangements or regulations.

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. Researchers in countries that lack internal capacity for certain research activities have prioritized laboratory capacity building and access to final products (e.g., vaccines, therapeutics, diagnostics) that cannot be developed in-country. In contrast, researchers in high-income settings have prioritized acknowledgement or co-authorship, or have seen the knowledge generated by pathogen sharing as a benefit. In addition, respondents noted that lower income countries may lack the resources, experience, legal expertise or negotiating leverage to secure benefits for their country. This disparity can create barriers for fair PBS. It can also lead researchers and commercial actors to seek pathogens elsewhere (#30), an option that is sometimes not possible for specific outbreaks or scientific purposes.

Importantly, while substantial disparities in research capacities persist, many respondents from both HICs and LMICs 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). An emerging demand from many pathogen-sending countries is tying capacity building, infrastructure development and training with pathogen sharing, under a larger strategy of building up national capacity for in-country diagnostics and research in order to reduce the international traffic of pathogen samples in the future, as explained by a scientist from a developing country:

"Even if you are giving samples, then there should be a framework that says you are receiving the samples now, but you need to make that capacity available in the next one year … Fine, you don't have the capability to do this work here now, fine, we'll send you the sample, but sign an agreement that you get the sample, but the next year, you're going to make that capability available on the ground." (#38)

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. Intersecting with disparities in capacities, respondents from many countries reported not having the laboratory capacity needed to achieve biosafety and biosecurity standards for certain pathogens. There are very few labs in the world that are ranked BSL4 – laboratories capable of storing and conducting research on the pathogens that pose a high risk of severe or fatal disease in humans, are capable of aerosolized spread in a laboratory setting and for which there are no available vaccines or treatments [31]. As such, countries with limited laboratory capacity that experience outbreaks of pathogens requiring high-level containment, such as Liberia's experience with Ebola (see case study below), 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. Some noted that academic benefits may be offered in lieu of economic and material benefits, to the detriment of sending countries (#32), and others indicated different contractual practices when commercial use of pathogens or their sequences is proposed, where "as soon as there is any commercial use, then there's a different MTA attached to those sequences, which is fine from a researcher's perspective" (#45). Several respondents noted significant challenges in assigning value to pathogens, with one asking: "how much are you going to ask as a payment when you don't know actually the value of something?" (#24). The commercial viability of products dependent on pathogen samples (i.e., vaccines or diagnostics) is often variable and unpredictable, subject to various factors, including the existence of an ongoing outbreak and its severity. This leads to uncertainty and disagreement about valuation of

pathogens, complicating PBS negotiations. Such negotiations are further complicated by the presence of mutual distrust and questioning of the motives of commercial partners involved. For example, one industry representative noted that they would wait for a request from the government for collaboration rather than seeking it out, to increase the likelihood of a cooperative deal being reached by avoiding perceptions of profit-seeking (#51). Similarly, another respondent noted that even the term "benefit sharing" could carry a negative connotation among commercial actors, and that to avoid raising hackles, alternative terms would be used in commercial contexts (#26). In addition, for some respondents, the purpose of sharing pathogens with a commercial partner is to secure access to medical countermeasures rather than for profit.

In addition to the foregoing challenges, there are a few complications that arise when commercial interests are involved that are particularly relevant during outbreaks. 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 legislation around PBS, often contingent on the availability of legal offices and a sensitization of researchers to changing rules. An example of a changing rule includes national laws in India and Brazil that include joint venture provisions that require nationals to be counterparts, and therefore responsible and accountable for the application of their respective laws. Respondents noted that "for Indian resources, it's only Indian researchers who can access them or be associated in their research" (#48) and where joint venture laws exist, the purpose is "to have someone in Brazil to go after if we had any kind of problem in terms of national legislation" (#25). 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. Significant steps are being taken to sensitize

researchers to emerging legislation, with some institutions "deploy[ing] all the tools in order to help the researchers who are not used to work with the legal offices of their universities or institute comply to 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. Many respondents expressed concerns that Nagoya would introduce too much red tape into the sharing process and lead to an increased need to convince government officials of the importance of pathogen sharing, incurring delays and/or reductions in sharing. As one researcher noted: "once you get outside the immediate public health authority that understands virus sharing, you need more and more clarity on why these viruses need to be shared, you need to explain it in layman's terms … that it's for a global benefit and it benefits back to the country as well" (#20). 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 having a particular risk during outbreaks, where timely and widespread sharing is of critical importance.

