The Global Governance of Access to Countermeasures

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List of Abbreviations

BMGF	Bill & Melinda Gates Foundation
C-TAP	Covid-19 Technology Access Pool
CEPI	Coalition for Epidemic Preparedness Innovations
DG	Director General
DRC	Democratic Republic of the Congo
EU	European Union
FIND	Foundation for Innovative New Diagnostics
GDF	Global Drug Facility
GFATM	Global Fund to Fight AIDS, Tuberculosis and Malaria
GPMB	Global Preparedness Monitoring Board
HICs	High-Income Countries
ICG	International Coordinating Group on Vaccine Provision
IFRC	International Federation of the Red Cross
IP	Intellectual Property
LMICs	Low- and Middle-Income Countries
MERS	Middle East Respiratory Syndrome
MPP	Medicines Patent Pool
MSF	Médecins Sans Frontières
PAHO	Pan American Health Organization
PDP	Product Development Partnership
PIP	Pandemic Influenza Preparedness Framework
PPE	Personal Protective Equipment
R&D	Research & Development
SARS-CoV-1	Severe Acute Respiratory Syndrome-Coronavirus
UNICEF	United Nations International Children's Fund
UNOPS	United Nations Office for Project Services
US CDC	United States Centers for Disease Control and Prevention
US FDA	United States Food and Drug Administration
US FDA EUA	United States Food and Drug Administration Emergency Use Authorization
WHA	World Health Assembly
WHO	World Health Organization
WHO EUL	World Health Organization Emergency Use Listing
WHO PQ	World Health Organization Prequalification
WTO	World Trade Organization

1. Introduction

Access to countermeasures is critical for preventing, detecting and responding to disease outbreaks that may escalate into health emergencies. We use "countermeasures" to refer to personal protective equipment (PPE), therapeutics, diagnostics and vaccines. Not only are countermeasures necessary for direct response, such as protecting health workers or treating patients, they can also ease public panic, guide government responses, and restore economic and social activity.

Ensuring "access" – that countermeasures reach people in a timely manner, in adequate volumes, at acceptable levels of quality and at affordable prices – requires concerted international action. No country is self-sufficient in the research, development and production of all countermeasures. Lower-income countries, smaller (even wealthy) countries, and/or those without domestic manufacturing capacity for any given product face heightened difficulties securing access.

These challenges reach far beyond the health sector. Addressing them will often require engagement from ministries of finance, trade, research/science & technology, defence and industrial development – and indeed, heads of state. They touch on states' core interests in protecting their people's health and security, and in competing globally for economic resources and political influence. Countermeasures need to be understood as a strategic asset that states may share or hoard, not only according to public health logic, but also to pursue their global geopolitical interests [1,2]. Strong, principled, high-level leadership is necessary to ensure global access.

Current international frameworks governing access to countermeasures are thin, gap-ridden or simply non-existent. They largely rest on informal norms and voluntary funding, rather than binding rules or financing commitments. Strengthening global governance in this area will be difficult, especially with the rise of nationalism in influential countries [3] and weakened multilateralism. But failure to do so will mean prolonged pandemics, widescale and avoidable suffering, and heightened risk of future disasters.

Equitable access to countermeasures has been a major challenge in the Covid-19 pandemic, and high on the global political agenda. It was the central focus of the April 2020 UN General Assembly resolution 74/274 [4] and a contentious issue in the May 2020 World Health Assembly resolution [5] on Covid-19. Many new initiatives have been launched, including the Covid-19 Therapeutics Accelerator, Access to Covid-19 Tools Accelerator (including the Covid-19 Vaccines Global Access (Covax) Facility), European Union-led pledging conferences, WHO Technology Access Pool, UN Technology Access Partnership, regional, bilateral and private initiatives. These efforts all hold promise, but also raise many questions.

This paper analyses the global "system" for access to countermeasures. It aims to offer conclusions *broadly* relevant for preparedness. It does not provide an in-depth analysis of current Covid-19 access initiatives, but rather, seeks to discern what the current developments might mean for longer-term preparedness. This paper highlights eight key global governance challenges relevant for outbreaks in general, identifies areas of progress over the past 10-20 years, and suggests three priorities for high-level advocacy from the GPMB towards global leaders.

2. Main global governance challenges, progress and proposals

a) Challenge 1: Building access into the R&D process

We limit this discussion to how decisions made in the upstream R&D process can affect access downstream (this paper should be considered alongside the R&D paper).

Countermeasures are frequently developed in response to, rather than in anticipation of, outbreaks. This is often unavoidable, as even repurposed (let alone new) drugs cannot be proven to be safe and effective, nor can vaccines and diagnostics be developed, until after novel pathogens have been identified. Even for known pathogens, clinical trials are difficult or impossible to conduct until a sufficient number of infections has occurred. These features of countermeasure R&D mean that inevitably there will be time lags in development, and especially in the earlier stages of an emergency, uncertainty on product performance and scarcity of supply. It also implies heightened challenges for ensuring products are adapted for use in resource-poor settings, as the rush to identify any workable technology means other criteria (e.g. thermostability, low cost of goods, ease of administration) are likely to take lower priority.[1]

For example, the types of technologies pursued in vaccine R&D (e.g. live attenuated, DNA/RNA, or subunit vaccines) strongly affect ease of industrial scale up and cost of goods down the line [4]. Furthermore, traditionally, R&D policies (i.e. intellectual property, research funding) have focused on encouraging inventions, but not necessarily on ensuring widespread global access to them. Tension between these joint goals persists.

- **Progress:** There has been growing experience over the past two decades in how to integrate affordability and availability *ex ante* into the R&D process, rather than addressing these issues *ex post*. Some research funders, including the Bill and Melinda Gates Foundation (BMGF) and Wellcome Trust, have adopted access policies for grantees [6,7], the implementation of which offer examples of how funders can build access into their grants [7]. Product development partnerships (PDPs) for neglected diseases have included pricing, registration and supply conditions into contracts with firms engaged in R&D and manufacturing [8,9]. However, with the important exception of the Coalition for Epidemic Preparedness Innovations (CEPI) [10,11], access provisions have not regularly been incorporated into countermeasure R&D. Rather, they have been a somewhat unique feature of neglected disease R&D.

- **Proposals for consideration**: Recognizing that countermeasures entail significant costs and risks, public and philanthropic funders have frequently paid for early-stage R&D (i.e. research conducted in academic or public labs), and de-risked and subsidized the private costs borne by firms. For example, about $7.7 billion in public funding was mobilized for all stages of Covid-19 drug, vaccine and diagnostic R&D in the first half of 2020 [12] (comparable figures for private investment are not publicly available). This degree of engagement provides an important point

[1] For example, the rVSV-ZEBOV Ebola vaccine requires a heavy cold chain, and remdesivir (for Covid-19) was initially developed as an injectable requiring a clinical setting.

of leverage at which research funders can require up-front access commitments from developers and negotiate into funding contracts *ex ante* access provisions on IP management (see 2(g) below), sharing clinical trial data, technology transfer, supply, registration and pricing. Funders can also facilitate innovation by disallowing exclusive licensing of upstream or platform technologies.

As emphasized by the GPMB [13], securing access will require significant public funding beyond R&D alone. The greater the funding available, *ceteris paribus*, the easier it will be to secure these commitments. Given the large sums involved and the high public interest in the outcomes, transparency of these arrangements is critical for maintaining public trust. Requiring public disclosure of key information such as private R&D investments, manufacturing costs, and pricing can help to establish a fair division of risks and rewards borne by public and private actors. As access provisions and transparency in research funding contracts are a departure from standard practice, GPMB advocacy is needed to shift from business-as-usual.

Finally, Covid-19 has demonstrated the value of having a pre-established international pooled R&D fund for countermeasures with access conditions attached – that is, CEPI. Not only was CEPI quickly able to mobilize funding for Covid-19 related vaccine R&D and manufacturing, its grantees (such as the University of Oxford) have international access obligations. Evaluation of the real-world efficacy of these access provisions will be critical.

Ad hoc mobilization of funds to respond to each outbreak is slow and inefficient. Public funds from a single country alone are less likely to prioritize international access. Strengthening global preparedness therefore requires putting in place standing arrangements for pooled international funds covering the full range of countermeasures (beyond vaccines) with strong access provisions.

b) Challenge 2: Inadequate global and national supply

Global: The unpredictable timing of disease outbreaks makes it difficult to ensure that adequate volumes of countermeasures are manufactured globally. Even after technologies are developed, limited evidence about their performance can hinder manufacturing scale-up until there is greater clarity on which technologies countries should purchase, and subsequently, where reliable demand can be expected. (We exclude from the scope of this paper challenges relating to the selection of countermeasures when multiple options are available, where WHO guidelines play a clearly established role.)

Once outbreaks occur, demand for relevant technologies easily spikes far beyond supply. Manufacturing of pharmaceuticals, diagnostics, and vaccines has become increasingly concentrated in a few countries over the past decade, with India and China playing a growing role; this has allowed for efficient large-scale, low-cost manufacturing, but also heightened risks of supply ruptures [14]. Covid-19 has starkly illustrated both these challenges [15]. The rapid spread of the virus has created a simultaneous upsurge in global demand for scarce supplies of countermeasures,

giving rise to competition between (and even within) countries and export bans in producing countries seeking to ensure domestic populations are protected as a priority. It has also highlighted the fragility of global supply chains, when manufacturers of raw materials (e.g. chemicals for diagnostics and pharmaceuticals) and finished products (e.g. medical masks) in China slowed production in early 2020, followed by manufacturers elsewhere as the epidemic spread. Standard tools to ensure adequate supply, such as demand forecasting or advance purchase orders, have proven insufficient. Supply constraints may ease in later stages of an emergency, and stockpiles can then be created (see 2(e)), but action is needed to reduce the time delay to reach adequate supply.

