Public Health Emergency Archetypes and Supply Responses - Final Report

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Contents

Executive Summary

Public health emergencies (PHEs)—and, more specifically, outbreaks and epidemics of infectious disease—differ dramatically in their scale, mode and speed of transmission, geographic distribution, and affected populations, among other characteristics. These differences have important implications for efforts to ensure that Low- and Middle-Income Countries (LMICs) have timely and equitable access to the vaccines, drugs, diagnostics and other Medical Countermeasures (MCMs) needed to limit the impact of disease outbreaks. In order to inform the efforts to support equitable access to MCMs, we have developed a set of infectious disease outbreak categories or "archetypes" and used this framework to consider which strategies and tactics international and regional agencies, including UNICEF, should prioritise in which kinds of outbreaks. The focus of this analysis is not on the biological characteristics of outbreak-prone pathogens but on features that affect supply of MCMs to LMICs.

The categorisation of PHEs presented here is based on two main considerations: the *type of PHE* and the *status of MCM development and availability*. We first distinguish three broad types of outbreaks or outbreak pathogens:

1. Pathogens that cause rare and historically small outbreaks posing little threat to High-Income Countries (HICs), such as Ebola Sudan or Nipah virus
2. Those causing more frequent and larger outbreaks, of which cholera and yellow fever are examples
3. Pathogens with clear global pandemic potential, such as beta coronaviruses and certain influenza strains

From the perspective of MCM supply to LMICs, these categories of outbreaks differ profoundly in two related respects: the commercial potential of markets for MCMs and thus the engagement of private-sector product developers and manufacturers; and the likelihood that HICs will, on one hand, invest in the development and production of MCMs and, on the other, potentially monopolize supply of these life-saving tools.

We then consider the status of MCM development and availability for particular pathogens and distinguish three broad stages of development:

1. Early-stage R&D
2. Advanced clinical trials, when safety in humans has been established but definitive efficacy trials have not been completed
3. Licensed (or granted emergency use listing or authorization)

Combining these two three-part distinctions leads to nine provisional archetypes.

Each proposed archetype is associated with one or more characteristic *market challenges*. For example, pathogens causing rare and historically small outbreaks, for which there are no licensed MCMs, the primary challenges are the complete lack of commercial incentives to develop these products and the poor prospects for large-scale investment by HIC governments. Similarly, for pathogens in this category with licensed MCMs, the challenge is to ensure adequate supply is available despite highly unpredictable demand and, again, in the absence of commercial incentives for production. At the other end of the spectrum, for global pandemics, the main challenge for LMICs and agencies acting on their behalf is to

secure access in the face of competition from HICs and/or export bans. For outbreaks in the middle tier, with higher and somewhat more predictable demand, in some cases including demand from preventative campaigns or routine use, the challenge is to make markets for MCMs sufficiently stable and attractive to support a sustainable commercial market.

These very different market challenges are in turn amenable to quite different sets of market and policy interventions, or *supply levers*. We analyse the feasibility and likely effectiveness for each archetype of more than thirty such measures, ranging from procurement modalities such as advance purchase agreements and price-volume guarantees, to investment in building the capacity of regional manufacturers and incentives for technology transfer, to regulatory measures and potential provisions of an international pandemic treaty or accord. This analysis, which is summarized in a set of proposed supply *playbooks* for each archetype, demonstrates the importance of an explicitly differentiated approach to ensuring MCM supply in preparation for and in response to disease outbreaks of different types.

Importantly, we note that our analysis focuses on adequate and timely supply of MCMs to countries, not on the equally important factors that affect access to and impact of MCMs after arrival at a port of entry or national warehouse, including within-country distribution and cold chain, health worker training and infrastructure, appropriate use, and public attitudes toward and demand for these products. Addressing these barriers to access requires a different set of measures that are beyond our scope.

The objective of this analysis is to inform decisions by regional and international agencies on the best approaches to MCM supply in different kinds of outbreaks. Each pathogen and MCM is of course unique, but we believe the archetypes framework can provide a useful starting point and structure for these decisions. The analysis also has implications for the division of responsibilities across agencies in outbreaks, as the focus of some agencies on particular approaches to MCM development and supply means that these agencies may have a smaller or larger role in outbreaks where these interventions are more or less important. At the same time, the analysis highlights some important gaps in the international system, in that no agency is currently configured to play certain critical roles at the necessary scale, including building regional manufacturing capacity and facilitating tech transfer. Incorporating some of the insights from this work into current processes to define roles and responsibilities in pandemic preparedness and response can help to ensure that the resulting structures and partnerships are appropriate for the full range of potential outbreaks.

In presenting this analysis, we emphasize that it is not intended to prioritize particular pathogens or to provide guidance on the importance and appropriate use of particular medical countermeasures. The archetypes framework focuses instead on how best to ensure availability to LMICs of MCMs prioritized by governments and by technical and normative agencies such as WHO and Africa CDC.

Glossary – key terms

Public Health Emergency (PHE). The project focuses primarily on multi-LMIC outbreaks of infectious diseases, where UNICEF and our partners support preparedness and response. Small, single country outbreaks are often resolved by individual governments, with limited support from UNICEF and partners. As such, we hope this work might be useful to them, but they are not the primary intended audience. The project will not focus on health emergencies caused by non-health events, or Non-Communicable Diseases. We are focused on rapidly changing, non-routine events.

While recognising the different definitions of 'outbreak', 'epidemic', 'Public Health Emergency', 'Public Health Emergency of International Concern' (PHEIC) and 'pandemic', this project is not tied to any of the formal classifications.

Medical countermeasure (MCM). Medical countermeasures are medical products (biologics, drugs, devices) that may be used in the event of a PHE. Within supply, we will focus on vaccines, diagnostics, therapeutics, and Personal Protective Equipment (PPE).

Availability (of medical countermeasures). Whether a medical countermeasure can get to the port of entry of an LMIC. Demand-side issues (including community engagement and questions of in-country 'programming', 'delivery support', and health systems strengthening) are out of scope, although we recognise their enormous importance for driving access to medical countermeasures. Our focus, availability, stops short of full access considerations.

Market challenge. The key aspect(s) of development, licensure, production or procurement of medical countermeasures that is required to change to increase availability for LMICs. The description of the market challenge includes the desired outcome or change e.g., "expanded production capacity", as well as aspects of the supply, demand and financial context e.g., "lack of commercial incentives". NB. These are market 'challenges' not market 'failures' because many of them are not failures in the narrower neoclassical economic sense, instead market-related situations we would like to see change.

Supply levers. Supply levers include investment in, contracting and procurement of, medical countermeasures to combat an outbreak. These levers could be used to increase the likelihood of medical countermeasures coming to market/shorten the time to marekt or increase the availability of a medical countermeasure. Levers include grant funding for R&D or production capacity development, an Advance Purchase Agreement (APA), a technology transfer agreement, or vaccine donations. Different levers can achieve different objectives, carry different risks, and come with a variety of advantages and disadvantages.

Introduction

The international response to the COVID-19 pandemic, despite important successes, has highlighted profound inequities in access to Medical Countermeasures (MCMs), with many Low- and Middle-Income Countries (LMICs) receiving life-saving products, especially vaccines, months or years after High-Income Countries (HICs).[1] Many efforts are now underway to absorb the lessons from the COVID-19 experience and to build a stronger infrastructure for ensuring fair access to MCMs in future disease outbreaks. There have been more than thirty reviews and evaluations of the COVID-19 response, negotiations have begun on a pandemic accord, and both the G7 and G20 will focus on pandemic preparedness and response this year.[2,3,4,5,6] WHO is leading a comprehensive analysis of the capacities that countries and international organizations need to put in place to respond more effectively to future pandemics and is also developing an "MCM coordination platform" to coordinate efforts on MCM availability and access.

While understanding what did not work well in the response to the current pandemic is crucial, there is also a danger of focusing too much on PHEs that closely resemble this one, that is, of fighting the last war. Infectious disease outbreaks come in many kinds and the next pandemic may be very different from COVID-19 in ways that have important consequences for efforts to ensure equitable access to MCMs. Moreover, LMICs in particular currently suffer from, and will continue to be at risk of, disease outbreaks that may fall short of pandemic status but nonetheless impose a heavy burden on populations and economies. Thus the international community, and especially regional and international organizations focused on LMICs, including UNICEF, need to prepare for and respond to a broad range of outbreak and epidemic types.

We believe that planning for many different types of disease outbreaks can be facilitated by a systematic grouping of epidemics *according to characteristics relevant to the availability and supply of MCMs in LMICs*. We outline such a framework here and highlight some implications for approaches to supply and market shaping. After clarifying the scope of the analysis, we present the framework, consisting of a set of outbreak types, or *archetypes*, each characterized by a particular primary *market challenge*. We then analyze a large set of supply or market-shaping interventions and assess the relevance and likely effectiveness of each in addressing the market challenges associated with each archetypes. This analysis leads to a set of playbooks, or sets of supply interventions best suited to each type of outbreak. Finally, we summarize some key insights from this work and offer some recommendations.

[1] Hunter, D. J. et al (2022): Addressing vaccine inequality—Covid-19 vaccines as a global public good. Editorial. NEJM 386: 1176-79.
[2] Independent Panel for Pandemic Preparedness and Response (2021): Covid-19: Make it the last pandemic. Available at https://theindependentpanel.org/wp-content/uploads/2021/05/COVID-19-Make-it-the-Last-Pandemic_final.pdf
[3] Sachs, J.D. et al (2022): The Lancet Commission on lessons for the future from the Covid-19 pandemic. Lancet 400:1224-1280.
[4]Matsoso, P. et al (2023): Negotiating a pandemic accord: a promising start. BMJ 380:506.
[5] Kishida F. Human security and universal health coverage: Japan's vision for the G7 Hiroshima Summit. Lancet. 2023 Jan 28;401(10373):246-247. doi: 10.1016/S0140-6736(23)00014-4.
[6] Mandaviya, M. (2023). India plans to use its G20 presidency to build consensus on global health resilience. World Economic Forum. Available at: https://www.weforum.org/agenda/2023/02/india-g20-presidency-consensus-global-health-resilience/. Accessed, 27 March 2023.

The nine archetypes

The archetypes framework is built on a simple classification of outbreak pathogens coupled to an assessment of the status of MCM development and supply.

Pathogen tiers

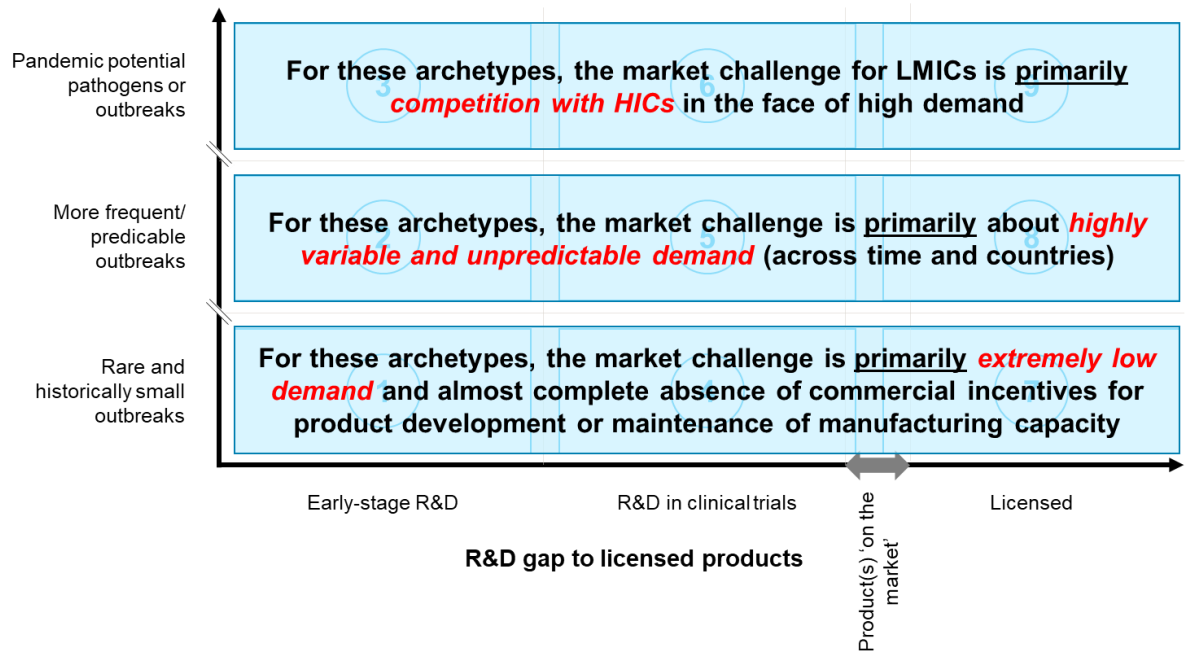
Disease outbreaks and the pathogens that cause them differ in many ways, including the type of pathogen and mode of transmission, the location of the outbreak, and health system capacity to respond. A number of organizations, including WHO, Africa CDC, US NIH, the European Commission's Health Emergency Preparedness and Response Authority, and the UK Research and Development Vaccine Network, have categorized and prioritized pathogens in various and valuable ways.[7,8,9,10,11] In our work with UNICEF Supply Division, the world's largest procurer of vaccines and a key supply partner in health emergencies, our focus is on access to MCMs. From this perspective, we believe that the critical characteristics of pathogens include the typical size and frequency of the outbreaks they cause and the likelihood that they will strongly affect HICs. On this basis, we propose a simple division of disease outbreaks into three categories or tiers, each associated with a particular *market challenge*.

1. **Rare and historically small**. This category includes pathogens such as the Ebola, Marburg, and Nipah viruses, which, at least to date, have caused outbreaks of hundreds or at most thousands of cases. Crucially, these pathogens pose little realistic threat to HICs, either because their vectors or animal reservoirs are ecologically restricted or because outbreaks are readily contained where health infrastructure is adequate. The volume of MCMs required for these diseases is so small—and the ability of affected populations and states to pay for them so limited—that the fundamental market challenge for these outbreaks is the *almost complete lack of commercial incentive* to develop or manufacture these products.
2. **More frequent, larger, and semi-endemic.** This category includes pathogens such as cholera, yellow fever, bacterial meningitis, and perhaps dengue and chikungunya, which cause more frequent and larger outbreaks and may be endemic in some countries. Like the rare and historically small outbreaks, these pose little current threat to HICs, although climate change could change that by expanding the range of mosquito vectors. Although the location and timing of these outbreaks is unpredictable, the required volumes of MCMs, averaged over year-to-year fluctuations, is sufficient to support a commercial market. In some cases, such as dengue, although international funding will still be required to ensure access for the poorest countries, unsubsidized markets in middle-income countries can help to sustain commercial viability. Here, the main market challenge is to *stabilize demand*, thereby making these markets more attractive to manufacturers and help to ensure reliable and sufficient supply.