Others expressed a desire for greater regulation of PBS. A few respondents expressed concern that Nagoya was being inadequately implemented or weakened during implementation, limiting its ability to produce more equitable benefit sharing. One noted that "It's a matter of the domestic implementation of the Nagoya protocol's objective of … meaningful benefit sharing for genetic resources (#27)"; another argued that it was within countries that legislation needed to be changed "to make sure that the international guidelines are working well (#5)." 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. For example, one respondent explained that "a flaw of Nagoya" is that "it's not prescriptive. It allows for too much space for countries to implement it and then it just becomes a mosaic … and I understand that from a company point of view, this is a nightmare (#25)."

Generally, revisiting normative frameworks around PBS was largely considered to be a priority issue, especially in terms of the governance of benefit sharing: as one respondent put it, "we have a framework in sample sharing but don't have a framework that's working well for benefit sharing" except on a "case by case" basis (#5). One respondent explained that "there's a great deal of impor-

tance in having an international norm and having something in writing" because that can provide countries with enough certainty and confidence to share (#7). After all, if you are sharing because you want to secure certain benefits for your population, then "you have to believe that the system works well enough for your population not to be forgotten about (#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: "everybody knows this needs to be done, but nobody really wants to do it (#7)."

5 | CASE STUDIES: PATHOGEN- AND BENEFIT- SHARING IN OUTBREAK RESPONSE

Though not exhaustive, these five categories were the core issues that surfaced through our interviews. 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 (see **Table 6**), 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 6: Development and health indicators for Brazil and Liberia (2018) [32]

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)[16]	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

16 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, the topic itself was sensitive for Brazilian scientists, made more-so by the political climate in Brazil.

5.1 Case Study 1: PBS during Liberia's EVD epidemic (2014–2016)

Context

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 [33], [34]. 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 [35]. In total, the epidemic caused an estimated 28,600 cases and 11,325 deaths [36], [37]. While the response to the West African epidemic attracted criticism for being late and expensive [17], 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 [38].

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	**Governing framework**	**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 governance in the wake of Liberia's EVD epidemic

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 [39]:

> *"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

Interviews demonstrated 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 vaccine was partly developed in Liberia, legal provisions for access to it were not included in existing PBS or other arrangements (#64) and it has yet 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 NRL. 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 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 [40] and amendments to address biosafety and biosecurity in Liberia's Title 33 Public Health Law are before the national legislature. Till present, there are no policies or regulations specific to PBS, and legal resources are 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.

5.2 Case Study 2: PBS during Brazil's Zika epidemic (2015–2016)

Context

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 [41]. 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 [41]. 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.

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 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.	On November 17th, 2015, the Biodiversity Law came into force, establishing the rules for access to genetic resources and benefit 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.	"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 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, I would say, 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)."

PBS Governance in the wake of Brazil's Zika epidemic

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 is a party to the CBD, but not the Nagoya Protocol as of November 2020; 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 [42]. 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.

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 registra-

tion 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).

5.3 PBS in outbreak response

Despite stark differences between Liberia's EVD and Brazil's Zika outbreaks – including different national capacities for outbreak response 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 precipitat-

ing 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 limit 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 health response to the Zika epidemic [43].

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 the next epidemic, 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 legislations 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.

6 | GOVERNING PATHOGEN- AND BENEFIT- SHARING: WHAT ARE THE OPTIONS?

"Everyone knows it's a problem and it's such a damn big problem that it's really hard to start turning those conversations into some sort of tangible outputs (#26)."