National:[2] Countries without pre-existing manufacturing capacity (the majority), lower-income countries and/or smaller countries face difficulties competing as buyers on the global market. For Covid-19, stiff competition among countries for a limited supply of countermeasures has led to bidding wars [16–18] and priced many actors out of the market [15,19], to the point where intelligence agencies and militaries have become openly involved with procurement [20,21].

Export restrictions can further limit access to both raw materials and finished products. During the 2009 H1N1 pandemic, Australia and Canada restricted vaccine exports to meet domestic demand first [22]. An even broader array of export restrictions has been imposed in response to Covid-19. By August 2020, at least 94 countries had imposed export restrictions on a range of goods, including PPE, medical equipment (e.g., ventilators), therapeutics, and diagnostics, as well as some food products and raw materials [23]. For example, India restricted exports of over two dozen active pharmaceutical ingredients, antiseptics, PPE, and ventilators [23]. Similarly, the EU restricted exports of PPE to states outside the bloc, providing legal justification for such restrictions while calling for solidarity within the block [24,25].

- **Progress:** Regarding export bans, criticism and exhortations at global level have (to date) yielded little concrete progress. Trade rules generally include flexibility to impose restrictions in emergencies [26]. Raising concerns in dispute settlement proceedings at the World Trade Organization, for example, takes years with uncertain outcomes. The strong political incentive to restrict countermeasure exports in emergencies will persist. The EU's recent success in easing export bans within the continent suggests regional approaches may be more promising, though still by nature limited.

  International investments in technology transfer increased capacity to manufacture pandemic influenza vaccine in multiple regions, increasing from 1.5 billion to 6.3 billion doses from 2006-2015.[3] Outside of influenza, however, little progress has been made. Rather, the growing

[2] National supply chains fall outside the scope of this paper's focus on transnational challenges requiring improved governance.

[3] Global capacity has increased more than four times since 2006 and the start of the WHO's Global Action Plan (GAP) for Influenza Vaccines [27]. In 2006, it was estimated that global capacity was 500 million doses of seasonal vaccine and 1.5 billion doses of pandemic vaccine; by 2015, it had increased to 1.467 billion doses of seasonal vaccine and 6.372 billion doses of pandemic vaccine. During the 10-year duration of the GAP, its technology transfer initiative provided funding to 14 vaccine manufacturers in developing countries, leading

concentration of manufacturing has increased the risk of shortages of even regularly used medicines. Interest in local production has grown in some countries, which have invested in national/regional pharmaceutical manufacturing capacities to reduce dependence and increase security of supply [29]. Six international organizations launched a joint initiative on local production at the 2019 WHA [30]. Reliable, timely information on production capacities and volumes remains difficult to find, though efforts to improve this situation have been launched [31].

- **Proposals for consideration:** Strengthening preparedness to address supply challenges will require addressing both international rules and production capacities. The GPMB should advocate for intergovernmental agreements to manage countermeasure export restrictions, at a minimum within regions or other country groupings. Compliance with such rules will be easier if there is adequate production capacity regionally and globally. The GPMB should therefore advocate for building more redundancy – and thereby resilience – into the system by investing in countermeasure production capacity (and facilitating the requisite technology transfer when relevant), including surge capacity for emergencies.[4] Countries could make funding contributions to build regional production capacity conditional upon guarantees that they could access supply when needed. Success with influenza vaccines is an important precedent, but is somewhat unique in that production facilities can manufacture seasonal influenza vaccines continuously (stay "warm"), and pivot to pandemic influenza vaccine when the occasion arises. For other pathogens and for non-vaccine countermeasures, analogous approaches need to be identified. Paying for excess capacity will largely fall to the public sector and should be considered a societal investment in preparedness. Finally, the GPMB could play a key monitoring role by calling for the creation of centralized information sources mapping and tracking production capacities, as has been done for artemisinin and antiretrovirals (see 2(e)).

c) Challenge 3: Ensuring quality products

Emergencies strain quality assurance systems. Quality assessment of a wide array of countermeasures may become less stringent in urgent situations and/or hit delays. Early warning systems can easily be overwhelmed. Low-resource settings may be particularly vulnerable to substandard or falsified products, particularly when there are shortages [33]. The development of new technologies, such as complex vaccines, pose new challenges for regulators who may not have familiarity with or procedures to assess novel production processes.

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to six of these countries gaining local licensure to produce local vaccines [28]. Nevertheless, the majority of vaccine production remains in high-income countries – 17 manufacturers in LMICs countries have a combined capacity of 450 million doses of seasonal vaccine; the other 1.017 billion doses are from manufacturers in high income countries [27].

[4] In April 2020, the Netherlands and Sweden raised the possibility of negotiating a new agreement on trade in "essential health goods" at the WTO [32]; further details were not available at the time of writing.

Yet without quality assurance, risks to individuals and health systems grow (e.g. when diagnostics give false positives and negatives), people can be harmed (e.g. by substandard or falsified medicines), and the public can lose trust in technologies (e.g. exacerbating vaccine hesitancy).

Covid-19 has highlighted these challenges. The rapid development of many new diagnostic tests coupled with limited capacity of regulatory authorities has produced bottlenecks. In-person inspection of manufacturing plants has been hindered by travel restrictions or quarantine policies [34]. Contamination of the US CDC's diagnostic kits reportedly delayed the roll-out of testing across the US in early 2020 [35]. There have been reports of substandard PPE and hand sanitizer [36–38], black market remdesivir and tocilizumab sales [39], and falsified dexamethasone [40]; such reports seem likely to grow as the epidemic progresses and evidence on therapeutics develops.

- **Progress:** Emergency use of investigational interventions or off-label use (e.g. WHO's EUL and US FDA's EUA) have increased flexibility by regulatory authorities in emergencies, although robust debate remains about the appropriate balance between speed and risk, and political influence on technical regulatory decisions [41]. The WHO Prequalification (PQ) and Collaborative Registration Procedure [42] facilitate national regulatory review and international procurement; however, WHO PQ has been limited to a short list of health conditions of interest to donors. Non-state actors can also support regulatory authorities: by August 2020, the Foundation for Innovative New Diagnostics (FIND, a PDP) had published performance data on over 50 Covid-19 diagnostics in coordination with WHO [43,44]. International and regional networks can facilitate regulatory cooperation, such as the African Vaccine Regulatory Forum, which strengthened national capacities and harmonized standards to accelerate review of the Ebola vaccine [45], or the International Coalition of Medicines Regulatory Authorities, which is facilitating alignment on Covid-19 vaccine data requirements and trial design [46]. Finally, the WHO Global Surveillance and Monitoring System gathers and rapidly shares information between Member States when substandard or falsified products are detected. However, overall, it remains to be seen how well current arrangements can handle the expected upsurge of demands on regulatory systems.

- **Proposals for consideration:** Strengthening networks to increase information-sharing between regulatory authorities, and improve the coherence of assessment, licensure, control, and surveillance of countermeasures is still needed. Coordinated regulatory guidance (e.g. acceptable trial designs) and the sharing of key information (e.g. details on submissions, decision rationales, advice on approaches and methodologies) needs to be improved. Support for surge capacities of quality assurance bodies and early warning systems will be needed. Given that regulatory issues are often overlooked in global health security discussions, the GPMB could advocate for regulatory capacity to be seen as integral to preparedness and appropriately financed**.**

d) Challenge 4: Ensuring affordable prices

Emergencies create conducive economic conditions for price spikes and unaffordable pricing: demand for countermeasures increases rapidly and becomes less price-sensitive (inelastic), while

supply is often scarce in the early stages before production can ramp up (see 2(b) Challenge 2). The risks are even more acute under monopoly or oligopoly conditions, which frequently characterize therapeutics, vaccines, and to a lesser extent, diagnostics (e.g. those on closed platforms).

To counteract price-gouging (and the related practice of artificially restricting supply), some national authorities regulate prices of essential goods, restrict consumption,[5] and/or monitor supply during crises such as natural disasters and epidemics [47]. However, no such price-regulating or competition (anti-trust) authority exists at global level. Furthermore, affordability must be determined relative to a particular buyer, and will differ based on the level of wealth of a country, the extent to which public or private insurance shields individuals from bearing the full costs, and competing demands for resources (among other factors), making it difficult to assess or achieve for all [48]. For example, debates over Gilead's pricing of remdesivir for Covid-19 highlight deep disagreements on how prices should be set in health emergencies: Gilead argued that the price (for "developed countries") of 2340-3120 USD/patient (6 vials) was far below the costs savings due to earlier hospital discharge, while critics argued that public investment in the R&D and the cost of production justified a tenfold-lower price [49–51].

- **Progress:** There has been very little progress at the international level in addressing high prices for countermeasures particularly during emergencies. Reputational risk for sellers perceived to be profiting from disaster can be a powerful constraint. But 'naming and shaming' relies on the availability of timely, accurate information on prices, costs, and profits that is often unavailable; and it does not always work. There is no international organization with the mandate to track – let alone to regulate – countermeasure prices. Some companies have announced that they will price Covid-19 drugs and vaccines on a "no-profit" basis during the pandemic (e.g. AstraZeneca, Johnson & Johnson, and Novartis [52–54]), but questions have been raised on how costs or profits will be assessed and how long such commitments will last. Not all firms have made such commitments and one company (Pfizer) said its vaccine will be priced for-profit [55]. Licensing and technology transfer agreements with manufacturers in developing countries have been announced to expand supply (e.g., AstraZeneca/Oxford's agreements with India's Serum Institute and Brazil's Instituto Butantan) [52,56,57]. The degree to which they will lower prices depends on many factors, including degree of competition in each national market, cost of goods, and willingness of the producer or regulator to restrain pricing. The situation remains that there are no international rules or organizations with the mandate to ensure affordable prices for countermeasures.