[7] WHO: Prioritizing diseases for research and development in emergency contexts. Webpage. Available at: https://www.who.int/activities/prioritizing-diseases-for-research-and-development-in-emergency-contexts. Accessed March 27, 3023.
[8] National Institute of Allergy and Infectious Diseases (2021): NIAID Pandemic Preparedness Plan. https://www.niaid.nih.gov/sites/default/files/pandemic-preparedness-plan.pdf
[9] Africa CDC (2023): Risk ranking and prioritization of epidemic-prone diseases. Available at https://africacdc.org/download/risk-ranking-and-prioritization-of-epidemic-prone-diseases/
[10] Health Emergency Preparedness and Response Authority (HERA). HERA factsheet – HEALTH UNION: Identifying top 3 priority health threats. Available at: https://health.ec.europa.eu/document/download/18c127ce-da4b-4e4e-a27c-f7b93efb2980_en?filename=hera_factsheet_health-threat_mcm.pdf. Accessed 27 March 2023.
[11] The UK Department of Health and Social Care (DHSC). The UK Vaccine Network. Working Group 1- Identify and prioritise human and zoonotic diseases. Available at: https://www.gov.uk/government/groups/uk-vaccines-network. Accessed 27 March 2023.

3. **True pandemics.** COVID-19 and a potential global flu pandemic are the canonical examples of this upper tier of outbreaks, which affect hundreds of millions or even billions of people, including those in HICs as well as LMICs. For these outbreaks, scope and duration and hence demand for MCMs remain unpredictable, but there is a potential for large commercial returns to product developers and manufacturers. Critically, there is every expectation that HICs will invest large sums in R&D and in creating attractive markets for suppliers. Thus, for LMICs and organizations acting on their behalf, the fundamental challenge in these cases is to *secure adequate and timely supplies of MCMs in the face of competition from HICs*, as the struggle for COVID-19 vaccines demonstrated.

Figure 1: Market challenges for the tiers of the archetypes framework



Where pathogens fall in this categorization is of course determined in turn by underlying biology: animal reservoirs, vectors, modes of transmission, and so on. But the essential point is that the market challenges associated with each derive more directly from the higher-level characteristics emphasized here, and pathogens of very different types, such as yellow fever and Meningitis A, can pose similar market challenges.

Although other considerations enter into this categorization, the demonstrated or potential threat that a pathogen poses to HICs is the factor with the greatest implications for supply to LMICs, as will be discussed further below. An obvious challenge is that it may not always be clear in advance or in the early stages of an outbreak if HICs will be strongly affected. Although easily transmitted respiratory viruses such as influenza and coronaviruses threaten all countries, this is less clear for some other pathogens. Until last year's epidemic, Mpox was virtually unknown in the US and Europe. Conversely, although we categorize Ebola as unlikely to strongly affect HICs, it was considered at least a theoretical threat at the time of the West Africa outbreak, and it remains on the US government's list of priority pandemic pathogens. Yellow fever, limited in recent times to Africa and Latin America, once caused devastating outbreaks in the US, as

did malaria. The conditions that currently limit pathogen ranges can change again as vector and host species' ranges shift and new health system vulnerabilities appear in rich as well as poorer countries. The challenge that this uncertainty creates is compounded by the fact that what matters for LMIC supply is, at least in part, the *perception* of threat to HICs, as this concern can drive both investment in product development and stockpiling/hoarding of available MCMs.

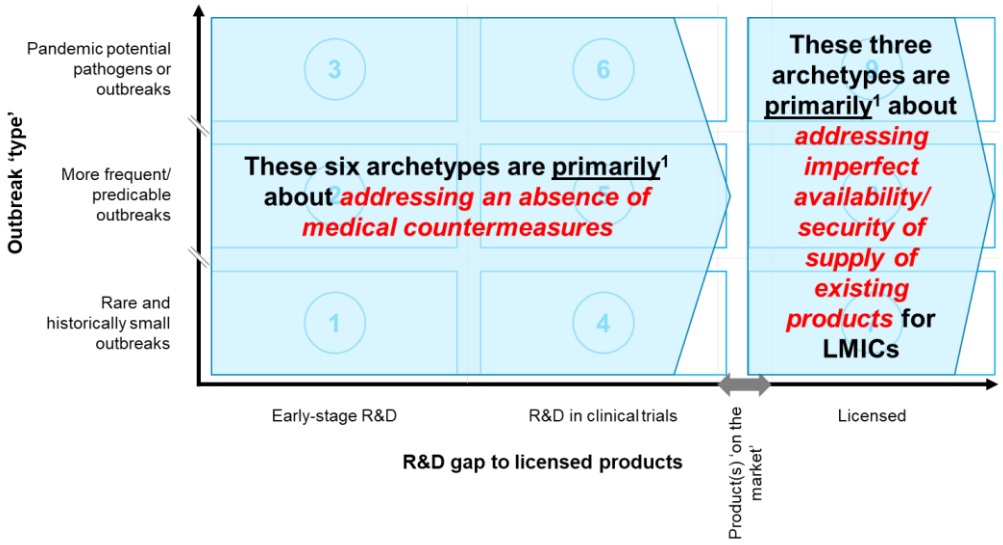
Status of MCM development and supply

The division into three tiers based on the characteristics of pathogens can be complemented by a second axis based on the status of particular countermeasures, with its own implications for market shaping priorities.

1. For some outbreak pathogens, we have no MCMs of needed types and R&D is at a very early stage. For example, there are no specific drugs for yellow fever, dengue, or chikungunya. This would be true as well, of course, of a previously unseen pathogen — "disease X", especially if it did not belong to a well-understood pathogen family.
2. For others, some MCMs have advanced to clinical trials and enough safety data is available to move to an efficacy trial when an outbreak occurs. Sudan Ebola vaccines are a good example of countermeasures in this category. Vaccines for pathogens from families for which effective vaccines have already been developed, such as influenza viruses or novel coronaviruses similar to COVID-19 could also be placed in this group.
3. Finally, adequate MCMs already exist for some pathogens—in these cases the emphasis can be on ensuring sufficient supply available to LMICs.

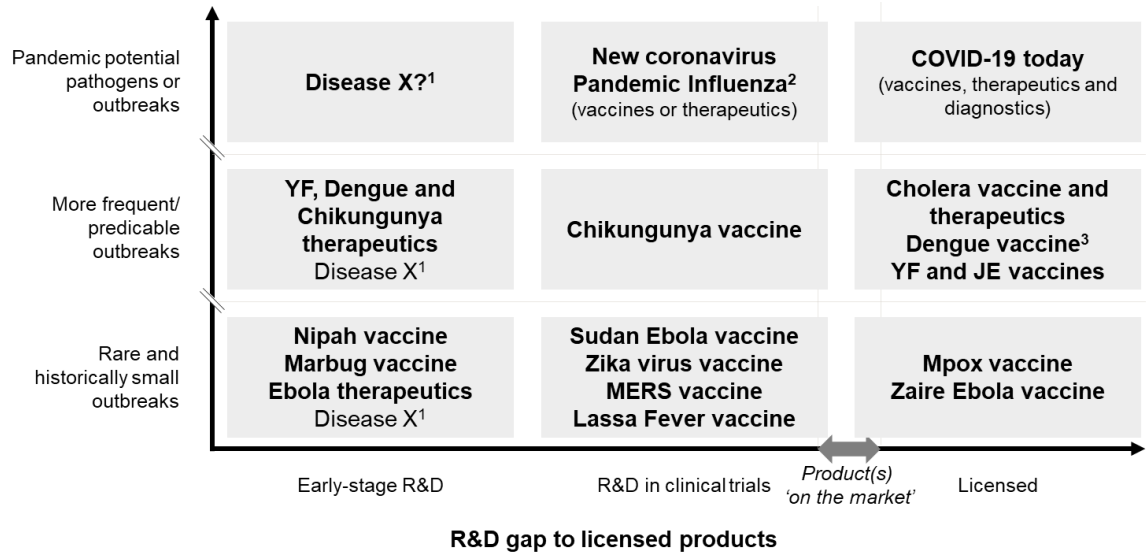
It is important to stress that as no MCM is perfect, there may be good reasons to support the development of improved—more effective, more affordable, easier to deliver--products even when a useful drug or vaccine is available. Thus MCMs for a particular pathogen may be simultaneously at different development stages. For the purposes of the archetypes framework, however, the emphasis is on whether or not a useful product is available and, if not, on the development status of the most advanced plausible candidate or candidates.

Figure 2: Market challenges by the stage of development of the MCM



Combining these two dimensions, we arrive at a three-by-three matrix of categories, which we call health emergency archetypes. Figure 3 displays the nine archetypes, with illustrative examples of pathogen-MCM combinations corresponding to each.

Figure 3: The PHE archetypes with example pathogen-MCM combinations mapped on



1. For a truly novel disease, there will be no R&D at all. And of course, the disease could end up in any of the rows. It is highlighted in archetype 3, as it would be a pathogen of this type that would drive a major supply response from the international community
2. With the rapid potential development of mRNA vaccines, the time taken to reach Phase 2/3 will be small, and the likelihood of success very high, hence being categorised here
3. There is only one Dengue vaccine on the market, with a specific target population. See https://www.who.int/news-room/questions-and-answers/item/dengue-vaccines

Analysis of supply levers

The framework defines a set of nine PHE archetypes on the basis of pathogen and MCM characteristics; each of these archetypes is associated with one or more market challenges to timely and adequate supply of MCMs to LMICs in an outbreak. To understand the implications of these differing challenges for market intervention and to provide guidance to governments and regional and international agencies, we analyzed the relevance and likely impact of a diverse list of supply or market-shaping interventions, which we call "supply levers". These range from R&D push and pull incentives and procurement modalities to intellectual property provisions, approaches to promoting tech transfer, and support of regional manufacturing (see Table 1). After defining each lever and describing how it can promote MCM development, supply, or LMIC access, we have analyzed the circumstances in which its use is appropriate. In particular, we have assessed both the feasibility and likely impact of each lever for each of the archetypes in both preparedness and response. This analysis is presented in summary form in the two "heat maps" in Annex A, the more detailed description and analysis of each supply lever is available in Annex D. To make the implications for policymakers more accessible, we have also highlighted the supply levers that our analysis suggests should be prioritized for each archetype—we call these "playbooks": see Tables 2 & 3. Finally, we have drawn out some of the higher-level findings from this analysis as a series of insights and recommendations (see next section).

This analysis is subject to numerous caveats and elaborations, as each of the market shaping levers can be structured and applied in different ways;[12] their effectiveness often depends on how much funding is devoted to them; and an overall rating inevitably requires weighing on a common scale advantages and disadvantages of quite different types. The purpose of this analysis is not to promote or discourage the use of particular instruments in general or to reach definitive judgments about which to use in which circumstances, but to highlight the ways that the value of various supply levers differs across outbreak types.

Table 1: Supply levers

No.	R&D levers
1	R&D Push Funding (by LMIC-focused agency)
2	Publicly funded IP for R&D
3	Access provisions in R&D push funding
	Procurement-related levers
4	Advanced Purchase Agreement (APA)
5	Advanced Market Commitment (AMC)
6	Price-Volume Guarantee
7	Demand pooling and pooled procurement – LMIC-wide
8	Demand pooling and pooled procurement -- regional
9	Ex ante commitment to devote share of supply to LMICs (Berlin Dec.)
10	Putting donation infrastructure in place
11	Donations
12	Putting a resale market in place
13	Resale market

[12] For example, an APA is classically considered a 'pull' mechanism, but if you link an APA to a stockpile, and have substantial pre-payment this is effectively 'push' funding/contract manufacturing. The details are crucial.
Similarly, the COVAX 'AMC' (https://www.gavi.org/gavi-covax-amc) is not an AMC at all, but a set of manufacturer-specific APAs.

14	Pre-emptive Long Term Agreement negotiation
	Stockpiles
15	Stockpile - investigational
16	Stockpile - licensed
	Financing levers
17	Rapid response fund for MCM procurement
	Manufacturing levers
18	Contract manufacturing (no expectation of ongoing market)
19	Reservation of additional manufacturing capacity for surge
	Tech-transfer related levers - 'owner side'
20	Tech transfer and IP licensing - Incentives/funding to share technology
21	Tech transfer and IP licensing - TT/licensing as condition of APA
	Tech-transfer related levers - 'bridging'
22	Tech transfer and IP licensing - Patent pools and TT hubs
23	Tech transfer and IP licensing - Brokering advance TT and licensing agreements
	Tech-transfer related levers - recipient side
24	Tech transfer to a high-volume manufacturer (without regional security of supply focus)
	Regional manufacturing levers
25	Tech transfer to regional manufacturer focusing on regional supply
26	Non-product specific investment in and capacity-building for regional manufacturers
27	Subsidy for procurement from regional manufacturers to build capacity
28	Non-binding regional procurement compact
	Regulatory levers
29	Regulatory agency capacity strengthening - to oversee manufacturing
30	Expedited regulatory approvals in country of use
31	(Clinical) Policy/Guideline development
	Possible treaty provisions
32	Tech Transfer requirement
33	Ban on export bans
34	HIC dose-sharing requirement
35	Pandemic IPR waiver
	Other levers
36	Publishing market information
37	Demand forecasting
38	Advocacy/soft power

Application of the framework to different types of MCMs

This framework was developed primarily on the basis of experience with vaccines, but we believe it should be useful for medicines and, with modification, for diagnostics as well. The basic drivers of differences across the archetypes are important to all three categories of MCMs: the lack of commercial incentives to develop products for pathogens causing small outbreaks in LMICs; the primary focus of HICs on MCMs for pathogens seen as a threat to their populations; the potential for competition with HICs to limit supply to LMIC in pandemics. There are differences as well, however. A new diagnostic can generally be brought to market at much lower expense than a new drug or vaccine, potentially creating commercially viable markets for smaller outbreaks. The role of patents as barriers to expanding supply, including regional supply, differs across the MCM categories. The international's community's division of labor also differs, with the roles of the various agencies in financing, R&D, procurement, delivery support, regulation and oversight clearer and better developed for vaccines than for drugs or diagnostics. Finally, for diagnostics, use cases may be an important determinant of market challenges, as the potential demand for a diagnostic used in widespread population screening may be much greater than for one used for clinical confirmation. These differences across the MCM types undoubtedly affect the assessment of supply levers for different archetypes and may require some revision of the archetypes themselves, especially for diagnostics.

Insights and recommendations

In many ways, the 'playbooks' are the main recommendations from this work, as they provide detailed guidance on approaches to driving development and delivery of MCMs for each archetype, in preparedness as well as response. But the analysis also leads to a number of conclusions at a higher level listed below Tables 2 and 3.