One of the tasks set out in this research project was to identify workable solutions for the key issues identified in PBS and formulate tangible options that respondents identified as needed for their resolution. 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. In this section of the report, we first identify key debates in the interaction of existing rules for PBS, and in so doing explore the PIP+/PIP-like policy option for governing PBS. Secondly, we identify and 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. An in-depth analysis of the strengths and weaknesses of these proposals is beyond the scope of this paper; we present here this spectrum of options to stimulate further analysis and debate.

6.1 Interaction of existing rules and the PIP+/PIP-like option[17]

Current PBS practices should be understood in the context of existing rules and frameworks. We discuss each one in turn here, starting with the IHR (2005), then PIP Framework (2011), and then the CBD (1992) and its Nagoya Protocol (2011).

17 In this section, we use PBS when discussing access and benefit-sharing as it relates specifically to pathogens and ABS when referring, more broadly, to the CBD and Nagoya Protocol approach to all genetic resources.

There has been some discussion in the academic literature about using the IHR (2005) as a legal basis for pathogen sharing. 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 (see **Box 2**) 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).[18] 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.

Box 2: Articles and provisions in international legal regimes with implications for PBS

THE INTERNATIONAL HEALTH REGULATIONS (IHR) (2005) [10]

Article 6.2: Notification: Following a notification, a State Party shall continue to communicate to WHO timely, accurate and sufficiently detailed public health information available to it on the notified event, where possible including case definitions, laboratory results, source and type of the risk, number of cases and deaths, conditions affecting the spread of the disease and the health measures employed; and report, when necessary, the difficulties faced and support needed in responding to the potential public health emergency of international concern.

THE NAGOYA PROTOCOL (2011) [12]

Preamble: Mindful of the International Health Regulations (2005) of the World Health Organization and the importance of ensuring access to human pathogens for public health preparedness and response purposes.

Article 3: *Scope*. This Protocol shall apply to genetic resources within the scope of Ar-

18 Specific knowledge cited in this section that is not attributed to an interviewee (using #) comes from the experience of the investigators and co-authors of this report.

ticle 15 of the Convention and to the benefits arising from the utilization of such resources. This Protocol shall also apply to traditional knowledge associated with genetic resources within the scope of the Convention and to the benefits arising from the utilization of such knowledge.

Article 4.4: *Relationship with International Agreements and Instruments*. This Protocol is the instrument for the implementation of the access and benefit-sharing provisions of the Convention. Where a specialized international access and benefit-sharing instrument applies that is consistent with, and does not run counter to the objectives of the Convention and this Protocol, this Protocol does not apply for the Party or Parties to the specialized instrument in respect of the specific genetic resource covered by and for the purpose of the specialized instrument.

Article 8(b): *Special Considerations*. In the development and implementation of its access and benefit-sharing legislation or regulatory requirements, each Party shall: (a) […]; (b) Pay due regard to cases of present or imminent emergencies that threaten or damage human, animal or plant health, as determined nationally or internationally. Parties may take into consideration the need for expeditious access to genetic resources and expeditious fair and equitable sharing of benefits arising out of the use of such genetic resources, including access to affordable treatments by those in need, especially in developing countries; […].

Article 19: *Model Contractual Clauses*. 1. Each Party shall encourage, as appropriate, the development, update and use of sectoral and cross-sectoral model contractual clauses for mutually agreed terms. 2. The Conference of the Parties serving as the meeting of the Parties to this Protocol shall periodically take stock of the use of sectoral and cross-sectoral model contractual clauses.

Article 20: *Codes Of Conduct, Guidelines And Best Practices And/Or Standards*. 1. Each Party shall encourage, as appropriate, the development, update and use of voluntary codes of conduct, guidelines, and best practices and/or standards in relation to access and benefit-sharing. 2. The Conference of the Parties serving as the meeting of the Parties to this Protocol shall periodically take stock of the use of voluntary codes of conduct, guidelines and best practices and/or standards and consider the adoption of specific codes of conduct, guidelines and best practices and/or standards.