- **Proposals for consideration:** In the absence of a transnational price regulating authority, international strategies to address the affordability of medicines have included: donations (usually time- and volume-limited), tiered pricing, facilitating competition, and information (we address international subsidies, pooled procurement, and IP licensing separately below, and

[5] For example, limiting consumer purchases of paracetamol or toilet paper.

exclude from the scope national strategies such as reference pricing). All these could be adopted for countermeasures. The most appropriate strategy depends on the particular technology and outbreak, but information is critical for all of these. The GPMB should therefore advocate for the creation of an observatory to increase information available on prices, which would provide key intelligence to monitor, understand and take action; gathering and analysing this information has proven feasible and valuable for vaccines [58] and medicines for HIV, tuberculosis (TB) and malaria [59]. The GPMB should also advocate for increased transparency regarding the costs to develop and/or manufacture countermeasures, which would provide objective benchmarks regarding the fairness of prices [51]. Member states called for significantly increasing the transparency of pharmaceutical markets in WHA Resolution 72.8 (2019) [60].

e) Challenge 5: Limited international pooled procurement, stockpiling & related financing dedicated to countermeasures

International procurement of countermeasures has been limited, and for most pathogens, international stockpiles of countermeasures do not exist. UNICEF, UNOPS and WHO have engaged in some procurement during emergencies, but for countermeasures there has been no large-scale equivalent to Gavi (for vaccines, via UNICEF), the Global Fund (GFATM), Unitaid or Global Drug Facility (GDF) (for drugs and diagnostics for HIV, TB and malaria). A key exception is the PAHO Strategic Fund (modelled off the PAHO Revolving Fund for vaccines), which is not limited to a disease or single technology, but is limited to the Americas.

By coordinating and/or pooling procurement internationally, these organizations are able to improve supply security and obtain more affordable prices for participating countries. Some operate on a cost-recovery basis, while others subsidize lower-income countries. They also carry out other key market-shaping functions: e.g. pooling fragmented demand, forecasting demand to help producers plan supply, supporting national procurement agents to use information on patent status (e.g. via the Medicines Patent Pool [MPP]) and quality (e.g. via WHO PQ), coordinating with WHO to ensure affordable supply can respond to changing normative guidance, monitoring R&D pipelines to plan for production and uptake of new products,[6] and in general, providing the global community with expertise on various aspects of global commodity markets. The absence of any analogous organization for outbreaks means no entity is continuously working to address access barriers between emergencies, nor developing in-depth knowledge of relevant market actors and forces.

[6] For example, dolutegravir was considered a potentially useful new treatment for HIV when it was in late-stage clinical development. The Medicines Patent Pool, GFATM and UNITAID worked with WHO so that when WHO guidelines changed to recommend use of dolutegravir for first- and second-line treatment, patent licenses had already been negotiated for generic manufacturers to have competitive, low-priced generic production ready and country-level grants were in place to procure the drugs.

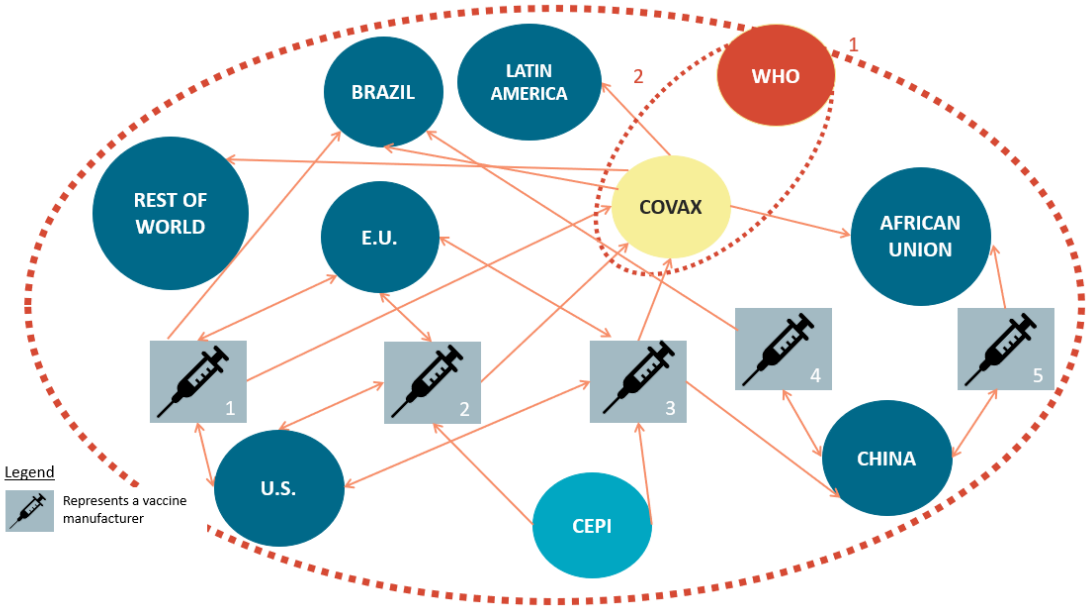
When an emergency strikes, *ad hoc* financing and organizational arrangements must be made with limited market intelligence.[7] Financing needs can be significant, but without organizations with pre-existing mandates on countermeasures, there is no centre of gravity for resource-mobilization.

- **Progress:** WHO, Gavi, GFATM, Unitaid [61], the European Union [62,63], African Union [64,65] and PAHO [66] have all become actively involved in addressing Covid-19 access challenges through pooled procurement and related financing. Gavi, GFATM and Unitaid are focusing on vaccines, diagnostics and therapeutics under the ACT Accelerator, respectively, and have pivoted from their original mandates to cover a new disease area and/or a broader group of countries. These developments raise two key questions. First, can or should these initiatives address the needs of all countries, or retain their previous focus on LMICs? High-income countries (HICs) generally procure for themselves, and have done so for Covid-19 health technologies, which can raise challenges for equitable global allocation (see discussion in next section 2(f) Rationing). Second, a key question arises regarding the role China will play as a potentially major supplier of health technologies. For example, of the thirteen Covid-19 vaccine candidates in Phase 2 or 3 as of July 2020, six involved a lab or firm in China. Similarly, of the more than 800 diagnostics being tracked by FIND's SARS-COV-2 Diagnostic Pipeline database, at least 110 are being developed by Chinese companies [67]. Whether China will supply vaccines through bilateral or multilateral agreements, or both, remains unclear. Overall, the global landscape is a patchwork of national, regional and global initiatives, as illustrated in Figure 1 below.

  Regarding stockpiles, international countermeasure stockpiles have been established in the past [68]: WHO manages a vaccine stockpile for yellow fever, cholera and meningitis (see 2(f)), and is entrusted to do the same should countermeasures for pandemic influenza be developed under the 2011 Pandemic Influenza Preparedness (PIP) Framework. WHO also managed the *ad hoc* stockpile of donated H1N1 vaccines created in the 2009 pandemic. Gavi stockpiles Ebola vaccines, as does the Global Polio Eradication Initiative for mOPV2 [69,70]. Each of these covers a vaccine specific to a pathogen. However, no international organization is mandated to stockpile and/or procure products across multiple pathogens of pandemic potential, nor for non-vaccine countermeasures, nor covering all countries [71].

[7] For example, on numbers and quality of suppliers, estimated demand, timeframes for production, and supply chains for raw materials.

Figure 1. COVID-19 Vaccine Supply Relationships – a simplified depiction[8]



- **Proposals for consideration:** Given the patchwork of procurement initiatives that has emerged for Covid-19, stewardship – that is, monitoring how well the sum total of these initiatives is addressing global needs and prompting action when the system falls short – is a critical governance function [72]. The GPMB may wish to take on this stewardship function itself, as all other major global health actors are directly involved in one or another procurement initiative. Furthermore, longer-term preparedness requires making clear arrangements for stockpiling of countermeasures. Stockpiles for all WHO-identified priority pathogens of pandemic potential could be established as global public goods that would be available to all countries, not only LMICs, and financed on a sliding scale. Further analysis is required to determine which organizations should be mandated to manage these stockpiles. Finally, the GPMB should advocate for clear arrangements for pooled international procurement of countermeasures in future emergencies to be made part and parcel of preparedness. The experience with Covid-19 will generate important learning regarding the best approaches.

[8] Figure 1: This figure is a simplified depiction of the multiple bilateral and multilateral arrangements for Covid-19 vaccine access, based on publicly available information as of August 2020. Procurement and distribution of Covid-19 vaccines is likely to be fragmented – with multiple states and clubs acting to acquire vaccines for certain populations. While the WHO has put forward a draft Global Allocation Framework to provide guidance on how vaccines could be equitably allocated worldwide, it is not a legally binding framework that states have agreed upon and it remains unclear to what extent states, vaccine producers, or others will adhere to its guidance (see possibilities 1 and 2 in the red dotted line). Some actors have funded vaccine R&D, indicated by an arrow from the actor to a firm. Some are procuring vaccines directly from firms, indicated by an arrow from the firm to the state. And some states have done both, indicated by a bi-directional arrow.

f) Challenge 6: Rationing access to scarce products internationally

The scarcity of countermeasures, particularly at the earlier stages of an emergency, implies the need for rationing. But who should get priority access when demand outstrips supply? Experience suggests it will be law of the jungle unless more equitable, structured arrangements are made.

During the height of panic in 2009, wealthy countries secured most of the world's H1N1 vaccine supply. Only after it became clear that H1N1 was relatively mild did those countries, whose populations were then less willing to be vaccinated, donate unused vaccines to WHO for developing countries; those vaccines did not arrive until 2010. Looking back, WHO DG Margaret Chan noted that "Vaccine supplies would have been too little, too late, with large parts of the developing world left almost unprotected" [73].