Table 2: Preparedness 'playbooks'

Pandemic potential pathogens or outbreaks	• Non-product specific investment in and capacity-building for regional manufacturers • Rapid response fund for MCM procurement • Regulatory agency capacity strengthening - to oversee manufacturing • Demand pooling and pooled procurement - LMIC wide • Ban on export bans • HIC dose-sharing requirement • Ex ante commitment to devote share of supply to LMICs (Berlin Dec.) • Putting donation infrastructure in place in advance	• Non-product-specific investment in and capacity-building for regional manufacturers • Rapid response fund for MCM procurement • Regulatory agency capacity strengthening - to oversee manufacturing • Demand pooling and pooled procurement - LMIC wide • Ban on export bans • HIC dose-sharing requirement • (Clinical) Policy/Guideline development • Tech transfer and IP licensing - Brokering advance TT and licensing agreements • Reservation of additional manufacturing capacity for surge • Tech transfer to regional manufacturer focusing on regional supply • Tech transfer to a high-volume manufacturer (without regional security of supply focus) • Ex ante commitment to devote share of supply to LMICs (Berlin Dec.) • Putting donation infrastructure in place in advance	
More frequent/ predicable outbreaks	• R&D Push Funding • Publicly funded IP for R&D	• R&D Push Funding • Stockpile - investigational • Reservation of additional manufacturing capacity for surge • Publicly funded IP for R&D • Non-product-specific investment in and capacity-building for regional manufacturers	• Stockpile, restructured to smooth demand and enhance market stability • Reservation of additional manufacturing capacity for surge • Non-product-specific investment in and capacity-building for regional manufacturers
Rare and historically small outbreaks	• R&D Push Funding • Publicly funded IP for R&D • Regulatory agency capacity strengthening - to oversee manufacturing	• R&D Push Funding • Stockpile - investigational • Contract manufacturing (no expectation of ongoing market) • Reservation of additional manufacturing capacity for surge • Non-product-specific investment in and capacity-building for regional manufacturers • Publicly funded IP for R&D	• Stockpile - licensed • Reservation of additional manufacturing capacity for surge • Contract manufacturing (no expectation of ongoing market) • Non-product-specific investment in and capacity-building for regional manufacturers
	Early-stage R&D	R&D in clinical trials	Licensed

Table 3: Response 'playbooks'

Pandemic potential pathogens or outbreaks	• Advanced Purchase Agreement (APA) • Demand pooling and pooled procurement - LMIC wide • Demand pooling and pooled procurement - regional • Tech transfer to a high-volume manufacturer (without regional security of supply focus)	• Advanced Purchase Agreement (APA) • Demand pooling and pooled procurement - LMIC wide • Demand pooling and pooled procurement - regional • Tech transfer to a high-volume manufacturer (without regional security of supply focus) • Tech transfer to regional manufacturers	• Advanced Purchase Agreement (APA) • Demand pooling and pooled procurement - LMIC wide • Demand pooling and pooled procurement - regional • Tech transfer to a high-volume manufacturer (without regional security of supply focus) • Tech transfer and IP licensing - TT/licensing as condition of APA • (Clinical) Policy/Guideline development • Tech transfer to regional manufacturers • Donations
More frequent/ predicable outbreaks	N/A. No response with an MCM that has not been deemed safe for humans. (Advocacy/soft power, and R&D may help be prepared to respond to the next outbreak)	• R&D Push Funding (by LMIC-focused agency) • Using stockpile of investigational product (if established) to conduct efficacy and trial and combat outbreak under appropriate protocols	• Drawing on stockpile, if established • Reservation of additional manufacturing capacity for surge
Rare and historically small outbreaks		• R&D Push Funding (by LMIC-focused agency) • Contract manufacturing (no expectation of ongoing market) • Using stockpile of investigational product (if established) to conduct efficacy and trial and combat outbreak under appropriate protocols	• (Drawing down from the licensed stockpile assuming it has been set up in response) • Contract manufacturing (no expectation of ongoing market)
	Early-stage R&D	R&D in clinical trials	Licensed

How to think about markets for medical countermeasures

It may be obvious but bears repeating: we face public health emergencies of very different types. Outbreaks vary enormously in their scale and speed of spread. The recent Sudan Ebolavirus outbreak ended after only ~150 cases in the centre and west of Uganda. There are millions of cholera cases every year, with multiple countries affected. And there have been billions of COVID-19 cases so far, across countries at all income levels. These emergencies also differ in whom they affect: some strike only poorer countries[13]; whereas the COVID-19 pandemic reached every country on the planet.

These differences between outbreaks imply quite different market challenges for those seeking to develop and deliver MCMs for LMICs. For some kinds of outbreaks, the main challenge is the lack of commercial incentives for product development and supply, while for others the biggest challenge might be securing supply in the face of strong competition from better-funded countries.

The need for a tailored approach applies to both preparedness and response. It is too late for some preparedness investments as an outbreak rages, and some actions cannot be taken until an outbreak begins and the pathogen is known. Moreover, the most *relevant* market shaping levers differ across preparedness and response. For example, the establishment of large funds for rapid procurement is more important preparation for pandemics than for smaller outbreaks unlikely to affect HICs.[14] And the type of manufacturing facilities needed for ready reserves of investigational vaccines are different from those needed to supply a whole region with vaccines in a pandemic.

While each outbreak is unique, MCMs for particular pathogens can usefully be grouped into a small number of categories in ways that can usefully inform MCM supply strategies. Outbreaks, MCM pipelines and markets vary in many ways. However, the challenges in developing and testing novel therapeutics for Lassa and Nipah viruses are more similar than different, and the challenges facing UNICEF and other agencies engaged in MCM supply for these pathogens are very different from, for example, the challenges involved in securing access to COVID-19 therapeutics. This means we do not have to start from a blank slate each time, and we can prepare substantially now for what will likely be needed.

[13] Outbreaks only impacting HICs are out of scope for UNICEF, and therefore this work

[14] Conditional funding for medical countermeasures, and pooled procurement, are most useful when buyer power is low and/or rapid deals are needed. This is more likely in situations of high competition e.g., pandemics, than outbreaks of rare diseases where the international community is often the only buyer e.g., Zaire Ebolavirus

Moving to action in preparedness and response

We should develop playbooks, partnerships, policies and funding packages for each archetype. Playbooks, such as those included below, can facilitate thinking on supply strategies for outbreak MCMs, and, at a minimum, provide a useful structure for analyses of which market shaping levers to prioritize. Agreeing, codifying and practicing partially repeatable processes should make the international community more effective and efficient in preparing and responding to PHEs of various types.

Underpinning these playbooks is a need to think differently about our market health ambitions for outbreak MCMs. Markets for products needed in epidemics are qualitatively different from routine MCM markets. Most importantly, demand uncertainty is much greater, as neither the size nor the duration of an outbreak can be predicted with confidence. In addition, the urgency of a PHE can make agencies, governments, and the public less sensitive to prices, and lead to strong first mover advantages/product preferences that we would not normally see in conventional markets. For these and other reasons, some of the market attributes valued in healthy market frameworks, especially those related to competition, price, and sustainability, may not apply or be lower priorities for outbreak products. Gavi, UNICEF and others should consider whether Gavi Alliance vaccine Product Roadmaps[15], UNICEF Procurement Strategies and Market Notes are fit for purpose.[16]

An incremental re-arranging of today's partnerships and tactics will not be enough: the range of levers we have today for ensuring adequate and timely supply of MCMs for LMICs is too limited. The current system relies too much on uncertain 'charity'[17] from high-income and producing countries and from big pharma, invests too little in development of MCMs for pathogens that primarily threaten LMICs, and fails to ensure sufficient supply of established MCMs for outbreak diseases. Furthermore, regional R&D, procurement and delivery actors are both stronger and much more assertive than they were pre-COVID-19: a global, centralized, 'one-stop shop' approach to future outbreaks will not be supported by many LMICs or donors.

Sustained investment and new capacities are needed. The options we will have to respond to future outbreaks depends on what we do now. To break out of the current paradigm, sustained investment is needed. Furthermore, some of the most needed initiatives fall outside the core strengths of the main players in outbreak preparedness and response and will require new capacities and new divisions of labour. This is most pronounced in two related areas: technology transfer, both in advance of and during outbreaks, and building the capacity of new and existing regional manufacturers so that they can play a larger role in future outbreaks. Annex C presents some preliminary analysis of the most compelling roles for regional manufacturing in PHEs, with implications for the different archetypes.

What should the international community aim to achieve in each type of market?

For rare and historically small outbreaks, the international community should focus on bringing at least one effective product to market, relying primarily on push funding for product development and

[15] https://www.gavi.org/our-alliance/market-shaping/market-shaping-roadmaps
[16] https://www.unicef.org/supply/market-notes-and-updates
[17] It is worth noting that preparedness for, and response to, other types of PHE is often HIC donor-funded too e.g., research on Nipah virus vaccines by the US and global donors, or provision of Cholera vaccines funded by donors. However, without competition for these products, the dependence on HICs is much less pronounced than in pandemics. For the avoidance of doubt, we still see *a* role for donor funded purchasing of MCMs in outbreak preparedness and response: some very poor countries just do not have the financial capabilities for this, and so this form of 'charity' will continue to be needed. But, we do want to move away from a paradigm in which vast volumes of MCMs are purchased by HICs for their domestic populations, and then donated to LMICs. This is not reliable or often timely.

contracting production for stockpiles. Creating a 'commercial'[18] market with multiple competing suppliers is not a realistic objective for these products. Assuming a 'first past the post' or single-product market has wide-ranging implications.

- R&D funders and those running clinical trials may want to take a more aggressive approach to thinning the product pipeline. As the international community (HIC R&D funders, foundations, and international agencies) plays a much larger role in financing development of these products, they are in a position, and have a responsibility, to focus investment efficiently.[19] They need to make tough choices:
    - Is it better to select one product for a clinical trial, and hopefully gather enough data in a small outbreak, or to select multiple products and risk gaining insufficient data on any of them?
    - If there is one product that is 'good enough', is there still a case to fund development and trials of a second product with all the challenges of getting it to market?
- The risk to supply of having only one product but can be mitigated in various ways, including a large enough stockpile to weather temporary interruptions and a pre-agreed tech transfer agreement with a second supplier to be triggered if the preferred manufacturer fails or chooses to leave the market.
- Having only one supplier also entails higher price risk, but this can be managed through access provisions in the R&D funding.
- Regional suppliers, especially those with public health missions, may have an important role for these products, as the demand risk may be too high, and volume too low, for conventional/globally-focused suppliers. Post COVID-19, there has been a significant interest in building regional manufacturing capacity, especially for vaccines, but the product focus and business models of these manufacturers are not yet clear. Production of MCMs for pathogens causing rare and historically small but regionally important outbreaks could be a major contribution to health security, but will require not only technical capacity but also either cross-subsidy from commercially viable products or ongoing support from the national, regional, or international level.

Where investigational products for pathogens that case small and rare outbreaks have been shown to be safe in humans, ready reserves should be established to allow clinical trials to be started quickly when an outbreak, as well as potentially to contribute to the response under compassionate use protocols. There is much to be worked out for these ready reserves, including which products to stockpile, how insurance and liability should be managed, funding, and replenishment in the case that there are no outbreaks and products expire.[20] CEPI, Gavi and UNICEF are actively looking at stockpiles, including of

[18] These markets are 'commercial' in the sense that a product comes to market and is sold, or commercialized. But they are not 'commercial' in the sense of being an attractive market that players would compete to enter, and desire to remain in relative to other opportunities they could pursue. We assume that buyers would have to pay a 'COGS + premium" to keep manufacturers in these markets.

[19] International actors do fund R&D, and provide Target Product Profiles (which is engagement before PQ) but this influence is usually relatively small compared to industry investment. However, for the small and rare outbreak-MCMs, industry investment is low, and so this paradigm is reversed. The international community needs to recognise this reality and the choices it entails.

[20] For example - Who should decide which pathogens need Phase 1 vs Phase 2 clinical trial material reserves? Where should material be stored? What are the minimum requirements for candidate material? What number of doses is needed for an investigational reserve? Who should make this decision? Who should pay for what? Who should be responsible for operationalizing and maintaining the reserve? (e.g., import/export, labeling, delivery, quality monitoring, returns and disposal) What insurance and liability agreements are needed and how will they be established? Who should be responsible for defining the minimum requirements?

vaccines against these small and rare outbreaks. And Africa CDC is exploring stockpiles against its priority pathogens, some of which fall into this group.

For the middle 'tier' of PHEs, the international community should intervene just enough to support a quasi-stable market, by better linking up programmatic, policy and market shaping actions. These are a complicated and somewhat heterogenous group of markets, as in some cases products are used routinely and in preventative campaigns as well as in outbreak response. While for most there is currently no important HIC market, for some there may be significant markets in UMICs. Importantly though, demand for these products is, on average, sufficient to warrant ongoing production and to support more than one supplier, unlike products for rare and historically small outbreaks.

The international community could do more to smooth demand across time, countries, and the different uses, using such tools as larger and differently structured stockpiles[21], demand risk-sharing with suppliers and third parties, and modulation of demand for preventative campaigns. Too often these are treated like routine markets, with manufacturers asked to assume all demand risk, with the result that manufacturers produce less or expand capacity more slowly than they otherwise might, which in turn exacerbates supply shortages.

For true pandemics, the objective is to secure timely and adequate supply for LMICs, and a wide range of tools will be needed. These include rapidly accessible funding for early deal-making, dose-sharing commitments, and arrangements for donations, but also expanded regional manufacturing capacity and greatly accelerated technology transfer both to regional suppliers and to high-volume suppliers capable of rapidly increasing global supply. Some of these tools can only be put in place through substantial preparedness investments, without which the international community will be stuck with the same limited set of options available in the COVID-19 pandemic.

Substantial work is underway here, with too many initiatives to list[22], but it is not yet clear who will take responsibility for some of the most needed actions, especially concerning tech transfer and regional manufacturing, or that sufficient funding will be made available.

The international community must be prepared to pay for flexibility: in pandemic response, as the best balance of tools will depend in part on characteristics that may not be clear at the start. For example, if the R&D success rate is high and many product developers bring MCMs to market quickly and in high volumes, the best levers may be those focused on more equitable distribution of these MCMs, such as dose-sharing commitments, donations, and resale. But if only one or a few products reach market, rapid technology transfer to additional suppliers, including regional manufacturers, will be essential. As a result, it is important that preparation for pandemic response emphasizes flexibility and readiness to deploy a variety of levers depending on how the pandemic evolves.[23]

[21] There are stockpiles for some vaccines in this category, including cholera, and M-R. However, these stockpiles are primarily treated as programmatic tools "How many units do I need on hand as a minimum at any one time?" rather than functioning as both programmatic and market shaping tools, "How many units can I commit to for the next ~5 years, based on historical and assumed future demand [so that I can incentivize manufacturers to stay in the market, and/or increase production capacity]?"

[22] Key initiatives include the G20 MCM Coordination Platform, G20 Joint Financing for Health Task Force, G7 Delivery Platform, WHO Interim MCM Coordination Platform, WHO INB-hosted negotiation of a Pandemic Accord, WHO HEPR, WHO PRET, X-Vax, the Pandemic Fund, PAVM, CEPI's 100 Days initiative, Gavi 5.1 strategy, European Commission's HERA and many more

[23] This is less true of other types of outbreaks

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Annexes

A. Heat map scoring of supply levers by archetype

B. Market health considerations for outbreak products

C. Insights on regional manufacturing

D. Supply levers – descriptions and analysis

A. Heat map scoring of supply levers by archetype

The scoring of the market shaping levers is split out into two scores:

1. **Relevance for the market challenge in question and effectiveness at overcoming it (and therefore driving equitable availability of MCMs for LMICs).**

This combines elements of applicability, relevance and 'strength'. One score is given for each archetype for preparedness and another for response.[24]

2. **Feasibility of deploying the market shaping lever in question.**

This scoring includes elements of technical and political feasibility. Here one score is given across all archetypes for preparedness, and one for response.