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). **Table 7** presents selected respondents' perspectives on building PIP+ or PIP-like policy options to address PBS more broadly.

Table 7: Perspectives on PIP+ or PIP-like policy options

Problem of political readiness	"I think most people in the field think we need some type of PIP-like framework… everybody knows this needs to be done, but nobody really wants to do it (#7)." "A PIP framework type of instrument is a possibility, but I think we are not there yet…In the PIP, I think it was in a way more ready-made in the sense that there was a network of laboratories that are meeting regularly, they were sharing, they meet twice a year to make recommendations, and the PIP framework was really to put in place some terms and conditions because this system of sharing was really important for them to develop the [influenza] vaccine. I think for the other pathogens, I think we need to unpack currently what is happening and take into account that a lot of this sharing is happening with national laboratories, from one national laboratory to another national laboratory (#14)." "Is [PIP] an approach that can be used beyond pandemic influenza viruses? Not at a functional level but more on a political level, there is no appetite for this. No one wants to spend political capital on either expanding PIP (I've heard people say non-starter, not going to happen, forget about that), or extracting from PIP and creating a different framework for non-influenza pathogens. Same sort of thing, nobody's interested. There isn't a center of gravity there that someone's going to pick up on and run with...And so if you don't have political, you know, appetite or a willingness to expend political capital on using PIP to create something else, it's going to be Nagoya or sovereignty by default (#11)."
PIP-like + GISAID-like	"The PIP framework and the GISAID system…is a very good way forward [that] would work for many pathogens... I do think that many of the concerns of countries of commercial use of pathogens can be covered with a database like GISAID (#45)." "A framework that would have the same specification as GISAID… it depends if some countries move forward, like was the case with GISAID, and others join, or if it's a centrally negotiated agreement to put in place a repository that could be public access instead of being public domain for the other pathogens (#39)." "In GISAID, there's an explicit restriction for commercial use. So, as long as you use these sequences for research, and public health responses, such as under the PIP framework, then you can do whatever you want to do. But as soon as there is any commercial use, then there's a different MTA attached to those sequences. Which is fine from a researcher's perspective (#45)."

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. The rules of the game are relatively clear for influenza, where the predictability around access to medical countermeasures and funds gathered from partnership contributions is built into the system. That said, some of the key principles agreed in the PIP Framework – especially putting PBS 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. Using PIP as a model for a more general PBS instrument would nevertheless not be straightforward, but rather require clarity on its legal nature and scope, the conditions for sharing and the benefits attached to it, the role of WHO and inevitably its relations with the Nagoya Protocol (#4). Given 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, there does not seem to be much interest to invest political capital for a serious discussion on a "new PIP" even though there is a general agreement about the need for clarity, predictability and equity on the international legal terms for PBS.

The CBD, adopted in 1992, and its Nagoya Protocol negotiated in parallel to the PIP Framework, adopted in 2011 and in force for 124 parties as of the end of March 2020, dominated the interviews as the legal instrument that is 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 in the mind of the CBD's drafters. Selected interviewee perspectives are summarized in **Table 8**. 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). They argued that, given the flexibilities of the Nagoya Protocol (see next section), there is no inherent conflict with public health needs; the Nagoya Protocol provides clarity as a general regime and more time should be given to its implementation (#32). Both sides agreed, however, that national implementation is uneven and fragmented, with lack of clarity and different approaches that create confusion and unpredictability and can deter scientific cooperation. Some highly biodiverse countries such as Brazil are not parties but have enacted Nagoya-style legislation that is not published in the CBD ABS legislative clearing house and not yet well understood internationally (#2).