In 2014, only small supplies of experimental therapies were available for Ebola; stocks were reserved for international actors but very few reached nationals of the three hardest-hit West African countries [74]. WHO's ethics advisory panel opined that experimental therapies could be offered to patients, but did not reach agreement on who should get priority access [75]. These are complex, difficult questions at national level; ethics-based rationing between countries may be even more challenging, and very tough to enforce. Yet without explicit governance arrangements to prioritize access to supply, rationing will happen *de facto* – without clear principles or legitimate processes.

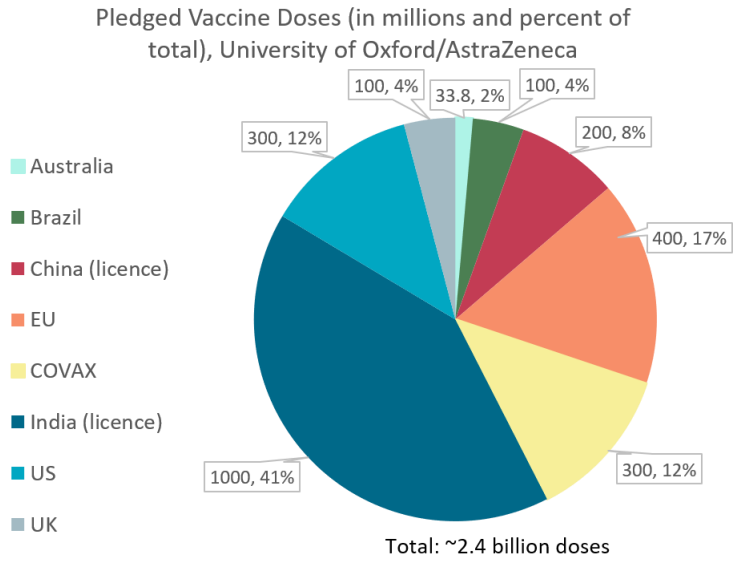
- **Progress:** Relevant governance arrangements have been developed for select vaccines. The International Coordinating Group on Vaccine Provision (ICG) was established by IFRC, MSF, UNICEF and WHO in 1997 initially to manage an international stockpile of meningitis vaccines, later expanded to cholera and yellow fever vaccines [71]. Upon country request, the ICG approves the release of vaccines from the stockpile conditional upon certain criteria.[9] While the ICG is not explicitly asked to ration between countries, this has become necessary when demand exceeds supply, e.g. during the 2016-7 simultaneous yellow fever outbreaks in Angola, Brazil, and DRC [76]. ICG governance has recently been reformed to make it more transparent and accountable [77]. The PIP Framework also established principles for allocating countermeasures provided to WHO in the event of an influenza pandemic. Concrete application of principles is to be made by "experts with transparent guidelines."[10] However, this priority-setting system has not yet been tested.

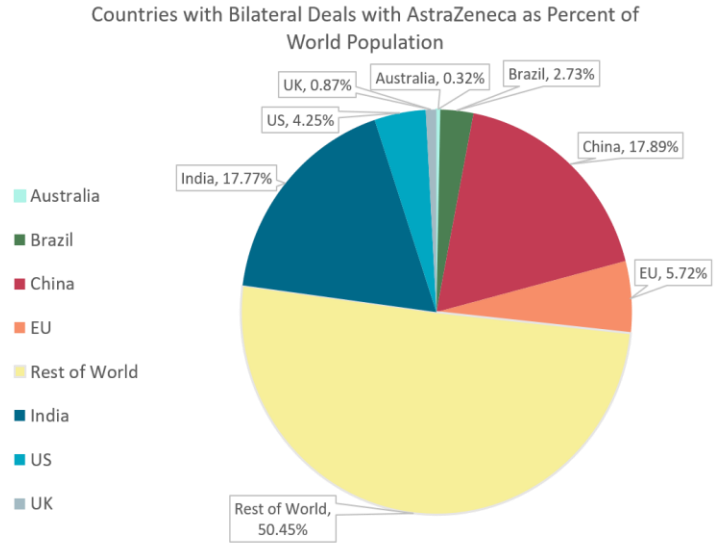
[9] For example, plans for mass vaccination, ability to conduct a vaccination campaign and adequate storage.
[10] Guiding Principles for use of PIP Partnership Contribution "Response" Funds (October 2014): "PIP Framework section 6.0.2 (iii) prioritize important benefits, such as and including antiviral medicines and vaccines against H5N1 and other influenza viruses with human pandemic potential as high priorities, to developing countries, particularly affected countries, according to public health risk and needs and particularly where those countries do not have their own capacity to produce or access influenza vaccines, diagnostics and pharmaceuticals. Prioritization will be based on assessment of public health risk and need, by experts with transparent guidelines;' ….Criteria to allocate benefits: Development of criteria will be based on assessment of public health risk and need, by experts with transparent guidelines, provided in the Framework (see above). This will require information about, inter alia, the level and extent of disease transmission, clinical and virological characteristics of the pandemic virus, its spread, and the development status of countries. Additionally, at the time of the pandemic event, updated information on the production capacities of

Finally, WHO released ethical guidance on how to approach rationing for Covid-19 countermeasures at both national and international levels [79]. The key question is how this guidance will be operationalized. In June, WHO published the draft "Global Framework to Ensure Equitable and Fair Allocation of COVID-19 Products" [80] with an initial focus on vaccines. As depicted in Figure 1 above, it remains unclear what proportion of global vaccine supply may be governed by this framework, whether total supply or only that handled by the Covax facility. Concerns have also been raised regarding the possibility that within Covax self-financing countries would have preferential access over donor-financed LMICs, and regarding the extent to which the WHO equitable allocation framework would apply [81]. Experience to date with one of the most advanced vaccine candidates, from Oxford/AstraZeneca, suggests that countries with the resources or production capacity to secure early supply will take a disproportionate share of production, leaving a fraction for the rest of the world, as illustrated in Figure 2 below. Similar challenges are likely to arise for other products.

manufacturers of pandemic products will be necessary. Allocation of benefits will also take into account national pandemic preparedness plans, e.g. regulatory capabilities and plans for deployment of vaccines, antivirals, diagnostics and other pandemic-related products" [78].

Figure 2.[11] Doses vs Population: Case study Oxford/AstraZeneca vaccine candidate





- **Proposals for consideration:** The GPMB should advocate for the application of WHO's ethical allocation guidelines to the global supply of countermeasures, not merely a subset of it. GPMB could track how well relevant actors adhere to those guidelines, and recognize those that

[11] Figure 2: this figure depicts the proportion of vaccines going to individual countries vs those allocated through the multilateral Covax facility, compared to population size, using the Oxford/AstraZeneca vaccine candidate as a case study. The figure is based on publicly available information as of August 2020 [82–88]. News reports have also indicated an arrangement between AstraZeneca and a South Korean company to manufacture the vaccine candidate; however, at the time of publication, details were not available on the number of doses covered by this agreement [89].

do, while naming and shaming those that do not, such as countries that hoard supply. All decision-makers with influence over the allocation of countermeasures should be asked to publicly justify their policies and decisions based on ethical principles. Beyond the Covid-19 crisis, future preparedness will require that governments agree *ex ante* upon rules or principles for international rationing of scarce countermeasures. Transparent and accountable governance mechanisms for rationing will also need to be established for any international stockpiles.

Transversal issues

This section covers two issues that cut across more than one of the six challenges identified above: intellectual property management and pathogen- and benefit-sharing.

g) Challenge 7: Intellectual property management

There is a vast literature and robust public debate on how IP can best be managed to achieve the joint societal goals of innovation and access to technologies [90].[12] This brief assessment focuses on IP management for access to countermeasures.

IP rights, particularly patents, provide incentives for countermeasures innovation by granting time-limited monopolies that allow firms to recoup their R&D investments through product sales. However, monopolies can pose a number of challenges in emergencies, including limiting the number of manufacturers and countries that can supply a product and concentrating sellers' market power when the risk of abusive pricing is high (see 2(d)). Monopolies can also slow down scientific progress and follow-on innovation if rights-holders restrict others from using patented knowledge.[13]

In addition, patents alone will not drive sufficient private investment into R&D for outbreaks, because of high uncertainty regarding the market – e.g. if, when, and how many people will need a therapeutic or vaccine.[14] Therefore, public and philanthropic R&D funding often plays a much larger role for countermeasures than for standard commercial R&D, with the defence sector an important player (see 2(a)). Nevertheless, it has been standard practice that firms retain patent monopolies on the end products. Global access provisions in IP licenses or research funding contracts has not been the norm for countermeasures, and changing these practices has not been easy. For example, as a major funder of vaccine R&D for pathogens of pandemic potential – with global access a core objective – CEPI has wrestled with finding an access policy that both public interest stakeholders and commercial partners find acceptable [11].

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[12] See literature syntheses across a range of topics at the website of the Knowledge Network for Innovation and Access to Medicines, a project of the Global Health Centre: https://www.knowledgeportalia.org/

[13] One response to this concern has been the creation of READDI - Rapidly Emerging Antiviral Drug Discovery Initiative - an open science drug discovery partnership launched to develop drugs in anticipation of future viral pandemics.

[14] Market dynamics for PPE and diagnostics are likely to differ from those for drugs and vaccines since PPE has uses outside of outbreaks and diagnostics can be developed much more quickly and at lower cost than drugs and vaccines.

The Covid-19 emergency seems to have shifted attitudes quickly regarding patent monopolies for countermeasures [91]. In the first half of 2020 alone, a number of high and middle-income countries amended their laws or policies to facilitate the granting of compulsory licenses.[15] Israel issued a compulsory license for lopinavir/ritonavir (LPV/r), an HIV drug then being tested for potential efficacy against SARS-COV-2. Shortly after, the patent holder Abbvie sent a letter to the MPP announcing it would no longer enforce its patent rights on the drug [92]. Novartis announced it would make available its IP related to the candidate therapeutic hydroxychloroquine [93].