As noted above, these scorings are necessarily approximations. This analysis is subject to numerous caveats and elaborations, as each of the supply levers can be structured and applied in different ways; their effectiveness often depends on how much funding is devoted to them; and an overall rating inevitably requires weighing on a common scale advantages and disadvantages of quite different types.

As such, these scorings should be seen as approximate, an attempt to capture big differences. For example, an APA is more complicated to put in place than a demand forecast, and negotiating a legally binding inter-governmental treaty is an order of magnitude harder again.

The purpose of this analysis is not to promote or discourage the use of particular instruments in general or to reach definitive judgments about which to use in which circumstances, but to highlight the ways that the value of various supply levers differs across outbreak types.

Table 4: Heatmap for preparedness

THE FULL HEATMAPS WILL BE INCLUDED OR ANNEXED AS A SEPARATE DOCUMENT – THIS IS A PLACEHOLDER

			Combined score for relevance of tackling the market challenge included in the archetype, and effectiver				
Archetype No. ->			1	4	7	2	5
Lever sub-group	Market shaping lever	Lever No.	Rare and historically small; early-stage R&D	Rare and historically small; R&D in clinical trials	Rare and historically small; licensed MCM	More frequent outbreaks; early-stage R&D	More frequent outbreaks; R&D in clinical trials
R&D levers	R&D Push Funding	1	1	1	4	1	1
R&D levers	Publicly funded IP for R&D	2	1	1	4	1	1
R&D levers	Access provisions in R&D push funding	3	3	3	4	3	3
Procurement-related levers	Advanced Purchase Agreement (APA)	4	4	2	4	4	2
Procurement-related levers	Advanced Market Commitment (AMC)	5	4	4	4	4	2
Procurement-related levers	Price-Volume Guarantee	6	4	4	4	4	4
Procurement-related levers	Demand pooling and pooled procurement - LMIC wide	7	4	4	3	4	4
Procurement-related levers	Demand pooling and pooled procurement - regional	8	4	4	3	4	4
Procurement-related levers	Ex ante commitment to devote share of supply to LMICs (Berlin Dec.)	9	4	4	4	4	4
Procurement-related levers	Donations	10a	N/A	N/A	N/A	N/A	N/A
Procurement-related levers	Putting donation infrastructure in place in advance	10b	4	4	4	4	4
Procurement-related levers	Resale market	11a	N/A	N/A	N/A	N/A	N/A
Procurement-related levers	Putting a resale market in place	11b	4	4	4	4	4
Procurement-related levers	Pre-emptive Long Term Agreement negotiation	12	4	3	4	4	3
Stockpiles	Stockpile - investigational	13	4	1	4	4	1
Stockpiles	Stockpile - licensed	14	4	4	1	4	4
Financing levers	Rapid response fund for MCM procurement	15	4	3	3	4	3
Manufacturing levers	Contract manufacturing (no expectation of ongoing market)	16	4	1	1	4	2
Manufacturing levers	Reservation of additional manufacturing capacity for surge	17	4	1	1	4	1
Tech-transfer related levers - 'owner side'	Tech transfer and IP licensing - Incentives/funding to share technology	18	4	4	4	4	3

[24] Some levers are only applicable in preparedness or response or obviously not relevant to the context. We have scored these cases as "N/A". It is also worth noting there are levers which are relatively weak across all archetypes, but possibly worth doing as part of a package of interventions because they are easy or quick to do

Table 5: Heatmap for response

THE FULL HEATMAPS WILL BE INCLUDED OR ANNEXED AS A SEPARATE DOCUMENT – THIS IS A PLACEHOLDER

			Combined score for relevance of tackling the market challenge included in the archetype, and effective				
Archetype No. ->			1	4	7	2	5
Lever sub-group	Market shaping lever	Lever No.	Rare and historically small; early-stage R&D	Rare and historically small; R&D in clinical trials	Rare and historically small; licensed MCM	More frequent outbreaks; early-stage R&D	More frequent outbreaks; R&D in clinical trials
R&D levers	R&D Push Funding (by LMIC-focused agency)	1	3	1	4	3	1
R&D levers	Publicly funded IP for R&D	2	NA	NA	NA	NA	NA
R&D levers	Access provisions in R&D push funding	3	4	4	4	4	4
Procurement-related levers	Advanced Purchase Agreement (APA)	4	4	3	3	4	2
Procurement-related levers	Advanced Market Commitment (AMC)	5	4	4	4	4	2
Procurement-related levers	Price-Volume Guarantee	6	4	4	4	4	2
Procurement-related levers	Demand pooling and pooled procurement - LMIC wide	7	4	3	3	4	2
Procurement-related levers	Demand pooling and pooled procurement - regional	8	4	3	3	4	2
Procurement-related levers	Ex ante commitment to devote share of supply to LMICs (Berlin Dec.)	9	4	4	4	4	4
Procurement-related levers	Donations	10a	4	4	4	4	4
Procurement-related levers	Putting donation infrastructure in place in advance	10b	N/A	N/A	N/A	N/A	N/A
Procurement-related levers	Resale market	11a	4	4	4	4	4
Procurement-related levers	Putting resale market in place in advance	11b	N/A	N/A	N/A	N/A	N/A
Procurement-related levers	Pre-emptive Long Term Agreement negotiation	12	4	3	4	4	3
Stockpiles	Stockpile - investigational	13	B/A	B/A	B/A	B/A	B/A
Stockpiles	Stockpile - licensed	14	4	4	1	4	4
Financing levers	Rapid response fund for MCM procurement	15	N/A	N/A	N/A	N/A	N/A
Manufacturing levers	Contract manufacturing (no expectation of ongoing market)	16	4	1	1	4	3
Manufacturing levers	Reservation of additional manufacturing capacity for surge	17	4	2	2	4	2
Tech-transfer related levers - 'owner side'	Tech transfer and IP licensing - Incentives/funding to share technology	18	4	4	4	4	3

B. Market health considerations for PHEs

The Gavi-UNICEF 'Healthy Market Framework'[25] establishes a common way of thinking about routine vaccine market health in LMICs, communicating Gavi Alliance assessments of individual markets, and improving thinking on the trade-offs between how different routine vaccine market elements. It has become the dominant framework for market shaping for MCMs for LMICs.

Figure 4: The Gavi-UNICEF Healthy Markets Framework

This project sought to interrogate whether this framework was for purpose for PHE-MCM markets. Table 6, below compares PHE-MCM markets with markets for MCMs for endemic pathogens, using the same pillars of market health (green = demand, purple = supply) as the Gavi-UNICEF framework.

Table 6: Market health considerations for PHEs

Characteristic	PHE markets	Markets for MCMs for endemic pathogens	Implications for PHE market shaping
Demand predictability and stability	Demand for PHE MCMS is highly unpredictable, as the timing, location, scale, and duration of outbreaks cannot be predicted with confidence. Most outbreaks are relatively short-lived, and some pathogens may disappear for long periods. This unpredictability is the defining characteristic of these markets.	Much more stable demand e.g., annual vaccination of a birth cohort	Even when there is some potential for high demand, demand *risk* for the producer is very high.

[25] https://www.gavi.org/our-alliance/market-shaping

Market size	Many PHEs are relatively small scale, with correspondingly small volumes of MCMs needed. For example, only 19,000 doses have been drawn down from the (Zaire) Ebola stockpile this year, with 6500 for outbreak response, some for vaccination or HCWs, and some to replace expiring doses. There are three exceptions: • True pandemics • Products used in preventative campaigns as well as outbreak response, e.g., Cholera vaccine • Diagnostics, where some products could be used for surveillance and response	Tend to be many orders of magnitude bigger than PHE markets e.g., global demand for DTP vaccination, or HPV	The small magnitude of demand can mean a limited commercial rationale for investment, with implications for almost all market health dimensions e.g., availability, affordability, supplier risk, long term competition and innovation etc.
Frequency of outbreaks	Outbreaks of some pathogens are in frequent, while others are more common and may have a seasonal pattern.	Some outbreak pathogens are also endemic in some countries. As a result, markets for MCMs for these pathogens may be larger and at least somewhat more stable.	Low frequency of outbreaks contributes to market uncertainty and creates challenges in sustaining supply. In addition, infrequency of outbreaks makes it difficult to plan and conduct efficacy trials, creating a barrier to product develop and new entrants.
Urgency	PHEs are, by definition, emergencies and the need for MCMs urgent. This means that getting to market and scaling up supply quickly are very high priorities. It may also entail some increased tolerance for sub-optimal products (efficacy less than desired, or not demonstrated as fully as other products).	Although speed to market may be important commercially in these markets, it is not the priority it is in PHEs. There is very limited willingness to relax standards or licensing norms, especially for vaccines given to health people.	May support those first to market (even with a suboptimal product); premium for technologies that can be developed and scaled quickly (especially in true pandemics).

Price insensitivity	Urgency, fear, and public awareness can make governments (and international agencies) much less price-sensitive than they would normally be. There are at least two reasons for this: fear of/desire to avert a worst case scenario, and overvaluing of epidemic deaths as opposed to deaths from routine causes that have been normalized.1 Price insensitivity is substantially driven by the perception of threat to HICs, even when an outbreak is initially affecting only LMICs.	Price/cost tends to be a dominant concern in decisions on MCMs for endemic LMIC diseases. HIV is a partial exception, for some of the same reasons as outbreak diseases.	May make some PHE markets more commercially attractive than a market of similar size for an endemic disease restricted to LMICs, but this consideration will in most cases be dwarfed by the disadvantages of these markets.
Supply shortage	When a pathogen of MCM is new, or demand exceeds a stockpile, there will be a period of supply shortage, which can be acute.	Supply shortages can occur, but relatively predictable demand and greater time for supply to adjust mean that they are rarer and typically less acute.	Supply shortage means competition among countries for access. If high-income countries are affected, competing with them for limited supplies may be the greatest challenge facing LMICs and int'l agencies acting on their behalf.
Trade/export bans	When there are shortages of PHE-relevant MCMs, producing countries may impose export bans on key inputs and/or finished products	Export bans are very unlikely.	Increased importance of mitigating geopolitical risk for PHE markets. This could be achieved through geographic diversity of manufacturing or through international agreements limiting export bans and setting norms for allocation of scarce supplies in an emergency.
Political pressure not to profit maximise	Suppliers could face public scrutiny and political pressure tp prioritize the public good in an outbreak, with calls for them to donate products or sell them at cost and to share IP and technology.	Much lower levels of public scrutiny in most markets, though there are notable exceptions (e.g., HIV, HepC).	This political scrutiny can support availability and affordability in the short term, but may send negative signals to manufacturers, and in the worse case discourage involvement in PHE markets.

These differences mean (as mentioned in the Insights) that full market health is neither appropriate nor feasible for most PHE markets. Figures 5 and 6, below, summarise how PHE market health should diverge from the fuller conception of market health relevant to routine vaccine markets.

Figure 5: The Gavi Alliance HMF - supply side

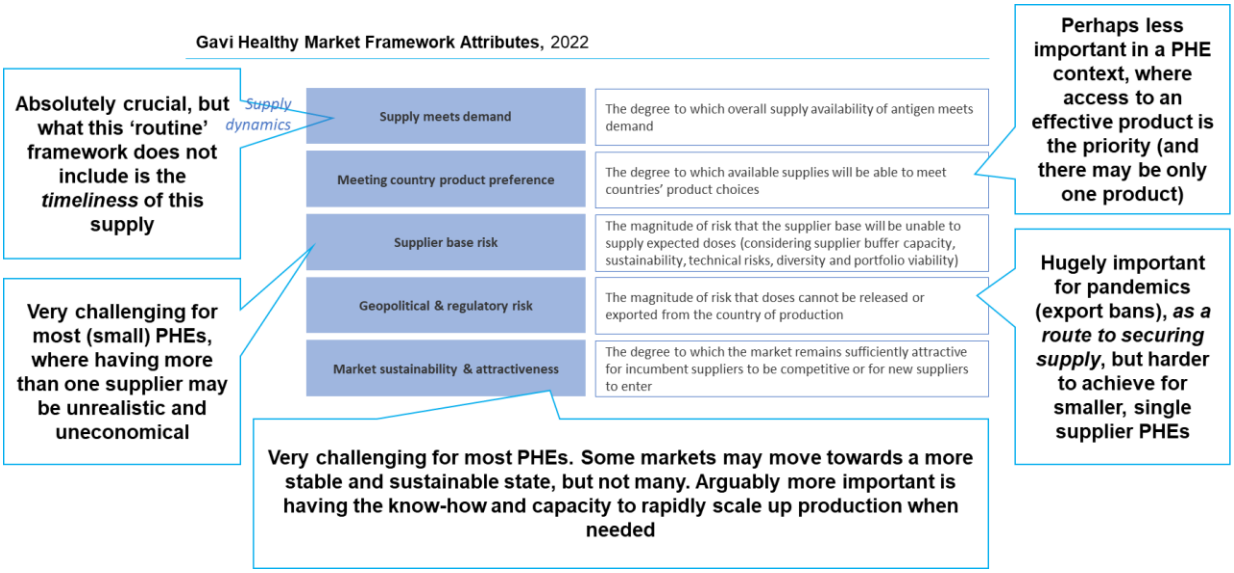
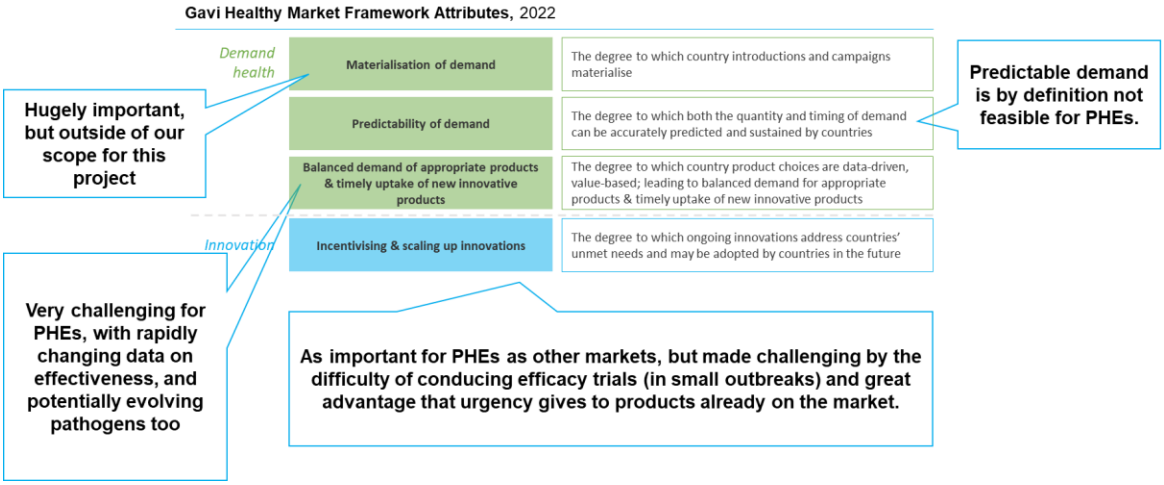


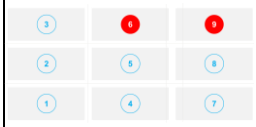
Figure 6: the Gavi Alliance HMF - demand side



C. Insights on roles for regional manufacturing

The COVID-19 pandemic has spurred considerable interest in strengthening African vaccine manufacturing to provide the continent with greater security of supply in future outbreaks. As with other approaches to MCM supply, greater reliance on regional manufacturing is probably more useful in some types of outbreaks than others. Our analysis suggests the case for regional manufacturing is particularly strong for six of the nine archetypes.