Table 8: Perspectives on Nagoya Protocol-related policy options

Pathogen "carve out" from the Nagoya Protocol	"I don't think that the Nagoya Protocol is adapted to public health and for the kind of work that we do ... I think there should be a completely different approach (#38)." "I think that viruses should not be part of Nagoya, and I think sharing viruses, from humans, for public health research, public health responses should be done without taking into account the privacy laws that exist for human samples ... Now we can do this one on one between scientists very easily. I think that this whole thing gets over-regulated and Nagoya gets used for things where it shouldn't be used for (#45)." "So, I think that almost when you talk about carve out or exemption or anything like that, that's something that for CBD people, is language that is alarming. It's not about carve out or exemption, it's about an alternative implementation that is consistent with and not contrary to, [the Nagoya Protocol] (#35)."
Specialized international ABS instruments (SII)	"The principles of Nagoya would still have to be applicable to whatever you are developing, so it's not about moving away from Nagoya as such, it's that ... we are creating an instrument that is more specialized, with regard to the scope of the instrument, and that would facilitate ... pathogen sharing, out of this whole bilateral basis mode of sharing. So, it's not about moving away from Nagoya ... whatever we develop has to be consistent and supportive of objectives of the Nagoya Protocol (#14)." "And there could be a future wherein you have one or more specialized instruments that relate to other potentially pandemic pathogens and I think that would be a good thing, but…the agreements themselves need to exist and they need to be clearly consistent with and not contrary to the Nagoya Protocol in order to proceed in that direction (#32)."

6.2 Formality and scope of international rules – the spectrum of options

Many interviewees highlighted as problematic the absence of clear international rules to govern PBS. At the same time, several respondents recalled the 4 years required to reach agreement on a set of rules for 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 not only a PIP-type instrument, but also a broader set of normative instruments, ranging from less to more formal, from few countries to all, and from select pathogens to all. **Table 9** presents selected perspectives on the below spectrum of options.

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. A concrete example in a related field is the "9 Points to Consider when Licensing University Technology" a 2007 statement initially negotiated between 12 academic institutions and issued by the Association of University Technology Managers (AUTM), which has been endorsed by over one hundred research institutes to improve access to health technologies developed from university inventions [44]. The Declaration of Helsinki on ethical principles for medical research involving human subjects [45] and the Council for International Organizations of Medical Sciences' (CIOMS) "International Ethical Guidelines for Health-Related Research Involving Human Subjects" (2017)[19] [46] are further examples of widely-referenced, codified non-binding sets of rules.

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 (see above). 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.

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19 The CIOMS guidelines include a section on the sharing of biological materials. Although the guidelines do not overtly engage with benefit-sharing, they include provisions on the use of MTAs, an emphasis on the rights of persons whose biological materials are used, and the use of ethics committees as governance mechanisms.

Table 9: 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 by an inter-governmental entity	"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 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)."

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 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).

In addition to a range in formality, international rules to govern PBS could also range in scope, in terms of countries or organizations included, types of pathogens, and/or intended use.:

Geographical scope: "Club models" of governance have increasingly been used to address global governance challenges when multilateral 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 around 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. This suggests that new international rules would be needed for pathogens of pandemic potential in particular. 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 (less specific terms).

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.

7 | CONCLUSIONS

The breadth of issues that surround PBS merit further research and discussion. Though policy options are many, the way forward is unclear—and the consequences of inaction need to be carefully considered. The ongoing pandemic outbreak of SARS-CoV-2 only underlines the need and urgency for finding governance solutions for PBS, and political appetite for multilateral instruments for PBS may be changing as a result. Our key conclusions for the way forward are as follows:

Traceability. Improving the tracking of both PBS will be necessary both to increase understanding of current practices, and to assess how well any future policies perform. More traceability and transparency of information on the movement of pathogen-samples and related benefits is feasible, as demonstrated by the PIP Framework. A traceability mechanism may be a component of a comprehensive negotiated framework, or a first step that could contribute to building one.

Leadership from a small group of countries. Given preliminary findings on the relatively small number of countries actively involved in global pathogen sharing, a relatively small group of stakeholders could start the process for developing normative frameworks for PBS governance. However, given that PBS is highly politicized, and that "club model" approaches could be seen as excluding opposing views, it will be critical to include a diversity of views and interests in early negotiations in order to avoid further entrenching existing tensions. Leadership from a small group of countries is needed.