Compulsory licensing is an important tool for governments to enable local production or importation of a product when not available on acceptable terms from the patent-holder. It will be especially effective for rapidly expanding access to products for which alternate supply exists or can quickly be brought online, such as small molecule drugs. But it cannot address all access challenges. For technologies where know-how, regulatory review of production quality (e.g. injectables), time lags, and/or economies of scale (e.g. vaccines) are important for production, the cooperation of the patent-holder for technology transfer and data-sharing is important for rapid results. Compulsory and voluntary measures – carrots and sticks – can complement each other for equitable access.

- **Progress**: In April, the MPP Board extended its mandate to negotiate voluntary licenses for Covid-19 related health technologies. A number of prominent US universities announced a Covid-19 Access Framework [94] with licensing principles for technologies related to the pandemic. A number of companies (mostly non-pharmaceutical) adopted the Open Covid Pledge to make intellectual property available free of charge for use during the pandemic [95]. WHO and about 40 Member States issued a Solidarity Call to Action [96] for the voluntary sharing of Covid-19 health technology related knowledge, IP, and data and a related Covid-19 Technology Access Pool (C-TAP) [97]. The initiative draws on existing mechanisms, such as the MPP and the UN Technology Bank-hosted Technology Access Partnership, launched in May to scale up local production in developing countries of Covid-19 countermeasures [98]. These initiatives hold promise, but a key question remains how many research funders and technology-holders will participate.

- **Proposals for consideration:** The GPMB could advocate for patent-holders to make their IP available through the WHO C-TAP, which would both reduce potential patent barriers to innovation and expand access by allowing for countermeasure production by multiple firms in different countries worldwide. Where patent-holders are unwilling to make IP available, the GPMB could encourage governments to take all necessary measures to facilitate access including but not limited to compulsory licensing, as is well-established under international law [99]. Governments and other funders could also reward inventors through alternate means, such as lump-sum payments (e.g. prizes or patent buyouts) to patent-holders in exchange for monopoly rights, allowing multiple suppliers to manufacture products [100]. Both for Covid-19 and future emergencies, the GPMB should encourage research funders and organisations out-licensing

[15] These countries are Canada, Chile, Colombia, Ecuador, France, Germany, Hungary, Israel. See details at https://www.knowledgeportalia.org/Covid-19.

upstream research (e.g., universities) to require pro-access IP management as a condition of receiving funding/licenses, and retain and use "march-in" rights if commitments are not met (see 2(a)). For preparedness more broadly, the GPMB should advocate for clear access and IP policies to be required for any entity mandated with facilitating countermeasure R&D or access.

h) Challenge 8: Pathogen- and benefit-sharing

Since at least 2007, when Indonesia decided to suspend international sharing of H5N1 influenza samples in order to negotiate better access to the resulting vaccines, ensuring pathogen- and related benefit-sharing (PBS) have been important global governance challenges [101]. This sub-section is based on not yet published empirical research conducted by three of this paper's co-authors on the drivers of PBS for outbreaks.

The timely international sharing of pathogens is critical, particularly in the early phases of an outbreak, to characterize new or mutating pathogens and to accelerate countermeasure R&D. Pathogen samples are also valuable for source countries, potentially facilitating access to countermeasures and other benefits. Yet, with the important exception of influenza, there are no clear international governing frameworks to ensure reliable, timely and equitable PBS.

What used to be a largely unregulated practice among scientists - with personal relations and trust playing a large role – has become more contested and legalized. Countries claim sovereignty over pathogens based on the UN Convention on Biological Diversity (CBD) and its 2011 Nagoya Protocol. Nagoya came into force in 2014, and many countries have only recently implemented it into their national legislation. These rules give more leverage to the providing state to seek "benefits" in exchange for access to pathogen samples, and have reportedly started to generate delays and uncertainty in pathogen-sharing. States have implemented Nagoya with and without specific provisions for pathogens or public health. Furthermore, our research found that the very concept of benefit-sharing is considerably less mature than that of pathogen-sharing. Understandings of what is or should be considered a "benefit" are diverse, ranging from access to research results to co-authorship in publications, from royalties to access to countermeasures.

Intergovernmental discussions to better govern PBS are underway in parallel within WHO and the CBD, but moving slowly. PIP, which is well-regarded but has not yet been tested in a pandemic, has been put forward as a possible model for other pathogens, but without concrete proposals.

The rapid development and increasing availability of genetic sequencing data (GSD) on pathogens creates new uncertainties. Nagoya and PIP explicitly only cover physical substances, leaving an absence of clear international rules regulating GSD. Researchers frequently share GSD on publicly available databases (mostly GISAID and GenBank), which facilitates understanding of pathogens and countermeasure development. However, countries may become less willing to share GSD if it is not linked (as physical samples can be) to benefit-sharing. GSD has become a contentious issue among PIP stakeholders. For the time being, GSD cannot fully substitute for physical samples, but it risks disrupting the delicate balance struck within PIP. Clear rules for GSD are needed.

Covid-19 has heightened attention again to PBS challenges. Chinese researchers publicly shared GSD in early January 2020, but there appear to have been delays in the sharing of physical samples internationally. The way the global community handles pathogen-sharing and access to countermeasures in Covid-19 can either build or destroy confidence. Reliable, equitable access to countermeasures for all countries would ease the path towards agreement on future frameworks to govern PBS, whereas failure to do so risks further polarization and gridlock.

- **Progress**: PIP was a landmark achievement for addressing PBS. However, despite calls to negotiate similar rules for other pathogens [74,102], there has been little movement since. The concerns raised by Nagoya implementation and the Covid-19 pandemic could provide a political push to bring key stakeholders to the negotiating table. GISAID was initially developed for influenza alone, but in January 2020 quickly adapted its platform to host SARS-COV-2 sequences; unlike other major databases, it requires users to agree to terms and conditions establishing ownership of the data, in principle allowing for future negotiation of related benefits. As of June 2020, GISAID hosted the highest number of publicly available SARS-CoV-2 sequences worldwide, six times more than any other database.[16]

- **Proposals for consideration:** The GPMB could advocate that, after years of foot-dragging, a group of committed stakeholders begin serious discussions on a global governance framework for PBS. Such a framework could not be negotiated within the health sector alone, however, but would also need to engage with Nagoya parties to secure a special status for pathogens, particularly in national implementing legislation. Rules and arrangements urgently need to be negotiated that streamline pathogen-sharing, and clarify and solidify benefit-sharing, striking a balance that is acceptable to both WHO's and Nagoya's stakeholders.

3. Discussion and Conclusions

Countermeasures have characteristics of global public goods – the existence of such technologies can strengthen global health security for all countries, but only if they can reliably expect to get access to them [105]. For many of the challenges identified here, lower-income, smaller and/or non-producing countries face particular disadvantages. But no country is entirely self-sufficient in the development and production of countermeasures. And all countries can be affected if an outbreak continues to spread anywhere in the world.

[16] As of June 18, 2020, 47,645 SARS-CoV-2 genomes had been uploaded to GISAID by researchers in 97 countries or territories; 7,280 had been uploaded to GenBank by researchers in 49 countries or territories [103,104]. Just five countries - the United Kingdom, the United States, Australia, the Netherlands, and Spain accounted for 75% (35,808/47,645) of all SARS-CoV-2 genomic sequences shared on GISAID, with relatively few from some current or past hotspots, such as Italy (157), Brazil (185), or Mexico (29). It is notable that GISAID appears to have become the preferred platform for GSD for SARS-CoV-2, hosting more than six times the number of genomes as GenBank; GISAID runs on a controlled open-access model that requires users to log into the site and agree to terms and conditions that establish ownership of the data, compared to GenBank, which does not.

Each of the eight challenges analysed above can impede access if unaddressed. Priorities among them will vary depending on the pathogen, stage of the outbreak, and specific technology. Yet across all of them, three overarching themes for preparedness emerge:

a. **Mandating organizations for countermeasures**: A relatively robust global ecosystem has been built to improve access to health technologies for HIV, TB, malaria, influenza, and maternal and child health. These have generally been conceived as part of development assistance, with a focus on LMICs. Covid-19 has highlighted the need to mandate organizations in advance to facilitate access to countermeasures, with the ability to address the needs of HICs as well as LMICs in an integrated manner. Two key lessons for future mandates emerge from CEPI: the value of a pre-existing international entity able to invest rapidly in R&D in response to a novel emerging pathogen; and the feasibility and potentially major payoffs of building access provisions into R&D funding. Both offer significant advantages over a country-by-country *ad hoc* approach to R&D and access. This type of preparedness needs to extend beyond vaccines, to include PPE, diagnostics and therapeutics. Further analysis is needed regarding the most appropriate organizations to take on future mandates on access to countermeasures, and how to strengthen access provisions to ensure they are the most effective.

b. **Negotiating international rules for access**: Political interest in access to countermeasures is currently high, but international norms and rules for access are either absent, weak, obscured within other rules, or displaced by corporate self-regulation. Neither innovation nor access to countermeasures are part of the International Health Regulations (IHR). IP rules include "flexibilities" for access, but access is not their core objective. Biodiversity rules are not adapted for health. There is a need, and unique window of opportunity now, to strengthen the framework of public international rules to ensure innovation with access. Topics covered in this paper for which formal or informal international rules are needed include: burden-sharing for R&D financing, access conditions on such financing, export restrictions, affordable pricing, technology transfer, principles for rationing, IP management, and PBS (including GSD). Any newly negotiated rules must co-exist and be coherent with existing regimes such as the IHR, CBD/Nagoya, IP, foreign direct investment, and human rights. Further analysis is required on the most appropriate normative instruments. But it is clear that negotiating international rules for innovation and access is an essential part of preparedness.

c. **Exercise stewardship over the system**: This analysis has found that the global "system" for access to countermeasures is fragmented in terms of information, rules, actors and technologies. In the current multipolar system characterized by the rise of nationalism, this fragmentation is likely to persist. There is an urgent need for an entity – perhaps the GPMB itself – to pro-actively exercise stewardship over the system to ensure that the whole is greater, and not less than, the sum of its disparate parts. Doing so requires much more "legibility" – increased investment in information and commitment to transparency is critical for guiding policies, targeting investments and building trust. Regular convening to agree upon organizational mandates and international rules, resolve differences and build consensus is a key stewardship function.

