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## Access by Design, Benefits if Convenient: A Closer Look at the Pandemic Influenza Preparedness Framework's Standard Material Transfer Agreements

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### Policy Points:

- Securing access to pathogen samples for research purposes is crucial for pandemic preparedness and responding to infectious disease outbreaks.
- The *Pandemic Influenza Preparedness Framework* (PIP Framework) is the only pathogen-specific international access and benefit-sharing (ABS) instrument.
- This analysis reveals that during an influenza pandemic, the PIP Framework will safeguard access to virus samples but may not be as effective in delivering the associated benefits, like vaccines and antivirals, to countries in need.
- The PIP Framework's deficiencies must be addressed before an influenza pandemic and before this ABS model is extended to other human pathogens.

**Context:** The World Health Organization (WHO) adopted the *Pandemic Influenza Preparedness Framework* (PIP Framework) after being forced to grapple with the demands of developing countries for the fairer distribution of vaccines and antivirals created using influenza viruses isolated from within their territories. Though adopted as a nonbinding resolution, the PIP Framework has been praised for its novel legal approach to access and benefit-sharing (ABS), using Standard Material Transfer Agreements (SMTAs) to create binding terms and conditions on both providers and users of PIP biological materials. The PIP Framework's SMTA1 regulates the movement of influenza viruses with human pandemic potential through the WHO's Global Influenza Surveillance

and Response System (GISRS) as it operates to monitor the spread of seasonal influenza and detect the emergence of pandemic strains. Member States give consent to the WHO to transfer their materials to third parties under the terms of a negotiated SMTA2. The SMTA2 details benefits such as vaccines and antivirals to be made available to the WHO for distribution in the event of an influenza pandemic.

**Methods:** I analyzed the PIP Framework, its SMTAs, and secondary sources to determine whether the PIP Framework will effectively function as an ABS instrument during an influenza pandemic.

**Findings:** The SMTAs do not create any direct or binding agreements between Member States and third-party recipients of influenza viruses. In the lead-up to and during a pandemic, the SMTA1 secures access to influenza viruses for the WHO, and the SMTA2 secures access for commercial users of virus samples, but the SMTA2 may be ineffective in securing tangible benefits for the sovereign providers of those materials.

**Conclusions:** As the international community starts to consider how to best regulate access to nonpandemic influenza pathogen samples, it is imperative that we first address the shortcomings of the only pathogen-specific international ABS instrument available, and we should do so before it is put to the ultimate test.

**Keywords:** access and benefit-sharing, PIP Framework, pandemic influenza, World Health Organization, genetic resources.

**I**N JANUARY 2007, THE INDONESIAN GOVERNMENT CHALLENGED the norms that had developed around sharing viruses with the World Health Organization's (WHO's) Global Influenza Surveillance Network (GISN) (now called the Global Influenza Surveillance and Response System, or GISRS) by asserting sovereignty over the avian influenza A (H5N1) viruses collected within its territorial borders.<sup>1</sup> Indonesia's admittedly "drastic decision" was precipitated by a series of perceived inequities, including the WHO's provision of an Indonesian virus strain to an Australian vaccine manufacturer that developed and patented a vaccine without Indonesia's consent.<sup>1,2</sup> Indonesia's position, supported by many low- and middle-income countries (LMICs),<sup>3</sup> was that developing countries are expected to provide their sovereign genetic resources without any guarantee that they will have fair and equitable access to the benefits associated with their use, like vaccines and antivirals.<sup>1</sup> LMICs are often the emergence sites for

novel and therefore scientifically valuable influenza viruses, so their engagement in surveillance and monitoring is central to pandemic preparedness.<sup>4</sup> They are also the countries least likely to possess vaccine-manufacturing capacity and are therefore highly reliant on the WHO for access to pandemic preparedness and response benefits like vaccines and antivirals.

In response to Indonesia's demands, the 60th World Health Assembly (WHA) adopted a resolution in May 2007 that addressed "the need for effective and transparent international mechanisms aimed at ensuring fair and equitable sharing of benefits" derived from the utilization of influenza samples.<sup>5</sup> That resolution became the blueprint for the *Pandemic Influenza Preparedness Framework* (PIP Framework), itself adopted as a nonbinding resolution (under Article 23 of the WHO Constitution) by the 64th WHA in May 2011.<sup>6</sup> The PIP Framework "recognize[s] the sovereign right of States over their biological resources" (Article 1.11) and "applies to the sharing of H5N1 and other influenza viruses with human pandemic potential and the sharing of benefits" (Article 3.1). The PIP Framework explicitly excludes from its scope "seasonal influenza viruses or other non-influenza pathogens or biological substances that may be contained in clinical specimens shared under this [PIP] Framework" (Article 3.2). In recognition of the new governance arrangements set out in the PIP Framework, the GISN was renamed the Global Influenza Surveillance and Response System, and Indonesia resumed sharing its influenza virus samples.<sup>7</sup>