Table 7: Roles for regionally distributed manufacturing for MCMs for PHEs

Role for regional manufacturing	**Market shaping levers to deploy…**		**Relevant to archetypes**
	…for preparedness	**…in response**	
Security of supply in the face of limited/uncertain commercial incentives (as a hedge in case other manufacturers withdraw)	• Tech transfer to regional manufacturers • Non-product specific investment in and capacity-building for regional manufacturers • Subsidy for procurement from regional manufacturers to build capacity • Regulatory agency capacity strengthening - to oversee manufacturing	• Where products already exist and technology has been transferred, none except purchase[26] • Product-specific tech transfer to regional manufacturers[27]	Rare and historically small outbreaks (bottom row), and more frequent outbreaks (middle row) 
Security of supply in the face of competition (as a primary channel of access) **AND** **Increasing the overall volume of supply**	• Tech transfer to regional manufacturers • Non-product specific investment in and capacity-building for regional manufacturers • Subsidy for procurement from regional manufacturers to build capacity • Non-binding regional procurement compact	• Where products already exist and technology has been transferred, none except purchase[28]	Pandemic potential pathogens and outbreaks (top row) 

[26] If preparedness investments in capacity have not been made, then it will likely be quicker and less expensive to secure supply through other means, such as contract manufacturing (rare and historically small PHEs), or tech transfer to a more capable, high volume supplier (more frequent PHEs and pandemics)
[27] This tech transfer would have to be quick to be impactful, which implies a high level of existing capability, that does not exist everywhere today
[28] If preparedness investments in capacity have not been made, then it will likely be quicker and less expensive to secure supply through other means, such as contract manufacturing (rare and historically small PHEs), or tech transfer to a more capable, high volume supplier (more frequent PHEs and pandemics)

	• Regulatory agency capacity strengthening - to oversee manufacturing	• Product-specific tech transfer to regional manufacturers[29] • Non-binding regional procurement compact	

[29] This tech transfer would have to be quick to be impactful, which implies a high level of existing capability, that does not exist everywhere today

D. Market shaping levers: descriptions and analysis

This Annex provides more detail on the 38 market shaping levers UNICEF has analysed to inform the PHE archetypes. In the tables that follow, each lever is described, with a short analysis of how it works, its benefits and drawbacks, and implications for its usefulness in different types of outbreaks.

This analysis is summarized in the heatmap (Annex A).

It is important to note that this analysis focuses on the effectiveness of the lever in promoting the development and timely availability of medical countermeasures to LMICs. An analysis that prioritized other market objectives such as affordability, sustainability, or ongoing innovation might lead to different conclusions.

List of levers

No.	R&D levers
1	R&D Push Funding (by LMIC-focused agency)
2	Publicly funded IP for R&D
3	Access provisions in R&D push funding
	Procurement-related levers
4	Advanced Purchase Agreement (APA)
5	Advanced Market Commitment (AMC)
6	Price-Volume Guarantee
7	Demand pooling and pooled procurement – LMIC-wide
8	Demand pooling and pooled procurement -- regional
9	Ex ante commitment to devote share of supply to LMICs (Berlin Dec.)
10	Putting donation infrastructure in place
11	Donations
12	Putting a resale market in place
13	Resale market
14	Pre-emptive Long Term Agreement negotiation
	Stockpiles
15	Stockpile - investigational
16	Stockpile - licensed
	Financing levers
17	Rapid response fund for MCM procurement
	Manufacturing levers
18	Contract manufacturing (no expectation of ongoing market)
19	Reservation of additional manufacturing capacity for surge
	Tech-transfer related levers - 'owner side'
20	Tech transfer and IP licensing - Incentives/funding to share technology
21	Tech transfer and IP licensing - TT/licensing as condition of APA
	Tech-transfer related levers - 'bridging'
22	Tech transfer and IP licensing - Patent pools and TT hubs
23	Tech transfer and IP licensing - Brokering advance TT and licensing agreements
	Tech-transfer related levers - recipient side
24	Tech transfer to a high-volume manufacturer (without regional security of supply focus)

	Regional manufacturing levers
25	Tech transfer to regional manufacturer focusing on regional supply
26	Non-product specific investment in and capacity-building for regional manufacturers
27	Subsidy for procurement from regional manufacturers to build capacity
28	Non-binding regional procurement compact
	Regulatory levers
29	Regulatory agency capacity strengthening - to oversee manufacturing
30	Expedited regulatory approvals in country of use
31	(Clinical) Policy/Guideline development
	Possible treaty provisions
32	Tech Transfer requirement
33	Ban on export bans
34	HIC dose-sharing requirement
35	Pandemic IPR waiver
	Other levers
36	Publishing market information
37	Demand forecasting
38	Advocacy/soft power

Lever Name	**1. R&D push funding (by LMIC-focused agency)**
Description/how it works	Direct financial support to an MCM developer to support R&D in order to incentivize or accelerate product development and/or to make the product more suitable for LMICs. In theory, could include other mechanisms for reducing R&D costs to product developers, such as tax breaks. For the purposes of this project, focus is on push funding from agencies focused on LMICs. In pandemics, the bulk of push funding is likely to come from HIC agencies motivated primarily by the needs of their own populations. HIC agencies can also be an important source of financing for development of MCMs for pathogens that do not pose a serious threat to HICs.
Benefits	By subsidizing R&D, push funding can induce product developers to undertake or accelerate development/adaptation of products needed by LMICs.
Drawbacks	• Transfers R&D risk entirely or in part to funders; requires funders to "pick winners". • Does not offer developers a return comparable to commercial markets. • By itself, does not ensure supply or availability to LMICs
Implementation constraints	Requires expertise to select which developers/product candidates to fund
Preparedness or response (or both)?	Can be both: • For a novel pathogen, push funding could take place during an outbreak e.g., COVID-19 drug and vaccine development • For a known pathogen, push funding can support product development in anticipation of an outbreak.
When should the international community use this lever?	• When there are no MCMs on the market or supply of available products cannot be expanded sufficiently and both market forces and funding from HICs are inadequate to drive R&D • When the MCMs that do exist are sub-optimal for LMICs because of presentation, cold chain requirements, dose regimen, or delivery model • As a way to secure access to supply through access provisions (see lever below: "Access conditions in R&D funding")

When should the international community not use this lever?	• When there are already a number of good MCMs available, or there is one good MCM with sufficient production capacity • When market forces are sufficient to incentivize development of the needed product • When extensive funding from HICs is already supporting the development of appropriate products (i.e. pandemics), especially when there are viable routes to access.
Examples	CEPI funding to Inovio to support early-stage development of Lassa and MERS vaccines

Lever Name	**2. Access to publicly funded IP for R&D (by LMIC-focused agency)**
Description/how it works	A substantial proportion of R&D on PHE-relevant pathogens, especially early-stage R&D, is funded by public sources. These funders could insist that this IP is made broadly available for further R&D. This could accelerate R&D by allowing more product developers to make use of this IP to pursue further development.
Benefits	• Can accelerate R&D for small and rare outbreaks, where IP is sometimes "trapped" when IP owners are not actively pursuing product development • Can accelerate R&D for other types of outbreaks as well by allowing more developers to make use of the IP, including to develop LMIC-suited products
Drawbacks	• Ensuring access to the publicly funded IP may not be sufficient to yield a product if other commercially protected IP is needed. • For pathogens causing small and rare outbreaks, access to IP will be insufficient without public funding for R&D and manufacture: IP is not the primary barrier. • Some product developers may be reluctant to accept public funds on these conditions and may therefore refrain from participating in the needed R&D.
Implementation constraints	• Resistance from industry • Need to weigh benefits of IP access against potential disincentives and choose in which circumstances and for which kinds of R&D to require access to IP.
Preparedness or response (or both)?	Mostly preparedness: as publicly funded IP is typically most relevant to early-stage R&D, most benefit when policy is in place in advance.
When should the international community use this lever?	• For pathogens causing small and rare as well as more frequent outbreaks to avoid trapping and to enable additional product developers • For pandemic-potential pathogens when there are gaps in HIC R&D funding
When should the international community not use this lever?	• For pandemics, where main HICs can be main source of funding. • For commercially borderline products, where interest of a developer in bringing a product to market depends on some degree of exclusivity • Products in later stage R&D – likely to be significant opposition from commercial actors who have invested up until that point • Products/pathogens where the obvious route to market e.g., only one suitable vaccine technology platform, is protected IP
Examples	NIH/FDA licensing of conjugation technology used in Meningitis A vaccine

Lever Name	**3. Access conditions in R&D push funding**
Description/how it works	By imposing conditions on grants or R&D contract, push funders can try to ensure that products arising from this funding are available to and accessible to LMICs. These conditions could include supply and price commitments or IP licensing/tech transfer to suppliers willing to serve LMIC markets.

Benefits	Can make it more likely that products resulting from R&D funding are available at an affordable price
Drawbacks	• Cannot guarantee access, as may be no wiling supplier or insufficient funding for purchase • Price and supply commitments may not allow competitive supply and therefore may not bring about lowest prices.
Implementation constraints	• Ability/market power to negotiate the access conditions • Information asymmetry: funder may have little information on cost of production and therefore appropriate access price
Preparedness or response (or both)?	Largely preparedness, with anticipated benefits in response
When should the international community use this lever?	For outbreak MCMs with potential HIC markets (i.e. pandemic products), to ensure that funded product developers serve LMICs as well as HICs.
When should the international community not use this lever?	• Generally not necessary for outbreaks not affecting HICs, as product developers already targeting LMICs. • Unlikely to be feasible when product developers have access to large amounts of funding from HICs without comparable conditions.
Examples	• CEPI funded nine COVID-19 vaccines candidates, across a range of developers and technology platforms. Some of the deals included (confidential) access conditions. • For non-outbreak products, access provisions are commonly attached to PDP support for R&D

Procurement-related levers

Lever Name	**4. Advanced Purchase Agreement (APA)**
Description/how it works	An APA is binding commitment to an individual supplier to purchase a specific product when the product becomes available, or at some future date (if the product is already on the market). Crucially, this commitment holds whether or not expected demand for the products materializes and whether or not the products are still needed. To distinguish these commitments from standard procurement contracts, the term is best used when the commitment is made well in advance of expected availability, in particular when the product has not yet come to market or when the necessary production capacity is not yet in place. It is most relevant when there is substantial demand risk, making the commitment valuable to the supplier. • APAs often involve some prepayment, but this is not a defining feature. • APAs signed before a product has come to market are typically conditional on regulatory approval. • Deals with suppliers may involve a mix of absolute purchase commitments and options to purchase additional volumes, thus allowing some sharing of demand risk.
Benefits	APAs have two main benefits. First, by creating firm demand in the face of the uncertainty typical of outbreaks, they can incentivize suppliers to invest in the R&D necessary to bring a product to market and/or to invest in additional production capacity—in this sense they are a classic pull mechanism. Importantly, in contrast to AMCs, APAs insulate suppliers from both aggregate demand risk (e.g., that the outbreak is smaller or ends sooner than expected) and competitive risk (that users will prefer other products). Second, in a context of supply shortage early in an outbreak, when new products are coming to market or production capacity for existing products is inadequate, APAs can allow buyers to secure supply in the face of competition from other buyers. Making a deal in advance of availability should guarantee the buyers a place in the production queue/a share of supply produced.

Drawbacks	The main risk of APAs for individual buyers is that is that they end up obligated to buy more than they need, either of a class of products (e.g., COVID-19 vaccines) or of specific products (e.g., Novavax's COVID-19 vaccine). This can happen in two ways: if APAs are signed before products come to market and more candidates than anticipated are successful, leaving the buyer with excess supply; or if demand (product specific or category wide) is lower than expected. Buyers can also end up paying higher prices than they might have paid if they had waited to sign contracts. From a broader market perspective, the use of APAs by all buyers, especially HICs, can result in a bidding war, driving up prices for everyone. For LMICs, the use of APAs by HICs can be a grave threat to access, as neither these countries nor their proxy buyers are likely to be able win a bidding war with HICs. Requires buyers to "pick winners", typically before product preferences are clear.
Implementation constraints	To enter into an APA, a buyer must be able to set aside the necessary funds to cover the commitment or credibly guarantee the commitment in another way. This credibility is crucial to the APA's power as an incentive. To be effective in securing supply in the fact of HIC competition, LMIC buyers must be able to pay competitive prices and be ready to enter in these commitments early in a pandemic (see "Rapid response fund for MCM procurement (#17 below). Buyers must also have the necessary capacity to negotiate this type of agreement and embed it in appropriate contractual language. Supplier commitments on delivery timing in APAs may be difficult to enforce, which can weaken the value of APAs in securing timely supply, especially when an LMIC or proxy buyer is in competition with HIC buyers who may be paying higher prices or have other market advantages. For suppliers, there is a risk that buyers will try to exit from purchase commitments if demand for the product falls, as has happened with COVID-19 vaccines.
Preparedness or response (or both)?	Primarily response. APAs are generally used during outbreaks, to drive R&D and production or to secure supply. Could possibly be put in place for existing or close-to-market products for pandemics, with purchase contingent on an outbreak. They could also be used before an outbreak to incentivize production for a stockpile, but this blurs pull and push funding e.g., an APA with prepayment for doses for a stockpile is essentially push funding for production costs.
When should the international community use this lever?	• To drive development or production of a product needed for an outbreak primarily affecting LMICs (but weigh also against push funding, contracted production, and other alternatives) or an LMIC-tailored product in a broader outbreak • To reserve some supply for LMICs in the face of competition from HICs during period of supply shortage.
When should the international community not use this lever?	• At very early stages of R&D, when scientific risk is very high—push funding is more appropriate in these circumstances. Also APAs have to be with firms that can manufacture at scale, so are not appropriate ways to support R&D by universities or biotech. • When supply is very constrained and competition with HICs too fierce. In these circumstances, LMIC buyers are likely to lose an APA bidding war and resources may be better spent on expanding supply through tech transfer (TT) and other means. • Towards the middle or end of a large outbreak, if HICs have clearly overbought, and donations or resale markets are likely to provide an adequate supply for LMICs • When there is an adequate supply of appropriate products—in this situation (COVID-19 vaccines in late 2022), there is no rationale for buyers assuming all demand risk
Examples	• COVAX APAs, especially those signed in advance of product approval • Gavi commitment to buy Merck Ebola vaccine after the West Africa trial

Lever Name	**5. Advanced Market Commitment (AMC)**

Description/how it works	An AMC is distinguished from an APA in that it is a commitment on the part of a buyer to industry as a whole, rather than to an individual supplier. The buyer commits in some way to buy—or create a market for—products meeting certain requirements regardless of who makes them. Two quite different types of AMCs are worth distinguishing. 1. In a "classic" AMC, price is specified but volume is not guaranteed. Instead, purchase at the agreed price is triggered by demand or need from eligible recipient countries. In this way the AMC sponsor commits to subsidizing these purchases and therefore ensures that *if demand materializes* it will be translating into purchase at the agreed price. In this way, suppliers are incentivized by the prospect of a commercially attractive market but are not protected against either demand or competitive risk. 2. In another type of AMC, a buyer commits in some way to buying qualifying products whether or not need or demand materializes, therefore protecting potential suppliers against demand uncertainty. Both price and volume could be set in advance, or the total to be spent on purchase fixed, with prices and volumes determined by an agreed process. This second type of AMC is the most relevant to disease outbreaks, since it protects product developers/suppliers (as a group) against the demand uncertainty characteristic of outbreaks. In both types of AMC, the commitment to industry as a whole is typically translated into bilateral supply agreements at some point; when this occurs is an important design choice.
Benefits	Like an APA, an AMC of the second type could in theory incentivize product development or production scale-up during an outbreak by reducing demand risk and increasing likely return to successful R&D. An advantage over bilateral APAs (and over R&D push funding) is that it does not require buyers to "pick winners". In theory, it leaves more room for market forces to drive product selection. And some designs can incorporate price competition.
Drawbacks	• From the perspective of an individual supplier, an AMC is a weaker demand signal than an APA, since it does not guarantee purchase of its product. This difference may be decisive in outbreaks. A consequence is that an AMC may have trouble attracting suppliers in competitions with APAs (firm commitments to particular suppliers) offered by other buyers. An AMC may be most appropriate where is it sponsored jointly by all potential buyers (where it is 'the only game in town'). • AMCs are complicated to design and challenging to make credible as legally binding commitments. This is particularly the case if prices are not specified in advance. As the main rationale for an AMC is to provide assurance to suppliers that there will be a market for their products, even in the very uncertain environment of an epidemic, this is an important challenge. • Especially when intended to incentivize R&D, an AMC would typically have to be very large to offer a strong incentive. Finding committed funding for such a large initiative would be very challenging. But it should be noted that to the extent that the large size required reflects R&D risk, the cost of an AMC would not necessarily be greater than the aggregate cost of achieving the same results through push funding.
Implementation constraints	• Sufficient funding for a large mechanism, untested in a PHE context • Design and legal complexity • Unfamiliarity of product developers and suppliers
Preparedness or response (or both)?	Response, although in theory buyers could announce in advance an intention to establish an AMC in a future outbreak, outline its general structure, and put in place some form of conditional funding that would become available at the start of an outbreak.