This brings us to our final **Proposal for consideration**: A forum is needed where diverse public and private actors may discuss and debate their respective problems and positions, build confidence and networks, mobilize resources, and find workable ways forward on specific concrete issues. The GPMB could advocate that WHO, alone or jointly with partners, convene stakeholders for focused dialogue on urgent or critical issues relating to innovation and access to countermeasures. A regular convening – rather than *ad hoc*, one-time meetings alone – would facilitate accountability and follow-up.

Covid-19 could be a turning point for access to countermeasures, but committed and forceful political leadership is necessary to turn the ship in the right direction. The GPMB can both provide and push for that leadership.

Works Cited

1 Moon S. The Vaccine Race: Will Public Health Prevail over Geopolitics? Glob. Chall. 2020.https://graduateinstitute.ch/communications/news/vaccine-race-will-public-health-prevail-over-geopolitics (accessed 20 Jul 2020).

2 Cohen Z, McGee L, Marquardt A. UK, US and Canada allege Russian cyberattacks on Covid-19 research centers. CNNPolitics. 2020.https://edition.cnn.com/2020/07/16/politics/russia-cyberattack-covid-vaccine-research/index.html (accessed 20 Jul 2020).

3 Bieber F. Is Nationalism on the Rise? Assessing Global Trends. *Ethnopolitics* 2018;**17**:519–40. doi:10.1080/17449057.2018.1532633

4 General Assembly Resolution 74/274. International cooperation to ensure global access to medicines, vaccines and medical equipment to face COVID-19 A/RES/74/274. 2020. https://undocs.org/en/A/RES/74/274

5 COVID-19 Response Draft Resolution proposed by Albania, Australia, Azerbaijan, Bahrain, Bangladesh, Belarus, Bhutan, Bolivia (Plurinational State of), Brazil, Canada, Chile, China, Colombia, Cook Islands, Costa Rica, Djibouti, Dominican Republic, Ecuador, El Salvador, Fiji, Georgia, Guatemala, Guyana, Honduras, Iceland, India, Indonesia, Iraq, Jamaica, Japan, Jordan, Kiribati, Maldives, Marshall Islands, Mexico, Micronesia (Federated States of), Monaco, Montenegro, Morocco, Nauru, Nepal, New Zealand, North Macedonia, Norway, Panama, Papua New Guinea, Paraguay, Peru, Philippines, Qatar, Republic of Korea, Republic of Moldova, Russian Federation, San Marino, Saudi Arabia, Serbia, Singapore, Sri Lanka, Thailand, the African Group and its Member States, the European Union and its Member States, Tonga, Tunisia, Turkey, Ukraine, United Kingdom of Great Britain and Northern Ireland and Uruguay. 2020. https://apps.who.int/gb/ebwha/pdf_files/WHA73/A73_CONF1Rev1-en.pdf (accessed 16 Jul 2020).

6 Bill and Melinda Gates Foundation. Bill and Melinda Gates Foundation Global Access Statement. Bill Melinda Gates Found. n.d.https://www.gatesfoundation.org/How-We-Work/General-Information/Global-Access-Statement (accessed 21 Apr 2020).

7 Wellcome Trust. Wellcome's approach to equitable access to healthcare interventions. Wellcome Trust. n.d.https://wellcome.ac.uk/what-we-do/our-work/access-healthcare-interventions/wellcomes-approach-equitable-access-healthcare-interventions (accessed 21 Apr 2020).

8 Drugs for Neglected Diseases Initiative (DNDi). 15 Years of Needs-Driven Innovation for Access: Key lessons, challenges, and opportunities for the future. Geneva, Switzerland: : DNDi 2019. https://www.dndi.org/wp-content/uploads/2019/10/DNDi_ModelPaper_2019.pdf (accessed 21 Apr 2020).

9 Foundation for Innovative New Diagnostics (FIND). Accessible pricing. FIND. n.d.https://www.finddx.org/pricing/ (accessed 23 Apr 2020).

10 CEPI. Why we exist. CEPI. n.d.https://cepi.net/about/whyweexist/ (accessed 21 Apr 2020).

11 Huneycutt B, Lurie N, Rotenberg S, *et al*. Finding equipoise: CEPI revises its equitable access policy. *Vaccine* 2020;**38**:2144–8. doi:10.1016/j.vaccine.2019.12.055

12 Policy Cures Research. COVID-19 R&D Tracker Update: 25 June 2020. Sydney, Australia: : Policy Cures Research 2020. https://s3-ap-southeast-2.amazonaws.com/policy-cures-website-assets/app/uploads/2020/07/09051858/COVID-19-RD-tracker-update1_25-June-2020.pdf

13 Global Preparedness Monitoring Board. The Global Preparedness Monitoring Board calls for a Scaled-Up Global Response to COVID-19: Estimated Costs and Funding Sources. Geneva, Switzerland: : GPMB 2020. https://apps.who.int/gpmb/assets/pdf/GPMB_6March2020statement.pdf (accessed 27 Apr 2020).

14 Turner T. COVID-19 and Drug Shortages: How to Prepare. Drugwatch.com. 2020.https://www.drugwatch.com/news/2020/04/06/covid-19-drug-shortages-how-to-prepare/ (accessed 27 Apr 2020).

15 Bradley J. In Scramble for Coronavirus Supplies, Rich Countries Push Poor Aside - The New York Times. N. Y. Times. 2020.https://www.nytimes.com/2020/04/09/world/coronavirus-equipment-rich-poor.html (accessed 21 Apr 2020).

16 Agence France-Presse. Solidarity? When it comes to masks, it's every nation for itself. RFI. 2020.http://www.rfi.fr/en/wires/20200403-solidarity-when-it-comes-masks-its-every-nation-itself (accessed 21 Apr 2020).

17 Okello C. Face masks from China intended for France 'hijacked' by US at the last minute. RFI. 2020.http://www.rfi.fr/en/europe/20200402-china-coronavirus-face-mask-france-stolen-us (accessed 21 Apr 2020).

18 Farrell H, Newman A. Will Governments Restrict Foreign Access to Pandemic Supplies? *Harv Bus Rev* 2020.https://hbr.org/2020/03/will-governments-restrict-foreign-access-to-pandemic-supplies (accessed 21 Apr 2020).

19 Diaz D, Sands G, Alesci C. Cost of protective equipment rises amid competition and surge in demand. CNN. 2020.https://edition.cnn.com/2020/04/16/politics/ppe-price-costs-rising-economy-personal-protective-equipment/index.html (accessed 21 Apr 2020).

20 Bergman R. Israel's Not-So-Secret Weapon in Coronavirus Fight: The Spies of Mossad. N. Y. Times. 2020.https://www.nytimes.com/2020/04/12/world/middleeast/coronavirus-israel-mossad.html (accessed 21 Apr 2020).

21 Barnes JE, Venutolo-Mantovani M. Race for Coronavirus Vaccine Pits Spy Against Spy. N. Y. Times. 2020.https://www.nytimes.com/2020/09/05/us/politics/coronavirus-vaccine-espionage.html (accessed 8 Sep 2020).

22 Moon S, Gordon R. Ensuring Vaccine Supply for the Next Pandemic Flu: Will the World Be Ready? Harvard Global Health Institute 2013. https://repository.gheli.harvard.edu/repository/10686/ (accessed 21 Apr 2020).

23 International Trade Centre. COVID-19 Temporary Trade Measures. Int. Trade Cent. Mark. Access Map. 2020.https://www.macmap.org/covid19

24 European Commission. Commission publishes guidance on export requirements for personal protective equipment. Eur. Comm. 2020.https://trade.ec.europa.eu/doclib/press/index.cfm?id=2123 (accessed 21 Apr 2020).

25 European Commission. Communication from the Commission to the European Parliament, the European Council, the Council, the European Central Bank, the European Investment Bank, and the Eurogroup: Coordinated economic response to the COVID-19 Outbreak. Brussels, Belgium: : European

Commission 2020. https://ec.europa.eu/info/sites/info/files/communication-coordinated-economic-response-covid19-march-2020_en.pdf (accessed 21 Apr 2020).

26 Pauwelyn J. Export Restrictions In Times Of Pandemic: Options And Limits Under International Trade Agreements. *SSRN* Published Online First: 18 April 2020. doi:10.2139/ssrn.3579965

27 McLean KA, Goldin S, Nannei C, *et al*. The 2015 global production capacity of seasonal and pandemic influenza vaccine. *Vaccine* 2016;**34**:5410–3. doi:10.1016/j.vaccine.2016.08.019

28 GAP Advisory Group. The ten years of the Global Action Plan for Influenza Vaccines. Geneva, Switzerland: : WHO 2016. https://www.who.int/influenza/GAP_AG_report_to_WHO_DG.pdf (accessed 27 Apr 2020).

29 Chaves LA, Chaves GC, Vianna MNS, *et al*. Medicines shortage in medical scientific journals: a literature review. *Physis Rev Saúde Coletiva* 2019;**29**. doi:10.1590/s0103-73312019290107

30 Saez C. Six International Organisations Pledge Collaboration On Local Production Of Medicines. Health Policy Watch. 2019.https://www.healthpolicy-watch.org/six-international-organisations-pledge-collaboration-on-local-production-of-medicines/ (accessed 27 Apr 2020).

31 Hammond E. VAXMAP - An Open Souce Map of COVID-19 Candidate Vaccines and Production Capacities. VaxMap. http://vaxmap.org/ (accessed 20 Jul 2020).