The WHO's GISRS has been in existence in various forms since 1952.<sup>8</sup> This worldwide collaborative network of laboratories operates to detect the emergence of any novel or potentially pandemic strains of influenza against the background of constantly evolving seasonal influenza viruses. The GISRS primarily comprises 144 National Influenza Centers (NICs) in 114 WHO Member States<sup>9</sup> and 6 regional WHO Collaborating Centers (CCs) in Atlanta, Beijing, London, Melbourne, Memphis, and Tokyo.<sup>10</sup> The NICs essentially act as sentinel nodes obtaining and analyzing influenza strains from local hospitals, clinics, and pathology labs and forwarding information and selected virus samples to the CCs for further analyses.<sup>9</sup> The GISRS network also includes H5 Reference Laboratories<sup>11</sup> as well as Essential Regulatory Laboratories, "which have a critical role at the global level for developing, regulating and standardizing human influenza vaccines" (PIP Framework, Article 4.3). The GISRS generates the epidemiological data and risk

assessments that inform the WHO's recommendations on the composition of both seasonal and pandemic influenza vaccines.<sup>12</sup> The GISRS then delivers those candidate vaccine viruses to pharmaceutical manufacturers to make the recommended vaccines. The overall aim of the GISRS is to provide advance warning of an influenza pandemic, and its partnership with commercial vaccine manufacturers is aimed at preparing the pharmaceutical countermeasures that can help the world to respond to and avert the catastrophic consequences of a 1918-style influenza pandemic.

As was highlighted by Indonesia in 2007, the virus-sharing practices of the GISN had developed informally over decades, and the rights and obligations of the providers of virus samples, the various laboratories within the GISN, and third-party recipients of virus samples from the GISN were never clearly or fully defined beyond the Terms of Reference for individual labs. The PIP Framework now codifies the operation of the newly rebranded GISRS, implementing Standard Material Transfer Agreements (SMTAs) to regulate the movement of PIP biological materials through the GISRS and provide greater clarity around the previously ambiguous terms and conditions associated with both providing and using influenza viruses. The PIP Framework asserts that WHO Member States should provide materials from all cases of H5N1 and other influenza viruses with human pandemic potential to the GISRS (Article 5.1.1). Providing materials for surveillance and response to the GISRS is consent to the onward transfer of their PIP biological materials to other GISRS laboratories under the SMTA1 (Article 5.4.1 and Annex 1) and then to third parties under an SMTA2 (Article 5.4.2 and Annex 2). (The consent-crystalizing transfer is from the NIC to the WHO CCs and H5 Reference Laboratories, Article 5.1.2.) The SMTA2 transfers these materials from the GISRS to parties that sit outside of the WHO-recognized GISRS network and its governance reach, including academic laboratories and research institutes, as well as diagnostic and vaccine manufacturers (Article 5.4.2 and Annex 2). In exchange, these third-party, non-GISRS recipients elect to provide certain benefits to the WHO, according to their capacities (Article 5.4.2 and Annex 2, Article 4). For instance, an influenza vaccine manufacturer may elect to donate a percentage of its vaccine production to the WHO in the event of a pandemic or grant royalty-free licenses to vaccine manufacturers in developing countries (Annex 2, Article 4.1.1[A]). Commercial third parties must also make a subscription payment, called a Partnership

Contribution, to the WHO as a part of their commitments to assist in funding the GISRS (Article 6.14.3).

The use of the SMTAs has been praised by commentators<sup>13,14</sup> as an innovative legal strategy for turning the nonbinding provisions of the PIP Framework resolution at the WHO into binding contractual obligations on the commercial recipients of PIP biological materials,<sup>13,15</sup> and as a fairer way of distributing the benefits associated with the use of sovereign genetic resources.<sup>16,17</sup> It should be noted, however, that there are many types of benefits generated and distributed through the GISRS, including epidemiological information, risk assessments, and data, as well as the provision of standardized reagents, technical support, and training to WHO-recognized laboratories within the GISRS network (see, for example, PIP Framework, Articles 6.0.2, 6.2.2, 6.2.3, 6.2.4, 6.4.1, and 6.5.1). Wilke<sup>14</sup> highlights the distinction between “diffuse” and “tangible” benefits of the PIP Framework, and in the context of the concluded SMTA2s, the term *benefits* is used to refer to the tangible benefits provided by commercial recipients of PIP biological materials, including diagnostic kits, antiviral medicines, and pandemic influenza vaccines.