When should the international community use this lever?	Not clear if ever the best strategy, but could be used • For R&D, especially when the scientific obstacles are modest (later stages) • When multiple suppliers are both desirable and feasible (i.e. for more frequent & larger but not for small and rare outbreaks) • When large volumes are desired (justifying multiple suppliers) • Best when all or most important buyers join • Better when suppliers would agree not to do bilateral side deals (e.g., regional buyers commit to a joint AMC with regional suppliers) • More useful when country preferences may vary but are unknown (making APAs with individual suppliers less attractive) • When most promising developers or products unclear, making an AMC more attractive than APAs
When should the international community not use this lever?	• When one supplier is clearly best-placed and sufficient, or when multiple suppliers are probably not needed (small and rare outbreaks) • When the R&D is very challenging and risky • When the AMC will have to compete against APAs
Examples	• Gavi's Pneumococcal AMC (Modified type 1 AMC) • UNICEF's Zika diagnostics APC (type 2) • Proposed COVID-19 vaccine AMCs (type 2--not implemented)

Lever Name	**6. Price-volume guarantee**
Description/how it works	A third party guarantees demand for an MCM in the event that the demand does not materialize from the agreed buyer(s), with the goal of reducing demand uncertainty for suppliers and thereby incentivizing their participation in R&D or manufacture. For example, a guarantor promises that if 10 specified countries buy less than 1m courses of a product, it will buy the remainder.
Benefits	• Encourages the producer to scale up production by removing the demand risk. From the seller's perspective, this is effectively an APA. • The buyer or buyers do not need to put up capital themselves – this is covered by the guarantor. • Instead of needing to commit financing for all of the guaranteed volume, the guarantor only has to cover the gap between this and the actual volume, taking into account the probability of shortfall. As such, a guarantor can guarantee much more product for the same volume of capital than a buyer would be able to.
Drawbacks	• Not appropriate when demand uncertainty is great, as cost to the guarantor is then very high. • As with APA, risk of paying for product that is not needed. Here this risk is borne by guarantor.
Implementation constraints	• Complex to design • Requires a willing guarantor
Preparedness or response (or both)?	In theory either, but much easier to design during an outbreak, when more is known about products and demand.
When should the international community use this lever?	• More predictable outbreaks where there are MCMs on the market. This could include products used in both preventative and response settings – here the risk of demand not materializing through either response or prevention should be low enough for the financial structure to work.
When should the international community not use this lever?	• Small and rare type outbreaks or pandemics, where demand uncertainty is too high. • Early-stage R&D/pre licensure products

Examples	• MedAccess – various including HIV diagnostics • UNICEF's Long-Term Agreement for rotavirus vaccines

Lever Name	**7. Demand pooling and pooled procurement – LMIC wide**
Description/how it works	A group of potential buyers join together to signal demand for a MCM and buy/procure that MCM together or through a proxy buyer. There are a range of models for pooled procurement: • Coordinated deal terms – buyers coordinate and potentially negotiate together, sending a stronger signal to sellers and increasing market power, but don't agree to share the product afterwards. • Aligned – buyers agree on a range of products (e.g., different COVID-19 vaccines), and each buyer then buys separately, but shares the supply with other buyers in the pool. In this model, the buyers do not combine but align their finances • Fully integrated – buyers combine finances and place one deal per product, then share the resulting supply. • Tiered. One proxy buyer buying on behalf of a set of countries could itself join a wider buying pool.
Benefits	• Gives buyers greater market power, helping them obtain better terms (price, delivery commitments, flexibility).[30] • Can help buyers mitigate R&D risk e.g, as can place bets on more products collectively than acting alone. • Can help buyers manage demand uncertainty e.g., if one country in the pool has more cases, supply can be diverted to them rather than each having to buy for their own worst-case scenario • Reduces transaction costs for suppliers • Can reduce transaction costs for buyers e.g., one deal team negotiating on behalf of governments, rather than each government having to do multiple deals
Drawbacks	• By definition, requires compromise from the buyers. For example, unlikely to be able to channel all demand to a domestic manufacturer and may have to compromise on product characteristics. • Disproportionately helps smaller buyers in the pool – bigger buyers might be able to move more quickly on their own and might be able to negotiate similar terms.
Implementation constraints	• Buyers have to agree on products and terms, and, in certain types of pooling, on mechanisms for sharing.
Preparedness or response (or both)?	Response, although pooling arrangement are best agreed in advance.
When should the international community use this lever?	• In outbreaks where there are few/no MCMs on the market but many in the pipeline e.g., early in COVID-19 vaccine development, when cooperating buyers can place bets on multiple candidates, either by individually making deals for products and agreeing to share or by collectively making deals for multiple candidates.. • In outbreaks where LMIC buyers are struggling with buyer power vs HICs (pandemics) e.g., COVAX or AVAT on COVID-19 • When demand is very varied and uncertain across buyers, where pooling can help to smooth demand for suppliers • Where there are large numbers of potential buyers, to reduce transaction costs for both buyers and suppliers
When should the international community not use this lever?	• When participants have not harmonized requirements and preferences or when there is insufficient trust (especially if pooling involves sharing)
Examples	COVAX, UNICEF procurement of routine vaccines for Gavi

[30] Except for the 'aligned' model

Lever Name	8. Demand pooling and pooled procurement – regional
Description/how it works	As LMIC-wide pooled procurement (#7), but regional.
Benefits	• Same as broader pooling (#7), although in general market power will be weaker. • Could be a vehicle for joint procurement from regional suppliers.
Drawbacks	• Same as broader pooling • Weakens potential buying power of LMIC-wide procurement mechanism; invites competition among regions
Implementation constraints	As #7
Preparedness or response (or both)?	Response, but best if arrangement put in place in advance.
When should the international community use this lever?	As for broader pooling, plus: • For outbreaks primarily affecting a region: some small and rare (e.g. Ebola in Africa), some more frequent. • If linked to regional manufacturing, when the latter is seen as important • When a regional perceives that it's supply security is insufficiently ensured by an LMIC-wide mechanism.
When should the international community not use this lever?	As for broader pooling, plus When an LMIC-wide mechanism can obtain better terms and can better meet the needs of participating countries
Examples	• EU COVID-19 Vx procurement • AVAT COVID-19 Vx procurement • PAHO's Revolving Fund

Lever Name	9. Advance commitment to devote share of supply to LMICs (e.g., 'Berlin Declaration')
Description/how it works	One or more MCM manufacturers agree in advance to make available a proportion of their supply to LMICs or some other category of eligible countries "in real time"—as they are produced.[31] (This lever concerns voluntary commitments by suppliers. Mandatory sharing, imposed on HICs by a pandemic treaty, is considered separately as lever #34.) The supply reserved for LMICs could be donated by manufacturers, purchased by LMICs or a proxy buyer, or purchased on behalf of LMICs by one or more HICs. The commitment may include other conditions, such as I&L agreements.
Benefits	• Ensures availability to LMICs of some supply at the same time as HICs, if participating product developers are successful in bringing products to market. • Ensures some supply for LMICs throughout an outbreak, e.g., if HICs place large deals catalysing production capacity increases, LMICs also have access to a share of this expanded supply.

[31] The Berlin Declaration does not state the proportion of production capacity, but some sources have mentioned 10%. It also does not spell out explicitly which countries would be eligible or who would buy at what price.

Drawbacks	• Only relevant to outbreaks where HICs are buying, as model depends on HIC purchase of unshared doses (and perhaps of LMIC share as well, and because in outbreaks not affecting HICs, 100% of production capacity would go to LMICs even without the commitment • Risk that the best or only MCMs that come to market are produced by manufacturers that not part of the scheme • Risk that the committed proportion of production capacity is not sufficient for LMIC needs • Risk that geographical restrictions leave out some countries. • Not enforceable: firms can renege in the face of HIC buying power and producing countries can impose export bans.
Implementation constraints	• Defining volume commitment (share of production), country eligibility, allocation rules, delivery timelines, price, and other terms, along with penalties for noncompliance • In more fragmented diagnostic and therapeutics markets (as opposed to vaccines), it may be challenging to get enough manufacturers on board to have a realistic chance of relying on such a commitment in an outbreak.
Preparedness or response (or both)?	Best established in advance, for use in response
When should the international community use this lever?	Pandemics, to ensure at least some supply when MCMs first become available and in case of continuing supply shortage
When should the international community not use this lever?	PHEs that only affect LMICs (and are not perceived as a threat to HICs) Even in pandemics where sharing commitments could be useful, LMICs and agencies acting on their behalf should not rely solely on this supply channel but should take multiple approaches to ensuring access.
Examples	IFPMA's 'Berlin Declaration'

Lever Name	**10. Donations infrastructure established in advance**
Description/how it works	Donation of surplus MCMs from HICs/producing countries to LMICs can be a useful tool in certain contexts (see lever #11). This lever concerns the design and establishment of an efficient system for managing donations in advance of an outbreak. This 'infrastructure' includes agreement on roles and responsibilities among potential HIC donors, potential recipients, and intermediaries such as WHO, Gavi, UNICEF, regional entities (Africa CDC, PAHO and others), as well as establishment of systems and processes for requesting, accepting and allocating donations, handling regulatory and liability issues, and distribution to LMICs.
Benefits	• Accelerates availability of donated doses to LMICs by reducing the transaction cost of donating MCMs for HICs/producing countries. • Could also make allocation more equitable if donors use the established system rather than bilateral channels. • If donations become available, could be an important source of supply for LMICs.

Drawbacks	• Donations are only useful when some countries, particularly HICs, have excess supply. Thus they are not useful for outbreaks affecting only LMICs, or for pandemics in which supply remains insufficient even for HICs. • For the same reason, LMICs cannot count on donations, which are not a reliable source of supply. • Donations will in general only become available when HICs are certain that they have more than they need. As a result, donations may not be timely. • Not useful if different products or presentations are needed by HICs and potential recipient countries. • Some potential to incentivize overbuying/overproducing if HICs/producing companies know it will be easy to donate their excess
Implementation constraints	Arrangements can be complicated, involving agreement among donors, producers, intermediaries, and recipient countries. But these processes have already been worked out as part of the COVID-19 response
Preparedness or response (or both)?	Preparedness for use in response. The 'infrastructure' is put in place in advance but used during outbreaks.
When should the international community use this lever?	• For potential pandemics that would threaten HICs, who may end up with excess supply. Most likely when R&D success is higher than anticipated, so that HICs end up buying more product than they need. • In outbreaks where LMICs are unable to obtain adequate supply through other means, either by competing successfully with HICs in markets or through dedicated regional supply.
When should the international community not use this lever?	• For outbreaks not likely to affect HICs • When HIC-favored products are not appropriate for LMICs.
Examples	N/A – has not been done ex ante yet. Some precedent through COVAX

Lever Name	**11. Donations**
Description/how it works	Donation of surplus MCMs from HICs/producing countries to LMICs can be a useful tool in certain contexts. This lever focuses on donations during an outbreak (a response action), while previous lever (#10) focuses on establishment of the necessary arrangements in advance.
Benefits	• Potentially important source of supply for LMICs if HICs have excess supply. • Free to LMICs
Drawbacks	• Only useful when there's excess supply/HICs overbuy. Thus not useful for outbreaks affecting only LMICs, or for pandemics in which supply remains insufficient even for HICs. • For the same reason, not reliable: LMICs cannot count on donations. • Not useful if different products or presentations are needed by HICs and potential recipient countries. • Typically not timely, as HICs will only donate when they are sure that they have sufficient supply for their own populations
Implementation constraints	Arrangements can be complicated because of I&L, product preferences, allocation, and this can introduce delays. Easiest if have worked out in advance.
Preparedness or response (or both)?	Response

When should the international community use this lever?	• In pandemics when HICs have excess supply. Most likely when R&D success rate is high. • Most important in cases where LMICs are struggling to obtain supply through other means, either by competing successful with HICs in markets or through regional supply
When should the international community not use this lever?	• In outbreaks not affecting HICs • In outbreaks when supply is insufficient even for HICs • When HIC-favored products are not appropriate for LMICs.
Examples	COVID-19, through COVAX and bilaterally

Lever Name	**12. Putting a resale market in place**
Description/how it works	Resale markets could be another way (in addition to donations) to facilitate flow of MCMs from HICs or other countries with excess supply to LMICs (or other countries) that need and want them (see lever #13). This lever focuses on the design of such markets and the value of putting arrangements in place in advance of an outbreak. The 'infrastructure' includes agreement on roles and responsibilities among producers, sellers, buyers, and intermediaries like WHO, Gavi, UNICEF, regional entities (Africa CDC, PAHO and others), as well as agreement on systems and processes for handling the MCMs for resale e.g., pricing, I&L, shipping etc.
Benefits	• Having market arrangement in place in advance could speed the access of MCMs to LMICs in the event of HIC over-buying and surplus.[32] • If surplus does become available on resales markets, could be another source of supply for LMICs.
Drawbacks	• As with donations, only relevant when some countries have excess supply, so cannot be counted on and will in general not be timely. • Unlike donations, require sufficient funding to purchase. • If overall supply is still constrained, prices on resale markets may actually be higher than directly from suppliers. • Might (weakly) incentivize further overbuying by HICs if they know they can easily recoup costs for these MCMs if they don't need them
Implementation constraints	• Should not be too difficult to create a parallel marketplace, and many of the issues will be similar to donations. • Requires agreement by suppliers to allow resale—may be more reluctant than for donations.
Preparedness or response (or both)?	Preparedness for use in response. The 'infrastructure' is put in place in advance but used during outbreaks.
When should the international community use this lever?	• Mostly pandemics, where there it is possible that some countries will have excess supply. • Outbreaks where it may not be possible for LMICs to secure supply by other means, as with donations.
When should the international community not use this lever?	• In most outbreaks not affecting HICs, where excess supply to some and insufficient supply to others is less likely • When LMICs cannot afford to buy at going prices and there is no source of funds to buy on their behalf.