32 Permanent Representation of the Netherlands to the EU (@NLatEU). Netherlands at the EU on Twitter: "In the long run, we must think about managing the vulnerability of world trade and progress from the current crisis-management mode to lasting risk-management and risk-mitigation. Therefore, the Netherlands proposes to investigate an Essential Health Goods Agreement. Twitter. 2020.https://twitter.com/nlateu/status/1250801248682438658 (accessed 21 Apr 2020).

33 Newton PN, Bond KC. COVID-19 and risks to the supply and quality of tests, drugs, and vaccines. *Lancet Glob Health* Published Online First: 9 April 2020. doi:10.1016/S2214-109X(20)30136-4

34 World Health Organization. Impact of COVID-19 on Prequalification activities. WHO. 2020.https://extranet.who.int/prequal/news/impact-covid-19-prequalification-activities (accessed 27 Apr 2020).

35 Gupta YK, Meenu M, Mohan P. The Tamiflu fiasco and lessons learnt. *Indian J Pharmacol* 2015;**47**:11. doi:10.4103/0253-7613.150308

36 Su A. Faulty masks. Flawed tests. China's quality control problem in leading global COVID-19 fight. Los Angel. Times. 2020.https://www.latimes.com/world-nation/story/2020-04-10/china-beijing-supply-world-coronavirus-fight-quality-control (accessed 27 Apr 2020).

37 BBC News. Countries reject Chinese-made equipment. BBC News. 2020.https://www.bbc.com/news/world-europe-52092395 (accessed 27 Apr 2020).

38 Tur JK. With no government oversight, profiteering industries flood Indian markets with toxic sanitisers. The Caravan. July 11.https://caravanmagazine.in/health/with-no-government-oversight-profiteering-industries-flood-indian-markets-with-toxic-sanitisers (accessed 20 Jul 2020).

39 Pandey V. India coronavirus: Life-saving Covid-19 drugs sold on Delhi black market. BBC News. 2020.https://www.bbc.com/news/world-asia-india-53304160 (accessed 20 Jul 2020).

40 Hopper E. Fake pharmaceutical industry thrives in West Africa. BBC News. 2020.https://www.bbc.com/news/world-africa-53387216 (accessed 20 Jul 2020).

41 Food and Drug Administration. Coronavirus (COVID-19) Update: FDA expedites review of diagnostic tests to combat COVID-19. FDA. 2020.https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-expedites-review-diagnostic-tests-combat-covid-19 (accessed 27 Apr 2020).

42 't Hoen EFM, Hogerzeil HV, Quick JD, *et al.* A quiet revolution in global public health: The World Health Organization's Prequalification of Medicines Programme. *J Public Health Policy* 2014;**35**:137–61. doi:10.1057/jphp.2013.53

43 Foundation for Innovative New Diagnostics (FIND). FIND evaluation update: SARS-CoV-2 immunoassays. FIND. https://www.finddx.org/covid-19/sarscov2-eval-immuno/ (accessed 27 Apr 2020).

44 Foundation for Innovative New Diagnostics (FIND). FIND evaluation update: SARS-CoV-2 molecular diagnostics. FIND. https://www.finddx.org/covid-19/sarscov2-eval-molecular/ (accessed 27 Apr 2020).

45 African Vaccine Regulatory Forum. African Vaccine Regulatory Forum (AVAREF) Strategic Plan, 2018 – 2020: New Plan to Accelerate Product development and Access in Africa. World Health Organization Regional Office for Africa 2017. https://www.afro.who.int/publications/african-vaccine-regulatory-forum-avaref-strategic-plan-2018-2020-new-plan-accelerate (accessed 21 Apr 2020).

46 International Coalition of Medicines Regulatory Authorities. International regulators align positions on phase 3 COVID-19 vaccine trials. Int. Coalit. Med. Regul. Authorities. http://www.icmra.info/drupal/en/news/22june2020_2 (accessed 20 Jul 2020).

47 FindLaw. Price Gouging Laws by State. FindLaw. 2020.https://consumer.findlaw.com/consumer-transactions/price-gouging-laws-by-state.html (accessed 21 Apr 2020).

48 Moon S, Mariat S, Kamae I, *et al.* Defining the concept of fair pricing for medicines. *BMJ* 2020;**368**. doi:10.1136/bmj.l4726

49 O'Day D. An Open Letter from Daniel O'Day, Chairman & CEO, Gilead Sciences. 2020.https://www.gilead.com/news-and-press/press-room/press-releases/2020/6/an-open-letter-from-daniel-oday-chairman--ceo-gilead-sciences (accessed 20 Jul 2020).

50 Sagonowsky E. Gilead's remdesivir rescued from 'scrapheap' by taxpayers, who deserve a better price: lawmaker. FiercePharma. 2020.https://www.fiercepharma.com/pharma/gilead-s-remdesivir-rescued-from-scrapheap-by-taxpayers-who-deserve-a-better-price-lawmaker (accessed 20 Jul 2020).

51 Hill A, Wang J, Levi J, *et al.* Minimum costs to manufacture new treatments for COVID-19. *J Virus Erad* Published Online First: April 2020.http://viruseradication.com/journal-details/Minimum_costs_to_manufacture_new_treatments_for_COVID-19/ (accessed 20 Jul 2020).

52 AstraZeneca. AstraZeneca takes next steps towards broad and equitable access to Oxford University's COVID-19 vaccine. 2020.https://www.astrazeneca.com/media-centre/press-releases/2020/astrazeneca-takes-next-steps-towards-broad-and-equitable-access-to-oxford-universitys-covid-19-vaccine.html (accessed 15 Jul 2020).

53 Johnson & Johnson. Johnson & Johnson Announces a Lead Vaccine Candidate for COVID-19; Landmark New Partnership with U.S. Department of Health & Human Services; and Commitment to Supply One Billion Vaccines Worldwide for Emergency Pandemic Use. Johns. Johns. 2020.https://www.jnj.com/johnson-johnson-announces-a-lead-vaccine-candidate-for-covid-19-landmark-new-partnership-with-u-s-department-of-health-human-services-and-commitment-to-supply-one-billion-vaccines-worldwide-for-emergency-pandemic-use (accessed 16 Jul 2020).

54 Liu A. Novartis promises zero profit for 15 symptomatic COVID-19 drugs in low-income countries. FiercePharma. 2020.https://www.fiercepharma.com/pharma/novartis-promises-zero-profit-for-15-symptomatic-covid-19-drugs-low-income-countries (accessed 20 Jul 2020).

55 Shapiro E. Pfizer CEO Bourla Raises Expectations for COVID-19 Vaccine. *Time* 2020.https://time.com/5864690/pfizer-vaccine-coronavirus/ (accessed 16 Jul 2020).

56 Associated Press. Brazil signs deal with AstraZeneca to produce experimental coronavirus vaccine. Bus. Today. 2020.https://www.businesstoday.in/sectors/pharma/brazil-signs-deal-with-astrazeneca-to-produce-experimental-coronavirus-vaccine/story/408244.html (accessed 20 Jul 2020).

57 Indian Company Starts Mass-Producing Coronavirus Vaccines Before Trials. Things Consid. 2020.https://www.npr.org/2020/07/08/889112811/indian-company-starts-mass-producing-coronavirus-vaccines-before-trials (accessed 20 Jul 2020).

58 Cernuschi T, Gilchrist S, Hajizada A, *et al.* Price transparency is a step towards sustainable access in middle income countries. *BMJ* 2020;**368**. doi:10.1136/bmj.l5375

59 World Health Organization. Global Price Reporting Mechanism for HIV, tuberculosis and malaria. WHO. n.d.https://www.who.int/hiv/amds/gprm/en/ (accessed 27 Apr 2020).

60 Seventy-Second World Health Assembly. Improving the transparency of markets for medicines, vaccines, and other health products. Geneva, Switzerland: : World Health Assembly 2019. https://apps.who.int/gb/ebwha/pdf_files/WHA72/A72_R8-en.pdf (accessed 27 Apr 2020).

61 World Health Organization. The Access to COVID-19 Tools (ACT) Accelerator. 2020.https://www.who.int/initiatives/act-accelerator (accessed 20 Jul 2020).

62 European Commission. Coronavirus: EU grants €314 million to innovative companies. Eur. Comm. - Eur. Comm. https://ec.europa.eu/commission/presscorner/detail/en/IP_20_1007 (accessed 20 Jul 2020).

63 European Commission. Coronavirus research and innovation. Eur. Comm. - Eur. Comm. https://ec.europa.eu/info/research-and-innovation/research-area/health-research-and-innovation/coronavirus-research-and-innovation_en (accessed 20 Jul 2020).

64 Africa Medical Supplies Platform. Made in Africa. Afr. Med. Supplies Platf. https://amsp.africa/ (accessed 20 Jul 2020).

65 Massinga Loembé M, Tshangela A, Salyer SJ, *et al.* COVID-19 in Africa: the spread and response. *Nat Med* 2020;**26**:999–1003. doi:10.1038/s41591-020-0961-x

66 Pan American Health Organization. Countries in the Americas pool efforts to ensure access to COVID-19 vaccines - PAHO/WHO | Pan American Health Organization. PAHO.

2020.http://www.paho.org/en/news/14-7-2020-countries-americas-pool-efforts-ensure-access-covid-19-vaccines (accessed 20 Jul 2020).

67 FIND. SARS-CoV-2 diagnostic pipeline. FIND. https://www.finddx.org/covid-19/pipeline/ (accessed 8 Sep 2020).

68 The Global Fund. COVID-19. Glob. Fund. 2020.https://www.theglobalfund.org/en/covid-19/ (accessed 27 Apr 2020).

69 Global Polio Eradication Initiative. OPV Cessation – GPEI. Glob. Polio Erad. Initiat. n.d.http://polioeradication.org/polio-today/preparing-for-a-polio-free-world/opv-cessation/ (accessed 27 Apr 2020).