Much of the praise for the PIP Framework relies on the assumption of a direct association between the Member States' providing access to their influenza viruses and the provision of associated vaccines and other benefits. Indeed, it was the lack of such an association that lay at the very heart of Indonesia's argument in 2007 that led to the adoption of the PIP Framework. The context of the PIP Framework negotiations and the full title of the *Pandemic Influenza Preparedness Framework for the Sharing of Influenza Viruses and Access to Vaccines and Other Benefits* tend to reinforce the perception that the PIP Framework creates a direct link between access to viruses and the sharing of associated benefits. This is also reflected in developments more broadly at the United Nations, where agreements such as the *Convention on Biological Diversity* (1992) recognize Member State sovereignty over biological resources and detail the exchange of access to genetic resources for related benefits.

Nevertheless, there has been little scrutiny of the PIP Framework's ability to meet its stated “objective of a fair, transparent, equitable, efficient, effective system for, on an equal footing: (i) the sharing of H5N1 and other influenza viruses with human pandemic potential; and (ii) access to vaccines and sharing of other benefits” (Article 2).

This article examines the access and benefit-sharing (ABS) provisions of the PIP Framework and its SMTAs. It should be noted that the PIP Framework is just one tool in the influenza pandemic and preparedness response toolbox (which includes Strategic Advisory Group of Experts on Immunization, the Global Action Plan to increase vaccine supply, and the WHO's *International Health Regulations*), but because it stands alone as an ABS policy for PIP biological materials, it is possible to analyze the ABS facets of the PIP Framework in isolation of these other instruments and bodies. Such analyses are necessary to identify and remedy the problems that could produce disastrous consequences when the PIP Framework is eventually subjected to the ultimate stress test—an influenza pandemic.

This section has provided a brief history of the PIP Framework and the operation of the GISRS. The next section will provide a textual analysis of the SMTA1 and SMTA2 contracts. It demonstrates that the SMTAs do not create any direct or binding agreements between the originating Member States as the providers of PIP biological materials and the recipients of those materials, and that the SMTA2 may not be effective in securing the promised benefits from commercial third parties in the event of a pandemic. Further textual analysis of the PIP Framework later in the article reveals that, like the SMTA2, the specific wording of the PIP Framework affords some flexibility to the WHO to avoid its stated responsibility during a pandemic, in this instance to trace Member States' virus samples as they traverse the GISRS. The penultimate section establishes that the act of providing viruses as essential inputs to the GISRS does not itself qualify Member States to receive any of the related benefits from the WHO, if indeed there is a pool of benefits to be distributed. The article concludes that while the PIP Framework was broadly conceived to perform as an access *and* benefit-sharing framework, it might be better conceptualized simply as an access framework. That is, in the lead-up to a potential pandemic, the virus samples that are required by the WHO and vaccine manufacturers to prepare for that pandemic have already been secured; however, there is no equivalent guarantee that any associated benefits promised through the SMTA2s will be forthcoming, leaving LMICs in particular dangerously underprepared for the pandemic. The predictable consequence is that the current WHO mechanisms need to be reconceived to respond to the next pandemic.

## Textual Analysis of the PIP Framework's SMTAs

### *The SMTA1 for Transfers Within the GISRS*

The principles of the PIP Framework include the explicit recognition of “the sovereign right of States over their biological resources” (Article 1[11]), indicating that Member States act as the original source and provider of their sovereign genetic materials. Article 5.1.1 provides:

Member States, through their National Influenza Centers and Other authorized laboratories, should in a rapid, systematic and timely manner provide PIP biological materials from all cases of H5N1 and other influenza viruses with human pandemic potential, as feasible, to the WHO Collaborating Centre on Influenza or WHO H5 Reference Laboratory of the originating Member State's choice.

Article 5.1.2 then states, in part, “Member States provide their consent for the onward transfer and use of PIP biological materials to institutions, organizations and entities, subject to provisions in the Standard Material Transfer Agreements.”

These provisions suggest that the originating Member States, defined as “the Member State where the PIP biological materials/clinical specimens were first collected” (Article 4.4), represent at least 1 of the parties to the PIP Framework's standardized agreements.

The “PIP biological materials” are defined by Article 4.1 of the Framework to mean:

virus isolates of wild type human H5N1 and other influenza viruses with human pandemic potential; and modified viruses prepared from H5N1 and/or other influenza viruses with human pandemic potential developed by WHO GISRS laboratories, these being candidate vaccine viruses generated by reverse genetics and/or high growth reassortment. Also . . . RNA extracted from wild-type H5N1 and other human influenza viruses with human pandemic potential and cDNA that encompass the entire coding region of one or more viral genes.