[32] Like donations, producing countries could re-sell products whilst still having insufficient supply for their own populations, but this seems unlikely

Examples	US-led medical countermeasure clearing house

Lever Name	**13. Resale markets**
Description/how it works	Resale markets could be another way (in addition to donations) to facilitate flow of MCMs from HICs or other countries with excess supply to LMICs (or other countries) that need and want them (see lever #12). This lever focuses on the use of such markets during an outbreak.
Benefits	• A potential source of supply for LMICs if some countries have excess supply • Allow overall supply and demand to come into balance and prices to adjust to market conditions
Drawbacks	• As with donations, only relevant when some countries have excess supply, so cannot be counted on and will in general not be timely. • Unlike donations, require sufficient funding to purchase. • If overall supply is still constrained, prices on resale markets may actually be higher than directly from suppliers. • Might (weakly) incentivize further overbuying by HICs if they know they can easily recoup costs for these MCMs if they don't need them
Implementation constraints	• Should not be too difficult to create a parallel marketplace, and many of the issues will be similar to donations, but easiest if put in place in advance. • Requires agreement by suppliers to allow resale—may be more reluctant than for donations.
Preparedness or response (or both)?	Response
When should the international community use this lever?	• Mostly pandemics, where there it is possible that some countries will have excess supply. Could also be relevant in some mid-tier outbreaks, especially where allocation of MCMs is not controlled by an international mechanism. • Outbreaks where it may not be possible for LMICs to secure supply by other means, as with donations. • When funding is available
When should the international community not use this lever?	• In most outbreaks not affecting HICs, where excess supply to some and insufficient supply to others is less likely • When LMICs cannot afford to buy at going prices and there is no source of funds to buy on their behalf.
Examples	US-led medical countermeasure clearing house

Lever Name	**14. Pre-emptive Long-Term Agreement negotiation**
Description/how it works	Negotiations that take place in order to establish an LTA - a written agreement between the purchaser and a supplier that covers all the commercial terms applicable to orders that may be issued for repeated purchase of predefined goods or services over a specific period of time. Unlike APAs, however, LTAs do not commit the buyer to specific volumes. Such LTAs could be negotiated for outbreak-relevant MCMs in advance of outbreaks, to reduce transaction times when outbreaks occur. This should speed time to availability of MCMs for LMICs. UNICEF, which uses LTAs, is the most likely buyer to use this approach, but in principle other buyers could do so as well.

Benefits	Once in place, LTAs reduces administrative time and costs required to place a purchase order and support availability of MCMs.
Drawbacks	• Putting an LTA in place entails significant transaction costs. As the agreement may never be used, products would have to prioritized. • Very weak as an inventive – does not do much to incentivize production or reserve capacity
Implementation constraints	Requires agreement on price, which may be difficult to obtain in advance of an outbreak, when little is known about demand.
Preparedness or response (or both)?	Preparedness
When should the international community use this lever?	• When products are on the market already, production capacity is sufficient, competition is not likely to be too high and APAs are not necessary to secure supply.
When should the international community not use this lever?	• If there is no product on the market or insufficient production capacity • When there is likely to be strong competition with HICs for available supply and other instruments such as APAs are necessary to reserve supply. • For extremely rare PHEs (the cost of negotiating the LTA is probably not worth it)
Examples	TBC

Stockpiles

Lever Name	**15. Stockpile – investigational ("ready reserve")**
Description/how it works	A store of a not-yet licensed MCM ready for rapid deployment when an outbreak occurs, either in an efficacy trial or to help control the outbreak under a compassionate use protocol. Mostly relevant for MCMs that have been proven safe in early-stage trials and for which there is some evidence of likely efficacy, from animal or immunological studies.
Benefits	• A stockpile allows an efficacy trial to begin as soon as possible, without delays caused by the need to manufacture the needed doses. • Allows the MCM to be used to help control the outbreak from the start, if the necessary regulatory approval is in place and under appropriate protocols.
Drawbacks	• May require regular renewal—and accompanying costs--if doses expire before an outbreak occurs. • Use in outbreak control involves some risk that MCM will not be effective. If a trial cannot be conducted, use may become "locked in" without strong evidence of efficacy.
Implementation constraints	• Deciding which of multiple candidates to stockpile • Determining appropriate criteria and obtaining regulatory approval for use in an outbreak.
Preparedness or response (or both)?	Preparedness, for use in response
When should the international community use this lever?	• In preparation for outbreaks for which there is a promising candidate that has demonstrated safety and some evidence of likely efficacy but no appropriate licensed product. • For outbreaks that are rare and typically short-lived, where it's particularly important to begin an efficacy trial as quickly as possible when an outbreak does occur.

When should the international community not use this lever?	• When there is an appropriate licensed product. • When there is no candidate ready for an efficacy trial or for use in outbreak control. • When the shelf life of the MCM is very short and outbreaks infrequent – as this will lead to high wastage. • When there is an ongoing outbreak, so available supply can be put to use immediately in a trial or outbreak control. • When factors other than supply availability are likely be rate-limiting.
Examples	• Ebola Sudan vaccines

Lever Name	**16. Stockpile - licensed**
Description/how it works	A store of a licensed MCM, ready for rapid deployment in event of an outbreak and replenished after doses are used or expire. The store can reside physically in one place or, more likely, consist of arrangements with manufacturers that have committed to making a certain volume available in a specified time. While the primary purpose of a stockpile is to ensure that supplies of the MCM are available quickly at the start of an outbreak, it can also serve as a kind of buffer, smoothing demand and allowing suppliers to better plan production.
Benefits	• A stockpile ensures a product is available right at the start of an outbreak • If accompanied by an appropriate allocation mechanism, a stockpile also ensures available supply for specific buyers/countries (though it is not impervious to export bans). • Allows smoothing of demand: while outbreaks create sudden surges in demand for doses, the stockpile can be replenished over a longer period of time. Moreover, it demand fluctuates annually but is more predictable over a longer time period, more regular replenishment may be possible.
Drawbacks	• A stockpile necessarily means some risk of expiry if the MCMs are not used. There are ways to minimize this risk, but it cannot be eliminated. • A too small stockpile will be quickly exhausted in a large outbreak; a too large stockpile will be wasteful, as more doses will expire.
Implementation constraints	• Setting the size of the stockpile • Establishing a rapid, equitable, and efficient mechanism for allocating supply from the stockpile during outbreaks, especially when supply is insufficient and rationing becomes necessary.
Preparedness or response (or both)?	Preparedness (stockpile agreed/planned in advance) for use in response
When should the international community use this lever?	• Outbreaks where there is an existing, effective MCM that can be deployed quickly • Outbreaks that grow very fast, where time to MCM availability is crucial, and especially those for which deployment of the MCM can help to contain the outbreak at an early stage • Most attractive for outbreaks where the risk of wastage can be minimized e.g., MCMs used for both routine/campaign and outbreaks, so that additional campaigns can be run in years with few outbreaks. • More frequent outbreaks for which smoothing of demand is feasible • Outbreaks for which the volumes of MCM required in an outbreak are within the range of feasible stockpile size—probably not most outbreaks with clear pandemic potential, such as pandemic flu or COVID-19. A possible exception could be a stockpile for a particular population, such as HCWs, which could help to ensure access in the face of HIC competition for limited supply. • Outbreaks where production capacity is not so elastic the potential wastage of the stockpile isn't worth the time-benefits of access through a stockpile • MCMs with longer shelf life

When should the international community not use this lever?	• When the shelf life of the MCM is very short and outbreaks infrequent – this will cause wastage. • When production can be rapidly scaled up, diminishing the added value of stored does. • Most pandemic-potential pathogens for which the MCM is unlikely to be able to prevent growth of the outbreak (e.g., current COVID-19 vaccines), as demand for the MCM would quickly exhaust a stockpile of feasible size.
Examples	• Yellow Fever vaccine • MenA vaccine • Cholera vaccine • Ebola Zaire vaccine

Financing levers

Lever Name	**17. Rapid response fund for MCM procurement**
Description/how it works	Governments and/or donors set aside money for procurement of MCMs that can accessed quickly when a pre-agreed trigger, such as a WHO declaration of a PHEIC, is met. This should enable deals to be placed more quickly than if fundraising is required, and placing deals earlier should allow LMICs to secure supply earlier.
Benefits	• Enables LMICs or agencies acting on their behalf to reach deals with suppliers more quickly and on more favorable terms, securing more timely supply • Eliminates or reduces the need for fund-raising during a pandemic • Potentially incentivizes development and supply capacity for LMICs by showing product developers that funds will be available for purchase.
Drawbacks	• Ties up capital • Depending on the trigger, access to the fund may be delayed or blocked altogether. For example, many important outbreaks are not declared PHEICs.
Implementation constraints	• Willingness of donors to commit funds in the necessary amounts: would have to be large to be useful • Agreement on trigger for releasing the funds and conditions for use when so many aspects of a future pandemic are difficulty to foresee.
Preparedness or response (or both)?	Designed and funded as part of preparedness, for use in outbreak response
When should the international community use this lever?	• Useful for all kinds of outbreaks, but particularly so in pandemics, when competition with HICs will likely be fierce and timing of deal signing therefore crucial to securing supply • For outbreaks in which rapid MCM deployment can contribute substantially to limiting spread(e.g. Ebola). • Where a stockpile is not in place
When should the international community not use this lever?	Less useful in small and middle-tier outbreaks, for which volumes (and funding) required are smaller and competition for limited supply with HICs not an issue.
Examples	N/A – not developed yet

Manufacturing levers

Lever Name	**18. Contract manufacturing**

Description/how it works	A funder pays a manufacturer to produce an agreed number of doses of an MCM for an agreed price, for a clinical trial or a stockpile or during an outbreak. The manufacturer does not market the product or sell directly to countries or in private markets, and the market is not competitive. This approach to obtaining doses can be distinguished from ordinary competitive markets or from markets created by pull incentives such as AMCs.
Benefits	Recognises that some medical countermeasure markets are not sustainable markets with viable long-term demand. Instead of using an APA with advance payments (really push funding dressed up as pull funding), this is cleaner, simpler push funding.
Drawbacks	• Forgoes potential benefits of supply competition • Eliminates or reduces incentive to produce more cheaply
Implementation constraints	• Ascertaining cost of goods, if contract is "cost-plus" or, more generally, determining reasonable price
Preparedness or response (or both)?	Both
When should the international community use this lever?	Primarily for rare and historically small outbreaks, where volumes are small and there is little prospective of commercially viable competitive supply
When should the international community not use this lever?	When demand is sufficient to support production on a commercial basis or when APAs, AMCs, procurement subsidies or other ways of supporting demand and transferring demand risk can make commercial production viable.
Examples	Not sure if has been used for stockpiles of licensed products but would be analogous to contract manufacture of trial lots.

Lever Name	**19. Reservation of additional manufacturing capacity for surge**
Description/how it works	Instead of buying a volume of product that may not be needed, the international community could pay to reserve manufacturing capacity for those products in case an outbreak exceeded a stockpile or other existing production channels. In return for the payments, the supplier agrees to be ready to produce the product for the buyer who reserved the capacity, if requested, instead of for other buyers or instead of using the capacity for other products. This is conceptually similar to having an option on volumes of the product in question, but implies a more timebound/urgent obligation on the part of the manufacturer
Benefits	• Will generally be less expensive than buying or committing to buy the product itself, especially if the reserved capacity can be used for a range of products • Secures supply for outbreaks that exhaust a stockpile
Drawbacks	• Supply from reserved capacity will not be available as quickly as supply from a stockpile. • Politically challenging, as the capacity you have reserved—and paid for—may not be used.
Implementation constraints	Decisions on which products, how much capacity, price
Preparedness or response (or both)?	Primarily preparedness, although could also be useful for more frequent outbreaks, where line between preparedness and response is blurred.
When should the international community use this lever?	Good for rare and historically small, and more frequent outbreaks where products are near to or on the market, as a complementary 'insurance mechanism' against an outbreak that exhausts a stockpile
When should the international community not use this lever?	• For products in early-stage R&D

Examples	CEPI is planning to do this for vaccines for small and rare outbreaks – see https://cepi.net/news_cepi/cepi-invites-vaccine-developers-and-manufacturers-to-join-global-outbreak-response-network/

Tech transfer related levers – originator side

Lever Name	**20. Tech transfer and IP licensing: incentives and funding to share technology**
Description/how it works	Tech transfer involves the active transfer of the knowledge and skills necessary to manufacture a product from the originator (or other entity) to another manufacturer. It must be accompanied by licensing of associated IP. The importance of tech transfer varies by product: for vaccines it has traditionally been considered essential, while for small molecule drugs IP is generally the main barrier for additional suppliers, as additional suppliers can often manufacture these drugs without assistance from the originator. Tech transfer may also be needed for contracted production but the term is more often used in connection with transfer to independent manufacturers. Direct funding or other incentives could make it more likely that product developers agree to license their IP and transfer technology to other manufacturers. These incentives could include subsidizing the costs of the transfer, receiving a share of revenues, or some sort of preferential procurement in unrelated markets.
Benefits	• Expands total supply by allowing additional manufacturers to produce a product that has already come to market (or is in development). • Less expensive and less risky than expanding supply through independent R&D • Could reduce costs if new suppliers have lower costs than originators. This is often the case with generic drug suppliers. • Could improve access for LMICs or specific regions if tech transfer recipients target supply to LMICs or specific regions, as may be required in licensing agreements. This objective may also be furthered by transfer to manufacturers located in LMICs or underserved regions. • Builds capacity for future products/technology platforms and outbreaks.
Drawbacks and risks	• Can be slow and expensive, depending in part on the preexisting capacity of recipient. • Depending on the cost structure of recipient, unit costs may be higher than originator cost or cost of that of contracted low-cost producers. • Typically requires separate regulatory approval, in the country where new producers are based and by WHO/countries where the products are being used • Donors could end up subsidizing tech transfer that would have happened voluntarily.
Implementation constraints	At least with some firms, reluctance to license of transfer technology may be so strong that cannot be overcome with feasible incentives.
Preparedness or response (or both)?	Potentially both, depending on nature of the tech transfer, and on whether relevant products or platform technologies already exist before an outbreak.
When should the international community use this lever?	Tech transfer can be useful when • Total supply is or is likely to be inadequate and additional manufacturers with the necessary capacity can be enlisted. • There are few successful or advanced product candidates, so expansion of supply through multiplication of products is a less promising strategy. • Existing supply is tied up by HICs or supplying countries or vulnerable to export bans Incentives can help when more tech transfer is desirable but cost is a barrier, or technology holders are unwilling to share but might be receptive to incentives.