There is agreement to build on. There is cautious optimism that, a decade after the PIP Framework, there is wide-spread acceptance of the importance of PBS being on equal footing. However, substantial efforts need to be devoted to clarifying benefit sharing as it relates to human pathogens.

Coherence within the complexity of existing rules. Though existing rules and their interactions are complex and need to be carefully studied in the development of new rules and frameworks, this need not block the development of specific rules for PBS so long as consistency with the objectives of the IHR, CBD and Nagoya Protocol is maintained. It will be critical to consider how to govern GSD alongside physical pathogen-samples, rather than leaving this issue on the sidelines. It remains an open question whether GSD would be better governed through a separate framework or integrated into rules pertaining to physical pathogen samples, but it is clear that the issue cannot be left unaddressed.

Time to move forward. Though there was considerable political hesitance to address the governance of PBS head-on—a hang-up from the difficulties of the PIP Framework negotiations—it is time to push for new international rules tailor-made for PBS. The Nagoya Protocol and Covid-19 pandemic may be the push that global health actors need to begin resolving the key issues associated with global PBS. 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. 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.

Directions for future research. This study has sought to fill gaps in the literature on PBS by investigating current practices of PBS and their drivers, at both international level and through two outbreak-specific case studies. Several areas of further inquiry would be useful. First, additional case studies of PBS practices would shed further light on these questions. For example, resource constraints prevented us from conducting a case study on PBS relating to MERS, but such a study could offer insights on practices in different regions of the world. Similarly, case studies on the drivers and practices relating to other pathogenic threats, such as antimicrobial resistance, would also be valuable. Second, understanding of the options for governance of GSD could be further improved through an exploration of the kinds of benefit sharing arrangements that have or have not been implemented. Finally, PBS practices relating to plant and animal health could uncover insights that would help to improve governance for human pathogens.

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9 | ANNEX

Annex 1: Interviewee characteristics

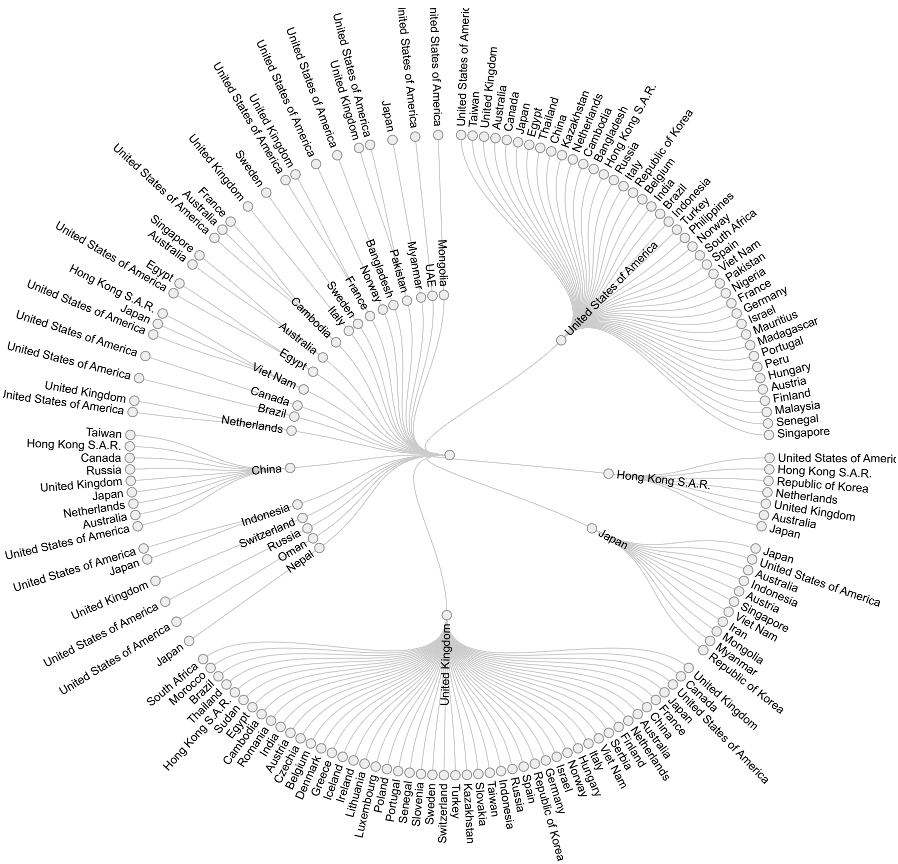
Characteristics	Phase 1 (N=53)		Liberia (N=20)		Brazil (N=13)	
	n	*%*	*n*	*%*	*n*	*%*
Sex						
Female	15	28	3	15	6	46
Male	38	72	17	85	7	54
Organization type						
Commercial	2	4				
Academic	13	25				
International	15	28				
Governmental	23	43				
National, governmental			10	50	1	8
National, non-governmental			3	15	0	0
National, academic			2	10	8	61
Regional			1	5	0	0
International, governmental			2	10	0	0
International, academic			2	10	3	23
International, pharmaceutical			0	0	1	8
Role						
Policy	23	43	7	35	1	8
Practice	12	23	6	30	8	61
Both policy and practice	18	34	7	35	4	31