The SMTAs themselves are directly addressed only in Article 5.4 of the body of the PIP Framework (Article 4.1 also makes mention of the SMTAs but does not address their use directly). Of the SMTA1, Article 5.4.1 of the PIP Framework states: “The Standard Material Transfer Agreement 1 (SMTA1) in Annex 1 will be used to cover all transfers of

PIP biological materials within the WHO GISRS for the duration of its applicability.”

Taken together, Articles 5.1.1, 5.1.2, and 5.4.1 can create the impression that originating Member States provide their sovereign genetic resources to the WHO using the SMTA1. This is only partly correct. The originating Member States provide their sovereign genetic resources “*through* their National Influenza Centers and Other authorized laboratories” (Article 5.1.1) (emphasis added), suggesting that the designated NIC is acting as an agent or trustee of the originating Member State for the purposes of the SMTA1. The NICs are “authorized and designated by the Member State and subsequently recognized by the WHO to perform a number of functions including providing PIP biological materials to the WHO GISRS in accordance with the terms of reference” (Article 4.3). The PIP Framework identifies NICs both as entities belonging to the Member State *and* as laboratories residing within the WHO’s GISRS network. To wit, Article 4.3, which provides definitions on “[i]nstitutions, organizations and entities,” states that the NIC is “recognized by WHO to perform a number of functions including providing PIP biological materials to the WHO GISRS,” indicating that NICs sit outside of the GISRS. However, it later states that “[t]he WHO GISRS comprises National Influenza Centers, WHO Collaborating Centers on Influenza, WHO H5 Reference Laboratories and Essential Regulatory Laboratories,” indicating that the NICs are within the GISRS. Lange notes that during the Director-General’s Interdisciplinary Working Group meeting in Singapore from July 31 to August 4, 2007, “participants could not even agree on which entities were part of the GISN (versus outside entities)” and it appears that the final wording of the PIP Framework captures that confusion.<sup>3</sup>

The Terms of Reference for NICs are contained in Annex 5 to the PIP Framework but outline only the role that NICs play in relation to the WHO GISRS. They do not elucidate the relationship between the NIC and its host country’s Ministry of Health. This is further complicated by the role the WHO plays in establishing and managing NICs in some host countries.<sup>18</sup> The Member State provides clinical specimens to the NIC as a matter of course, and an SMTA1 is not completed until the NIC provides those samples to other parts of the GISRS network. At no point does the originating Member State directly provide its sovereign genetic resources to the WHO or enter into a PIP Framework SMTA. The act of continuing to provide sovereign genetic resources through its NIC



can be considered approval of the arrangement (actual or constructive consent); however, as the NIC is considered to be a component of the GISRS network of laboratories, the sovereign authority over any genetic resources provided to the NIC is only as strong as the Member State's formal or informal agreement or understanding with that particular NIC. Functionally, though, "the PIP Framework largely depends on the decentralized operations of its constituent institutional components,"<sup>19</sup> and the NICs generally act independent of regular Member State direction or interference.<sup>20</sup>

As stated in Article 5.1.2, the SMTA1 embodies the consent of Member States for the onward transfer of PIP biological materials to other GISRS laboratories and eventually to third parties (with an SMTA2). The terminology in the PIP Framework is equivocal about the legal effect of the transfer of materials from the NIC to the broader GISRS. The NICs' providing physical materials to the CC or H5 Reference Laboratories is deemed approval for the onward transfer of PIP biological materials (Article 5.1.2) and might be sufficient to transfer title (sovereignty) of those materials to the WHO and its entities. The term "consent" used in Article 5.1.2 of the PIP Framework does not necessarily, however, suggest a transfer of complete title. This hesitation is reinforced by the reference in the SMTA1 that it is "to cover all transfers" (Article 5.4.1) and the Terms of Reference for the NIC that its activities "be consistent with the [PIP] Framework and the [SMTA1]" (Annex 5). The terms "cover" and "consistent" are precatory and may not be a formal and definitive transfer of title. Even if sovereign rights cannot be said to be extinguished at this (or any) point, the Member States have already consented to "the onward transfer and use" by the broader GISRS and third parties just by providing those materials (Article 5.1.2). Whether the Member State retains sovereign rights over its samples as they traverse the GISRS is a key legal issue that needs to be explicitly addressed. However, the point here is that even if a Member State does retain some legal authority over the samples that originate in its territory (whether that authority can be said to constitute sovereignty or ownership or something else), it has likely relinquished all functional control the moment those samples are within the GISRS network.