70 GAVI. Gavi Board approves new Ebola vaccine programme. 2009.https://www.gavi.org/news/media-room/gavi-board-approves-new-ebola-vaccine-programme (accessed 27 Apr 2020).

71 World Health Organization. International Coordinating Group for vaccine provision: Emergency Vaccine Stockpile. 2015.https://www.who.int/healthsystems/publications/SESSION2-ICG_vaccine_provisions_Emergency_Vaccine_Stockpiles.pdf (accessed 21 Apr 2020).

72 Frenk J, Moon S. Governance Challenges in Global Health. *N Engl J Med* 2013;**368**:936–42. doi:10.1056/NEJMra1109339

73 Chan M. H1N1 in post-pandemic period. 2010. doi:/entity/mediacentre/news/statements/2010/h1n1_vpc_20100810/en/index.html

74 Moon S, Sridhar D, Pate MA, *et al*. Will Ebola change the game? Ten essential reforms before the next pandemic. The report of the Harvard-LSHTM Independent Panel on the Global Response to Ebola. *The Lancet* 2015;**386**:2204–21. doi:10.1016/S0140-6736(15)00946-0

75 World Health Organization. Ethical considerations for use of unregistered interventions for Ebola virus disease: Report of an advisory panel to WHO. Geneva, Switzerland: : WHO 2014. https://www.who.int/csr/resources/publications/ebola/ethical-considerations/en/ (accessed 21 Apr 2020).

76 World Health Organization. Yellow fever global vaccine stockpile in emergencies. WHO. 2016.https://www.who.int/news-room/feature-stories/detail/yellow-fever-global-vaccine-stockpile-in-emergencies (accessed 27 Apr 2020).

77 World Health Organization. Reform of the International Coordinating Group for Vaccine Provision: a new framework for coordination, accountability and transparency. *Wkly Epidemiol Rec* 2019;**94**:591–600.

78 World Health Organization. Guiding Principles for use of PIP Partnership Contribution 'Response' Funds. Geneva, Switzerland: : WHO 2014. https://www.who.int/influenza/pip/guiding_principles_pc_response_funds.pdf?ua=1 (accessed 21 Apr 2020).

79 World Health Organization. Ethics and COVID-19: resource allocation and priority-setting. Geneva, Switzerland: : WHO 2020. https://www.who.int/who-documents-detail/ethics-and-covid-19-resource-allocation-and-priority-setting (accessed 23 Apr 2020).

80 World Health Organization. A Global Framework to Ensure Equitable and Fair Allocation of COVID-19 Products and Potential Implications for COVID-19 Vaccines. Geneva, Switzerland: : World Health Organization 2020. https://apps.who.int/gb/COVID-19/pdf_files/18_06/Global%20Allocation%20Framework.pdf?utm_source=POLITICO.EU&utm_campaign=18fd118248-EMAIL_CAMPAIGN_2020_06_22_04_52_COPY_01&utm_medium=email&utm_term=0_10959edeb5-18fd118248-189787901 (accessed 16 Jul 2020).

81 Third World Network. COVID-19: Questions over WHO's Global Equitable Allocation Framework & its workings. TWN Info Serv. Health Issues. 2020.https://twn.my/title2/health.info/2020/hi200702.htm (accessed 16 Jul 2020).

82 Karp P. Australian government announces Covid vaccine deals to provide 84.8m doses. The Guardian. 2020.https://www.theguardian.com/australia-news/2020/sep/06/australian-government-announces-covid-vaccine-deals-to-provide-848m-doses (accessed 8 Sep 2020).

83 Blankenship K. AstraZeneca reaches supply deal with Brazilian government to produce millions of doses of COVID-19 shot. FiercePharma. 2020.https://www.fiercepharma.com/manufacturing/astrazeneca-to-supply-millions-covid-19-shot-to-brazilian-government-swamped-by-new (accessed 16 Jul 2020).

84 Liu R, Burger L. AstraZeneca in first COVID-19 vaccine deal with Chinese company. Reuters. 2020.https://www.reuters.com/article/us-health-coronavirus-astrazeneca-kangta-idUSKCN2520Y1 (accessed 8 Sep 2020).

85 AstraZeneca. AstraZeneca takes next steps towards broad and equitable access to Oxford University's potential COVID-19 vaccine. AstraZeneca. 2020.https://www.astrazeneca.com/media-centre/articles/2020/astrazeneca-takes-next-steps-towards-broad-and-equitable-access-to-oxford-universitys-potential-covid-19-vaccine.html (accessed 8 Sep 2020).

86 Aakash B, Faulconbridge G, Holton K. U.S. secures 300 million doses of potential AstraZeneca COVID-19 vaccine. Reuters. 2020.https://www.reuters.com/article/us-health-coronavirus-astrazeneca-idUSKBN22X0J9 (accessed 15 Jul 2020).

87 Oxford University. Oxford University's COVID-19 vaccine: next steps towards broad and equitable global access. Univ. Oxf. 2020.https://www.ox.ac.uk/news/2020-06-05-oxford-university-s-covid-19-vaccine-next-steps-towards-broad-and-equitable-global (accessed 15 Jul 2020).

88 European Commission. Commission reaches first agreement on a potential vaccine. Eur. Comm. - Eur. Comm. 2020.https://ec.europa.eu/commission/presscorner/detail/en/ip_20_1438 (accessed 8 Sep 2020).

89 Reuters. South Korea's SK Bioscience in deal with AstraZeneca on vaccine. Reuters. 2020.https://www.reuters.com/article/us-health-coronavirus-southkorea-astraze-idUSKCN24M0ZF (accessed 8 Sep 2020).

90 World Health Organization, World Intellectual Property Organization, World Trade Organization. Promoting Access to Medical Technologies and Innovation - Intersections between Public Health, Intellectual Property and Trade. Geneva, Switzerland: : WHO, WTO, WIPO 2013. https://www.wipo.int/publications/en/details.jsp?id=305&plang=EN (accessed 27 Apr 2020).

91 't Hoen E. Covid-19 and the comeback of compulsory licensing. Med. Law Policy. 2020.https://medicineslawandpolicy.org/2020/03/covid-19-and-the-come-back-of-compulsory-licensing/ (accessed 27 Apr 2020).

92 Silverman E. AbbVie to allow generic copies of HIV pill in Israel after government license. STAT News. 2020.https://www.statnews.com/pharmalot/2020/03/20/abbvie-israel-hiv-kaletra-coronavirus-covid19/ (accessed 27 Apr 2020).

93 Novartis. Novartis to sponsor large clinical trial of hydroxychloroquine in hospitalized COVID-19 patients. Novartis. 2020.https://www.novartis.com/news/media-releases/novartis-sponsor-large-clinical-trial-hydroxychloroquine-hospitalized-covid-19-patients (accessed 27 Apr 2020).

94 MIT Technology Licensing Office. COVID-19 Technology Access Framework. MIT. 2020.https://tlo.mit.edu/covid-19-technology-access-framework (accessed 21 Apr 2020).

95 Open COVID Coalition. Open COVID Pledge. Open COVID Pledge. https://opencovidpledge.org/ (accessed 16 Jul 2020).

96 Word Health Organization. Solidarity Call to Action. World Health Organ. 2020.https://www.who.int/emergencies/diseases/novel-coronavirus-2019/global-research-on-novel-coronavirus-2019-ncov/covid-19-technology-access-pool/solidarity-call-to-action (accessed 16 Jul 2020).

97 World Health Organization. COVID-19 technology access pool. World Health Organ. https://www.who.int/emergencies/diseases/novel-coronavirus-2019/global-research-on-novel-coronavirus-2019-ncov/covid-19-technology-access-pool (accessed 16 Jul 2020).

98 UN Technology Bank for the Least Developed Countries. UN agencies launch Tech Access Partnership in joint effort to scale up local production of life-saving health technologies for COVID-19. UN Technol. Bank Least Dev. Ctries. 2020.https://www.un.org/technologybank/content/launch_tech_access_partnership (accessed 16 Jul 2020).

99 World Trade Organization. TRIPS and public health. n.d.https://www.wto.org/english/tratop_e/trips_e/pharmpatent_e.htm (accessed 27 Apr 2020).

100 World Health Organization. Research and Development to Meet Health Needs in Developing Countries: Strengthening Global Financing and Coordination. Report of the Consultative Expert Working Group on Research and Development: Financing and Coordination. Geneva, Switzerland: : WHO 2020. http://www.who.int/phi/cewg_report/en/ (accessed 21 Apr 2020).

101 Fidler DP. Negotiating Equitable Access to Influenza Vaccines: Global Health Diplomacy and the Controversies Surrounding Avian Influenza H5N1 and Pandemic Influenza H1N1. *PLOS Med* 2010;**7**:e1000247. doi:10.1371/journal.pmed.1000247

102 Review Committee on the Role of the International Health Regulations. Implementation of the International Health Regulations (2005). Report of the Review Committee on the Role of the International Health Regulations (2005) in the Ebola Outbreak and Response. Geneva, Switzerland: : WHO 2016. https://apps.who.int/gb/ebwha/pdf_files/WHA69/A69_21-en.pdf?ua=1 (accessed 27 Apr 2020).

103 GISAID. EpiCoV. GISAID. n.d.https://www.epicov.org/epi3/frontend#413f3b (accessed 21 Apr 2020).

104 GenBank. SARS-CoV-2 (Severe acute respiratory syndrome coronavirus 2) Sequences. NCBI GenBank. n.d.https://www.ncbi.nlm.nih.gov/genbank/sars-cov-2-seqs/ (accessed 27 Apr 2020).

105 Moon S, Røttingen J-A, Frenk J. Global public goods for health: weaknesses and opportunities in the global health system. *Health Econ Policy Law* 2017;**12**:195–205. doi:10.1017/S1744133116000451