List of Research Participants[20]

Abdullah Assiri	Christian Happi	Jonna Mazet	Peter Daszak	Steven Solomon
Anni-Riitta Virolainen-Julkinen	David Fidler	Jorge Bermudez	Raman Gangakhedkar	Suresh Jadhav
Arun Kumar	Dennis Carroll	Jurgen May	Ravindran Thayan	Tang Yi
Ben Neuman	Edward Hammond	Katherine Littler	Rebecca Katz	Tracy McNamara
Bernie Hannigan	Emily Erbelding	Makarim Wibisono	Richard Hatchett	Wenqing Zhang
Carlos Correa	Emmanuel Freudenthal	Marie-Paul Kieny	Richard Wilder	William Karesh
Carlos Morel	Igor Da Silva Barbosa	Mery Piña	Ron Fouchier	
Cathy Roth	Jari Jalava	Michael Shaw	Sangeeta Shashikant	
Chikwe Ihekweazu	Javier Gabaldon	Paula Barbosa	Stefano Ongarello	
Christian Haggenmiller	Jesse Goodman	Peter Bogner	Stephen Gunther	

20 We are grateful to the below research participants who generously shared their time and knowledge with us. We have included here only the names of 47 research participants who consented to be named in a final list of interviewees. This list excludes those who chose to remain anonymous and does not include research participants in the case studies.

Annex 2: Trajectories of IVPP sharing from sending (center circle) to receiving (outer circle) countries



Annex 3: Summary of Benefit Sharing Provisions in MTAs (N=26)

Benefits	Types of Provisions	Selected Text
Acknowledgement in Publications (n=17, 65%)	• Recipient acknowledges source of samples in all written or oral presentations on resultant research, unless otherwise requested (n=13, 50%) • Recipient acknowledges or provides co-authorship depending on level of involvement of provider (n=4, 15%)	• "The RECIPIENT agrees to acknowledge the source of the MATERIAL in any publications reporting use of it." (MTA #3) • "The Partners intend for authorship to be consistent with the International Committee of Medical Journal Editors (ICMJE). When appropriate under ICMJE standards, such articles or other publications are expected to include [Provider] author(s)." (MTA #25)
Access to Research Outcomes (n=15, 58%)	**Provisions for providers** • Provider to have access to research product for internal research purposes (n=3, 12%) • Provider maintains right to share any research results (n=3, 12%) **Provisions for recipients** • Recipient delivers report on research outcomes to provider (n=11, 42%) • Recipient to donate for free or at reduced costs resultant products to developing countries (n=3, 12%) • Recipient publishes research results in open access format (n=2, 8%)	• "The report shall include, but not be limited to, progress on the research and development involving the Materials or the Licensed Products and use of the Materials or the Licensed Products … 18. The Licensee is encouraged to publish the results of its research projects using the Materials or the Licensed Products." (MTA #6) • "The Recipient shall use all reasonable endeavors to ensure that the results of the Research Programme are, in accordance with normal academic practice, published in peer reviewed journals, scientific publications and open access databases as promptly as reasonably possible so, or to modify the publication to protect confidential or sensitive information … The Recipient shall send the [Provider] a copy of any reports or publications which describe work carried out using the Materials, as well as any supporting data, and [Provider] shall be entitled to use all such data, reports and publications and make them available to third parties." (MTA #15)