To reiterate, the SMTA1 defines the "Provider" of PIP biological materials as "the laboratory sending Materials," that is, any laboratory already within the GISRS (Annex 1, Article 1.1). "The Recipient is

the laboratory receiving Materials,” that is, yet another laboratory in the GISRS (Annex 1, Article 1.1). The SMTA1s are simply agreements between the various nodes of the extended GISRS network, and as such, any biological materials held by the NICs are already considered to reside within the GISRS. This is reinforced by the express inclusion of the NICs within the GISRS (Article 4.3). Accordingly, the Member State appears to have relinquished control (but perhaps not all sovereign rights) over its PIP biological materials well before any SMTAs are entered into. Furthermore, despite the scope of the PIP Framework’s being strictly limited to those viruses with pandemic potential, the NICs of individual countries must sometimes forward clinical samples to the CCs without having ascertained whether the strains therein qualify as “PIP biological materials.” The system therefore reinforces the sharing norms for *all* influenza samples while the PIP Framework applies only to those virus samples that are later designated as having pandemic potential. Anything not deemed to be “PIP biological materials” by the CCs is probably within the remit of the *Convention on Biological Diversity* and its *Nagoya Protocol on Access to Genetic Resources and the Fair and Equitable Sharing of Benefits Arising from Their Utilization*, and thus subject to regulation at the domestic level.<sup>21</sup> For this reason, the exclusion from the scope of the PIP Framework of “non-influenza pathogens or biological substances that may be contained in clinical specimens shared under this Framework” (Article 3.2) might strike originating Member States, particularly LMICs, as problematic as it renders uncertain the sovereign status of any *other* genetic resources contained in the clinical specimens provided to GISRS laboratories. It is challenging for a Member State to exercise legal authority and control over its sovereign genetic resources, should the State wish to do so, once those resources are no longer in its custody and control appears to have been ceded to the WHO.

### *The SMTA2 for Transfers Outside of the GISRS*

The SMTA2 governs the transfer of PIP biological materials from the GISRS network of laboratories to third parties. Article 5.4.2 provides: “The Director-General will, using the Standard Material Transfer Agreement 2 (SMTA2) in Annex 2, enter into agreements with entities outside

the WHO GISRS. Such agreements will cover all transfers of PIP biological materials to recipients for their duration.”

Importantly here, the term “recipients” has not been previously defined in the body of the PIP Framework. The SMTA2 lists the parties to the agreement as the “WHO and Recipient,” with the “Recipient” defined in the SMTA2 as those “entities that receive ‘PIP Biological Materials’ from the WHO [GISRS], such as influenza vaccine, diagnostic and pharmaceutical manufacturers, as well as biotechnology firms, research institutions and academic institutions” (Annex 2, footnote 1). The SMTA2 documents the terms and conditions attached to the materials exchanged between the WHO and the commercial or academic recipient of PIP biological materials and marks the departure of the materials from the legal entity of the WHO with its governance and accountability to Member States to a separate third-party entity.

The SMTA2 is indeed an inventive means to commit non-State actors to providing benefits into the PIP benefit-sharing system.<sup>13,14,22</sup> It is a hybrid standardized and negotiated contract as it requires the recipient party to agree to a few limited terms and conditions, and then choose a series of options for benefit-sharing. Standard contracts reduce transaction costs by removing the requirement to bargain and negotiate terms for each individual transfer event. They create “fewer legal, administrative and procedural complexities, which would imply less need for legal experts, consultants and formal bureaucracies to solve these complexities.”<sup>23</sup> Furthermore, standardized agreements are established practice in the biotechnology industry, creating legal certainty around the transfer of both physical and intellectual property, and establishing provenance for physical materials. So far, though, the process of negotiating SMTA2s for the PIP Framework has proven “complex and lengthy.”<sup>22</sup> This probably reflects the nature of the third-party entities and their extensive use of lawyers, as well as sensitivities to protecting their investments and assets in intellectual property.

As at June 2017, 11 vaccine and antiviral manufacturers (Category A) had signed SMTA2s with commitments to donate and reserve vaccines.<sup>24</sup> Just 1 diagnostics manufacturer (Category B) had signed an SMTA2 with a commitment to reserve diagnostic kits for the WHO,<sup>25</sup> and a further 63 SMTA2s had been signed by academic and research institutions (Category C), 26 of which offered benefits for the use of PIP biological materials accessed through the GISRS.<sup>26</sup> The 11 Category A SMTA2s between the WHO and the vaccine manufacturers are available online.<sup>27</sup>

However, the Term Sheets for all 11 SMTA2s have not been made available to the public. Apart from the negotiated articles stipulating the obligations of the company, the SMTA2s all follow the same structure and contain similar provisions.

By way of example, the Term Sheets of the SMTA2 concluded between the WHO and China National Biotech Group in 2016 “specify the terms for each of the Commitments,” that is, the obligations of the company to provide benefits to the WHO in the event of an influenza pandemic, and form the annexes of the agreement (Article 6.1).<sup>28</sup> Further, each SMTA2 indicates that the annexes are “an integral part” of the agreement (Article 6.1),<sup>28</sup> yet this integral information is not available for public scrutiny. In each of the 11 SMTA2s, the “[p]rovisions on liability and indemnity are contained in the relevant Term Sheets” (Article 8).<sup>28</sup> Every SMTA2 contains a provision on force majeure, stating that “[n]o Party shall be liable for any delay in the performance of or failure to perform its obligations under this Agreement, where such delay or failure is caused by Force Majeure” (Article 14).<sup>28</sup> For all but 1 of the 11 SMTA2s, the term “force majeure” is also defined in these confidential Term Sheets. From the available SMTA, between the WHO and Glaxo Group Limited on December 18, 2012, the definition in Article 3(d) provides:

“Force Majeure” shall mean any cause preventing either Party from performing any or all of its obligations under this Agreement which arises from or is attributable to acts, events, omissions or accidents beyond the reasonable control of the such Party, including strikes, lock-outs or other industrial disputes (whether involving the work force of the Party or any other party), acts of God, riot, war, embargo or requisition, acts of government, *disease (including influenza pandemic)*, shortage of materials (including suitable hens’ eggs and other raw materials), unavailability of transport, civil commotion, malicious damage, compliance with any law or judicial order or order of any government or quasi-governmental or other competent institution, rule, regulation or direction, accident, technical failure in the manufacture or development of the product to be supplied under the respective commitment, fire, flood, storm or default of suppliers.<sup>29</sup> [emphasis added]

That a manufacturer committed to delivering influenza vaccines and antiviral medicines to the WHO during an influenza pandemic (Article 5.1.1)<sup>29</sup> is not liable for failure to perform that obligation in the event of an influenza pandemic is plainly absurd. The SMTA2 is

specifically intended and designed to commit the manufacturer to providing products *during* an influenza pandemic, so an “influenza pandemic” cannot be considered to embody the “unexpected” or “unanticipated” element of the legal definition of the term “force majeure.”<sup>30</sup> Certainly, the same cannot be said of “acts of government” and “embargo or requisition,” which are worthy of mention here, given that “concern has been expressed by the industry that during an influenza pandemic, Member States with domestic [pandemic influenza vaccine] production within their territory would place restrictions upon exports of [pandemic influenza vaccine] that have been committed to the PIP stockpile, until domestic demand had been fulfilled.”<sup>31</sup> This is an understandable anxiety given the use of advance purchase agreements by developing countries during the concerns over H1N1 influenza in 2009.<sup>32-36</sup> In the midst of pandemic chaos, it is highly likely that domestic governments will requisition or nationalize their pharmaceutical manufacturers and deny access to vaccines and antivirals for other countries in favor of protecting their own citizens, irrespective of international public health priorities as determined by the WHO. It is difficult to rebuke the commercial parties to the SMTA2s for conceding the realities of an emergency situation. Nevertheless, including an influenza pandemic in the definition of “force majeure” does perhaps indicate a level of insincerity in their dealings with the PIP Framework and raise the question of the WHO’s role in agreeing to such limitations.

## **The Influenza Virus Traceability Mechanism Under Pandemic Stress**

Like the force majeure clauses in the agreed SMTA2s, there is an explicit recognition in the PIP Framework that certain aspects of the GISRS will not operate as planned under pandemic stress. The Influenza Virus Traceability Mechanism (IVTM) is defined as “an IT-based system for tracking the transfer and movement of PIP biological materials into, within and out of the WHO GISRS” (Article 4.4).<sup>6</sup> The tracing of PIP biological materials “in real time” as they traverse the various laboratories “within, and out of the WHO GISRS” (Article 5.3.1)<sup>6</sup> is particularly important to LMIC providers because the provision of samples through their NICs constitutes “their consent for the onward transfer and use of PIP biological materials to institutions, organizations and entities”

(Article 5.1.2).<sup>6</sup> Put simply, the action of providing materials *is* consent. The IVTM captures information about which GISRS laboratories and external parties have accessed particular strains of viruses. Providers can therefore ensure that their sovereign genetic resources have been used appropriately and in accordance with the provisions of the SMTAs and principles of the PIP Framework.<sup>37</sup> Importantly, however, this “transparent traceability mechanism” can be modified during an influenza pandemic. Article 5.3.3 of the PIP Framework provides that:

In order to ensure that the IVTM does not hinder the functioning of the WHO GISRS during pandemic influenza emergencies, as determined by the Director-General, the Director-General may temporarily modify the requirement to record all PIP biological materials. Such a modification must be limited to the pandemic virus strain or strains connected with the emergency.