Benefits	Types of Provisions	Selected Text
Cost Recovery (n=11, 42%)	• Recipient covers cost of shipping and handling (n=4, 15%) • Optional cost reimbursement for provider (n=3, 12%) • Provider does not charge recipient for shipping and handling costs (n=2, 8%)	• "The Original MATERIAL is provided cost-free; however, a handling fee may be charged for its preparation and shipment to the RECIPIENT." (MTA #16) • "The Materials are supplied at the Recipient's risk and without cost, but the Recipient shall reimburse [Provider] for any reasonable handling, transport and any other related costs that may be incurred when preparing and sending the Materials to the Recipient … [Provider] will arrange for delivery to be made through an approved third party and the applicant's institution will be liable for delivery payment within 28 days of their receipt. The researcher must confirm to [Provider] that the materials have arrived." (MTA #15)
Capacity Building/Training (N=2, 8%)	• Sample provider receives capacity building and training from recipient (n=2, 8%)	• "The project should contribute to building capacity, transfer of technology, training, and graduation of students and research fellows from [Country]. In particular, the [Country] co-investigators, students, and post-doctoral fellows shall be involved in the planning of projects and experiments, the generation of data, the analysis of data, and the preparation of publications." (MTA #22) • "[Country A] and [Country B] look forward to continuing to advance [Country B's] capabilities with respect to research and public health as identified in the Global Health Security Agenda (GHSA) targets and [Country B's] five-year GHSA roadmap, and thereby further the objectives of the International Health Regulations (2005) to improving detection, reporting, and response to public health emergencies of international concern (public health emergencies)." (MTA #25)

Annex 4: Summary of Benefit Sharing Options in the PIP Framework's SMTA2 [47][21]

	CATEGORY A (Select 2/6)	CATEGORY B (Select 1/6)	CATEGORY C (Consider)
1	Donate % of real-time vaccine production to WHO	Donate diagnostic kits to WHO	Consider contributing to the measures listed below, as appropriate: • Donations of vaccines; • Donations of pre-pandemic vaccines; • Donations of antivirals; • Donations of medical devices; • Donations of diagnostic kits; • Affordable pricing of pandemic products; • Transfer of technology and processes; • Granting of sublicenses to WHO; • Laboratory and surveillance capacity building.
2	Reserve % of real-time vaccine production at affordable pricing to WHO	Reserve diagnostic kits at affordable pricing to WHO	
3	Donate antivirals to WHO	Support laboratory and surveillance capacity strengthening	
4	Reserve antivirals at affordable pricing to WHO	Support transfer of technology, know- how and/or processes	
5	License on technology, know-how, processes or products needed for the production of influenza vaccines, antivirals or adjuvants to developing country manufacturers, on mutually-agreed fair terms	License on technology, know-how, processes or products needed for the production of influenza vaccines, antivirals or adjuvants to developing country manufacturers, on mutually- agreed fair terms	
6	Royalty-free license to developing country manufacturers or WHO for production of influenza vaccines, antivirals or adjuvants	Royalty free license to developing country manufacturers or WHO for production of influenza vaccines, antivirals or adjuvants	

21 This table is reproduced from the WHO's webpage on the SMTA2, accessed: https://www.who.int/influenza/pip/smta2/en/

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