Like the inclusion of pandemic influenza in the SMTA2’s definition of force majeure, this provision is recognition that the GISRS and the PIP Framework will be strained in times of pandemic stress. It is not clear from the text whether such a “modification” to the “requirement to record all PIP biological materials” might simply be a delay (ie, tracking information will not be published in real time but will eventually be made available) or a suspension of the requirement to record the movement of pandemic virus strains altogether throughout the course of a pandemic. The consent of providers for the onward transfer of their samples is predicated, at least in part, on their ability to know what happens with those samples once they are outside of their custody and functional control. At no other time are these PIP biological materials of greater value to the provider than in the lead-up to and during a pandemic, and this is precisely when there is, built into the PIP Framework, an expectation that the system will collapse.

### **There Is No Link Between Providing Access to Viruses and Receiving Benefits**

It is clear now that there is no direct agreement between the originating Member State as the provider and the commercial recipient of PIP biological materials. Their relationship is mediated through the WHO,

as the originating Member State never enters into a direct contractual or other agreement under the PIP Framework at all. To reiterate, the SMTA1 is an agreement between laboratories within the WHO's GISRS, and the SMTA2 is between the WHO and the commercial or academic recipient of PIP biological materials. This may seem an obvious point to some, but it is vitally important to make these contractual relationships explicit because even in assessments of the PIP Framework that conceptualize the WHO as an intermediary to the ABS transaction, there is an enduring perception that the provision of viruses from the originating Member State somehow qualifies that State for the benefits that are generated through the GISRS. Through its SMTAs, the PIP Framework creates the illusion of a quid pro quo, but in reality, the PIP Framework does not provide for any exchange of viruses for associated benefits.

During the negotiations for the PIP Framework, "Indonesia and many other developing countries [were] trying to create linkage [between virus sharing and benefit sharing]"<sup>3</sup> and "wealthy states like the United States, along with the pharmaceutical industry," opposed the reforms suggested by Indonesia and other developing countries.<sup>38</sup> These wealthy States "preferred the *status quo ante*, when virus sharing was unconditional and uncoupled from benefit sharing."<sup>38</sup> This "uncoupled" status was preserved when the Intergovernmental Meeting (IGM) in December 2008 established the principle that "benefits should not be provided in a preferential manner to the country from which the virus had originated, but rather as a pooled benefits system based on public health risk and need (aimed at developing countries)."<sup>3</sup>

Under pandemic situations, the PIP Framework does not provide any benefits that a Member State would not already qualify for outside of the PIP Framework. That is, originating Member States are providing inputs to the GISRS, but this action cannot affect their ability to receive specific benefits from the GISRS.<sup>3</sup> Article 1(8) of the PIP Framework (Principles) "recognize[s] that the benefits arising from the sharing of H5N1 and other influenza viruses with human pandemic potential should be shared with all Member States based on public health risk and need." Further, Article 6.1 states:

WHO will coordinate influenza pandemic preparedness and response in accordance with applicable International Health Regulations (2005) provisions and this Framework. As regards the benefits outlined in this Framework, WHO should pay particular attention to policies and practices that promote the fair, equitable and transparent

allocation of scarce medical resources (including, but not limited to, vaccines, antivirals and diagnostic materials) during pandemics based on public health risk and needs, including the epidemiology of the pandemic.

In preparing for and responding to an influenza pandemic, the WHO must allocate “scarce medical resources,” including those generated as benefits through the PIP Framework SMTA2, “based on public health risk and needs” (Article 6.1). The PIP Framework implies, but never explicitly states, that Member States must provide PIP biological materials to the GISRS in order to receive access to PIP Framework benefits. The PIP Framework defines only 3 benefits that appear to be tied directly to the specific materials provided by Member States: the active “participation of scientists to the fullest extent possible from originating laboratories . . . in scientific projects associated with” those materials (Annex 1, Article 5.2); access to the genetic sequence data and analyses derived from those materials (Article 5.2.1); and acknowledgment of “the contribution of collaborators” in downstream “presentations and publications” (Annex 1, Article 5.3). The latter 2 “benefits” are generally provided as a matter of scientific courtesy rather than in deference to the provisions of the PIP Framework. All tangible benefits, “including, but not limited to, vaccines, antivirals and diagnostic materials” are provided at the discretion of the WHO and must occur in accordance with sound scientific and public health reasoning (Article 6.1). This is reinforced in the section about the PIP benefit-sharing system, which will “prioritize important benefits, such as and including antiviral medicines and vaccines . . . to developing countries, particularly affected countries, according to public health risk and needs” and that “[p]rioritization will be based on assessment of public health risk and need” (Article 6.0.2[iii]). Therefore, the provision of viruses to the GISRS cannot qualify a Member State for PIP Framework–associated benefits. The corollary is that Member States cannot be legally precluded from receiving any “scarce medical resources” during an influenza pandemic even if they had not provided PIP biological materials to the GISRS. Indeed, Smith has noted that “[l]ittle that triggered or transpired during this controversy [Indonesia’s withholding virus samples from the WHO in 2007] would therefore violate the framework that supposedly resolves it.”<sup>38</sup> Access to viruses is not connected to the sharing of associated benefits under the PIP Framework and the WHO cannot be an intermediary in an access and benefit-sharing exchange if there is no direct or even theoretical



legal association between access and benefit-sharing. The WHO instead becomes the focal point of a constellation of uncertain legal rights and unenforceable obligations and the eventual target of opprobrium if it cannot deliver on the promises of the PIP Framework.

## Conclusion

The report from the 2016 scheduled review of the PIP Framework stated, “The success of the PIP Framework in ensuring better and more equitable access to viruses, vaccines, antivirals and diagnostics, has led some stakeholders to propose that the PIP Framework be expanded to include other infectious pathogens, whereas others have suggested applying the principles of the PIP Framework as a model.”<sup>22</sup> As the PIP Framework has not yet been put to the test under pandemic conditions, it is impossible to conclude that it has been successful in ensuring access to those tangible benefits for countries in need. This analysis indicates both that the PIP Framework has serious deficits—particularly with respect to the SMTAs—that must be addressed before an influenza pandemic and that the international community should be wary of applying this model to other pathogenic genetic resources without first addressing these problems.

The most likely areas for the emergence of new strains of influenza are LMICs<sup>39</sup> that are least equipped to address a pandemic threat. Considering the likely temporal course of an influenza pandemic, the GISRS will detect the emergence of a potentially pandemic strain when (and probably because) those emergent viruses are already in its possession. This means that the Member States with newly emerged (and therefore valuable) viruses will have already fulfilled their part of the PIP Framework's bargain: access.<sup>39</sup> However, the text of the PIP Framework and the SMTA2 acknowledges that the normal operation of the GISRS will be strained during an influenza pandemic, to the point that many of the Framework's obligations may not be met. This acknowledgment affords the WHO and commercial recipients of PIP biological materials a measure of operational freedom in responding to a pandemic. That is, the WHO will no longer necessarily be bound by the requirement to track samples using the IVTM, and it is uncertain whether vaccine manufacturers can be held accountable for *any* failure to meet their contractual obligations because of the force majeure clauses in the SMTA2.

Notwithstanding the fact that the provision of viruses to the GISRS in no way qualifies providing Member States to receive related benefits, the wording of the PIP Framework and SMTA2 is such that the WHO may not be able to secure the promised benefits to distribute, and even if it could, there are still major logistical barriers to efficient distribution, especially in LMICs.<sup>40</sup> In this sense, in the lead-up to and during a pandemic, the PIP Framework can be seen to exist solely as an access framework, rather than an access *and* benefit-sharing framework.

The continued cooperation of LMICs with the GISRS during a pandemic is most certainly predicated on an acknowledgment that Member States retain sovereign rights over their influenza viruses, that those viruses will be tracked through the GISRS, and that Member States will be eligible to receive benefits. If, however, LMICs lose sovereign control over their viruses, the IVTM is suspended by the WHO, and the force majeure clauses in the SMTA2s mean that vaccine manufacturers can wriggle out of any legal obligation to provide benefits, LMICs might be less inclined to continue to hand over their only bargaining chip so freely. In order to gain a measure of negotiating power during the course of a pandemic, LMICs might elect to stop sharing their viruses with the GISRS, hindering the WHO's ability to track the continuing spread and epidemiology of the virus. By this stage, however, the developed world will have already had advanced warning of the pandemic and started its own preparations.

The PIP Framework was supposed to have addressed the unfair distribution of pandemic influenza vaccines and antivirals. While it did secure both a level of legal legitimacy for the GISRS<sup>41</sup> and continued access to influenza samples from around the world, it could ultimately prove disastrously ineffective as a benefit-sharing instrument during a pandemic. Unless we critically evaluate the terms and conditions of the PIP Framework, particularly the SMTA2s, we are unacceptably relegating LMICs to the role of the "canary in the coal mine" for the developed world.

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