When should the international community not use this lever?	• When tech transfer is not the most efficient strategy or when resistance cannot be overcome by voluntary measures. This could include: • When existing supply is adequate or can be expanded more rapidly or cheaply by the original manufacturer. • When monopolization of supply by HICs or producing countries is not an issue or not likely to be an issue. • When no recipient with the necessary capacity to begin production in a timely manner is available • When the potential technology donor(s) is unwilling to transfer the technology e.g., if there is only one MCM on the market, underpinned by a 'dual use' technology
Examples	Brazilian government funding to support transfer of AZ and Sinovac vaccine technology to domestic producers.

Lever Name	**21. Tech transfer and IP licensing: tech transfer and licensing as purchase condition**
Description/how it works	In theory, an international buyer (or LMICs themselves) could make licensing and tech transfer a condition of purchase. Tech transfer could be to a specific manufacturer (mostly likely in the case of an individual LMIC), to recipients of a defined class, or to a patent pool or tech transfer hub. Tech transfer /licensing could be required from get-go or triggered in certain conditions, including failure to meet agreed supply terms. IP/tech transfer commitments in APAs have been a demand of access to medicine advocacy groups during the COVID-19 pandemic.
Benefits	• Putting tech transfer into APA terms (signed early in an outbreak) could accelerate tech transfer and IP-sharing during an outbreak • Might be more effective or cheaper than voluntary measures.
Drawbacks	• Technology holders have to agree/buyers have to have the market leverage to impose these terms. • Sellers may demand a higher price in exchange. • Compliance might be difficult to enforce. How do you distinguish legitimate delays in the transfer of technology from foot-dragging? What do you do if the firm is found not to be complying? • Could potentially disincentivize future outbreak R&D
Implementation constraints	• May be challenging to define the conditions in which agreements would be triggered. • Firms may be afraid to set a precedent that could lead to pressure to share IP and technology for non-pandemic products.
Preparedness or response (or both)?	Response, although policies could be announced ahead of time.
When should the international community use this lever?	• When TT/licensing is thought to be needed and voluntary measures are not working.
When should the international community not use this lever?	• When TT and additional manufacturers not a high priority • When requirement might deter sellers to LMICs/proxy buyers
Examples	None for international buyers?

Tech transfer related levers – bridging

Lever Name	**22. Tech transfer and IP licensing: patent pools and tech transfer hubs**

Description/how it works	Patent pools enable a hub-and-spoke and more standardized approach to licensing IP to multiple recipients and, in some cases, for multiple products. Instead of negotiating bilateral agreements with each potential recipient, technology holders "donate" IP to the pool, from which interested producers can in-license it on agreed terms. A technology transfer hub would in principle work in similar ways: once the "hub" had acquired the necessary know-how, it could retransfer it to other potential producers.
Benefits	• Could make IP-licensing much more efficient by reducing transaction costs. Potentially similar but probably lesser benefits for tech transfer • Could establish and consolidate norms. • Since in most cases, licensing and tech transfer would be restricted to certain regions or country income classes, could benefit LMICs.
Drawbacks	• The donation of the IP and technology would have to be voluntary, and therefore is subject to many of the same limitations as described above • Technology holders may impose geographic or other limitations. This could mean, for example, that UMICs are at risk of being left out.
Implementation constraints	• It is not clear how or how well the "hub" idea works for tech transfer, where time-consuming one-to-one work may be unavoidable.
Preparedness or response (or both)?	Both: • IP and know-how for existing products and platform technologies could be transferred to a pool outside of outbreaks. Pools and tech transfer hub infrastructure can be created ahead of time. • IP and know-how for new products developed during outbreaks can also be transferred to pool/hub.
When should the international community use this lever?	(As above on the general use case for tech transfer) • The hub model can be especially useful if transfer is needed and feasible to lots of manufacturers. This means high scale and probably low complexity products
When should the international community not use this lever?	(As above on the general case against tech transfer) • The hub model is especially weak when likely recipients are few, bilateral arrangements may make more sense.
Examples	• UNITAID Medicines Patent Pool, licensing to pool of Merck and Pfizer COVID-19 drugs • WHO RNA vaccine technology hub; flu vaccine hub

Lever Name	**23. Tech transfer and IP licensing - advance tech transfer and licensing agreements**
Description/how it works	The international community could broker tech transfer partnerships and licensing agreements in advance of an outbreak, with the ambition that these can rapidly be triggered when there is a pandemic, accelerating expansion of production and facilitating access to medical countermeasures.
Benefits	• Can support rapid scaling of production of medical countermeasures, potentially with access provisions too e.g., certain facilities dedicated to supplying LMICs or regions
Drawbacks	• The product developers participating in the partnership may not have a successful product candidate. In effect, the international community has to choose 'which horses to back' in advance of the outbreak with this lever
Implementation constraints	• The role for the international community is unclear, as much of this is about business-to-business deals and relationships, and is already happening e.g., AstraZeneca and SII partnering on an Ebola Sudan vaccine, following their partnership on COVID-19 vaccines.
Preparedness or response (or both)?	Preparedness, for use in response

When should the international community use this lever?	• Pandemics, where there is a need to rapidly scale manufacturing as soon as medical countermeasures are licensed, often with manufacturing in advance
When should the international community not use this lever?	• Not relevant for rare and historically small outbreaks, where there is no need for >1 manufacturer • Also not very relevant for more the more frequent outbreaks, where there is less urgency to rapidly expand production.
Examples	TBC

Tech transfer related levers – recipient side

Lever Name	**24. Tech transfer to a high-volume manufacturer (without a regional security of supply focus)**
Description/how it works	Transfer of the know-how and IP required to manufacture a MCM from the product developer or other current producer to another manufacturer, to enable that manufacture to also supply the product (after obtaining regulatory approval). For vaccines especially, removal of IP barriers is typically not sufficient, and active involvement of the originating manufacturer is usually necessary to enable production by others (see #20). This lever focuses in particular on transfer to high-volume suppliers, who may also be low-cost. May involve restrictions on the use of the transferred technology and the markets in which the product can be sold.
Benefits	Expansion of total supply, greater security and sustainability of supply, especially for LMICs, sometimes lower cost.
Drawbacks	• Can be slow, challenging, and expensive, although less so than transfer to less experienced manufacturers • Many high-volume producers of drugs and vaccines are located in countries with large populations and thus may be subject to export controls if these countries are affected by an outbreak.
Implementation constraints	• Willingness of originator to transfer technology and IP, especially if involves platform technologies useful for other products and markets • Willingness of recipient to accept transfer in the absence of additional incentives, if market is small, uncertain, or likely to be short-lived. • Capacity of recipient • Capacity of regulatory authority in country of recipient
Preparedness or response (or both)?	Both. If products already exist, best done as preparedness for an outbreak, but can be useful in an outbreak if fast enough, as demonstrated during COVID-19 outbreak.
When should the international community use this lever?	• Transfer to high-volume producers is most useful where large volumes are needed, i.e. for pandemics. • Most important when supply in a pandemic is limited and other approaches to securing supply for LMIC are less likely to be effective, for example when R&D success rates are low, few products are coming to market, and competition with HICs for available supply is particularly fierce. • Only useful for licensed or candidates in trials with good chance of success
When should the international community not use this lever?	• For early-stage products • For small and rare outbreaks, where high-volume production is not needed • Less important in pandemics if ample supply from originator manufacturers

Examples	Tech transfer of AstraZeneca's COVID-19 vaccine to Serum Institute of India

Regional manufacturing levers

Lever Name	**25. Tech transfer to a regional manufacturer focusing on security of regional supply**
Description/how it works	As tech transfer to a high-volume producer (#24), but to a manufacturer focusing on regional or possibly national supply
Benefits	Expansion of total supply, but primarily greater security of supply for the region or country
Drawbacks	• Can be slow, challenging, and expensive. • In most cases, regional supply will be more expensive than supply from a high-volume supplier or even the originator. • Benefits of regional supply depend in part on willingness and ability of supplier to supply beyond home country, and on willingness of other countries in the region to accept products from the regional rather than a global supplier.
Implementation constraints	• Capacity of recipient • Capacity of regulatory authority in country of recipient • Willingness of originator to transfer technology and IP, especially if involves platform technologies useful for other products and markets. Some originators may be more willing to transfer to a regional than to a high-volume supplier that may be or become a more direct competitor in lucrative markets • Willingness of recipient in the absence of additional incentives, if market is small, uncertain, or likely to be short-lived.
Preparedness or response (or both)?	Both. If products already exist, best done as preparedness for an outbreak, but can be useful in an outbreak if fast enough, as demonstrated during COVID-19 outbreak.
When should the international community use this lever?	• For small and rare and for more frequent outbreaks affecting the region where the supplier is located, where the main advantage of regional supply could be insurance against withdrawal of other suppliers. Regional suppliers with a public health focus could be particularly good candidates for tech transfer in these cases • In pandemics, where the objective is to provide the region with a dedicated source of supply • Only useful for licensed or candidates in trials with good chance of success
When should the international community not use this lever?	• For early-stage products • For more frequent outbreaks, where nonregional supply is secure and more affordable • Less important in pandemics if ample and secure supply from originator manufacturers or high-volume, nonregional suppliers
Examples	COVID-19 vaccine tech transfers from AstraZeneca to BioManguinhos and Sinovac to Butantan, although the two Brazilian firms have so far only supplied Brazil. In progress, various efforts to transfer technology for outbreak-relevant vaccine platform technologies to African manufacturers

Lever Name	**26. Non-product-specific investment in and capacity-building for regional manufacturers**

Description/how it works	The ability to bring on new manufacturers during an outbreak via tech transfer is limited by the capacity of the prospective recipients, particularly in certain regions. This constraint can be relieved by building this capacity in 'peacetime'. This capacity could either be general (Good Manufacturing Practices) or related to specific platforms (e.g., RNA vaccines, antibody drugs, lateral flow diagnostics). This is distinct from the transfer of the technology and know-how to make a specific product. This kind of investment could also allow the manufacturer to expand production capacity, lower costs, and strengthen its business model, making it more financially sustainable.
Benefits	• Allows more regional manufacturers to participate in tech transfer (or bring their own products to market), thereby increasing total supply of MCMs, providing greater regional security of supply, and, for small and rare outbreak MCMs, insuring against supply interruption caused by withdrawal of other, nonregional manufacturers.
Drawbacks	• Often very slow and expensive, typically takes years. • The value of the investment depends on the priority given to increasing geographic dispersion of suppliers, relative to greater reliance on proven high-volume, low-cost suppliers. • Requires a way to sustain suppliers between pandemics, ideally without disrupting other markets
Implementation constraints	• All the challenges to achieving international production standards and competitive costs in environments with likely weaker infrastructure, human resources, and governance • National Regulatory Agency capacity
Preparedness or response (or both)?	Preparedness only: takes too long to do during an outbreak.
When should the international community use this lever?	• When total supply capacity is deemed inadequate for a global pandemic. • When regional manufacturing capacity is considered important for supply security in future regional outbreaks or in global outbreaks as a hedge against HICs hoarding or export bans. • For small and rare or more frequent outbreaks affecting a region, when supply is insecure and a regional supplier is considered more likely to stay in the market.
When should the international community not use this lever?	• When existing supply capacity is adequate or can be expanded more rapidly or cheaply by the original manufacturer. • When cost is a priority • When there is no way to sustain the newly built capacity without exorbitant costs or damaging the health of other product markets
Examples	Various planned initiatives to build capacity of African vaccine manufacturers

Lever Name	**27. Subsidy for procurement from regional manufacturers**
Description/how it works	Regional suppliers, like other suppliers, cannot sustain themselves by producing outbreak MCMs alone, as demand for these products is too small or unpredictable. In most cases, to be viable they will need to find markets for other products such as routine vaccines. Producing for these markets will also allow them to build their capacity and ability to achieve international quality standards. Subsidies for national, regional, or international procurement of non-outbreak products from these manufacturers could be one way to allow them to compete successfully as they build their capacity.

Benefits	• Could help regional manufacturers to participate in national, regional, and international product markets between outbreaks, allowing them to sustain themselves and therefore be able to supply needed MCMs when outbreaks occur (see benefits of regional supply in #25, 26). • Could make supply of some non-outbreak products more secure both global and regionally by increasing number of suppliers.
Drawbacks	• Expense: subsidy might have to be considerable and sustained over a long time. • Subsidy could be difficult to withdraw once put in place and could create long-term dependence, weaken suppliers' incentives to become more efficient. • Could lead to the withdrawal of unsubsidized suppliers in certain markets—could be seen as unfair • Requires assurance that the subsidized suppliers will be willing to supply outbreaks MCMs when needed • In some cases, could entail subsidizing suppliers that don't require subsidy. • The value of the subsidy depends on the priority given to increasing geographic dispersion of suppliers, relative to greater reliance on proven high-volume, low-cost suppliers.
Implementation constraints	• Defining which suppliers qualify for the subsidy for which vaccines • Setting the size of the subsidy and criteria for reduction or termination
Preparedness or response (or both)?	Preparedness only
When should the international community use this lever?	• In contexts where regional supply is considered important (see #26) • Where relevant suppliers are ready to compete in national, regional, or international markets with (but not without) subsidy
When should the international community not use this lever?	• In contexts where regional supply is not judged a priority (see #26) • Where there are no regional suppliers ready to participate in non-outbreak markets even with subsidy • Where regulatory agencies are not strong enough (to allow WHO PQ) • When there is no assurance that the subsidized suppliers will be willing or able to produce outbreaks MCMs when needed
Examples	Proposed Gavi AMC for African manufacturers

Lever Name	**28. Non-binding regional procurement compact**
Description/how it works	A group of buyers/potential buyers. Such as. countries in a geographical region, pledge to purchase products from specific suppliers, such as suppliers in their region. This could help to de-risk demand for those suppliers and so may encourage R&D investment, and/or production capacity scale up. Could apply either to outbreak or non-outbreak products
Benefits	• Could help to bring private investment to regional manufacturers and thus reduce the need for international public investment to build the capacity of regional producers or defray the costs of technology transfer during a pandemic. Alternatively, could help to justify international investment by building assurance that products will find buyers. • Builds regional solidarity
Drawbacks	• Relatively weak, as compact is nonbinding: buyers may renege on their commitments to buy depending on the price at which products come to market, the availability of superior products, public preferences, or political considerations.

Implementation constraints	• Putting in place a sufficiently credible and durable compact backing by sufficient political commitment • Overcoming regional rivalries and mistrust • Commitment cannot be absolute: to be realistic it would have to include price, performance, delivery conditions, complicating design and allowing compact signers to opt out
Preparedness or response (or both)?	• Established as part of preparedness, primarily for use in response • Could theoretically be developed during an outbreak, but time and effort required makes this challenging
When should the international community use this lever?	• When there is a strong case for building regional capacity (see #26), yet a risk that countries will not choose the resulting products • When other, stronger levers are not available • When regional solidary and capacity for concerted action is already in place or there are associated political processes that reduce the risk of buyers reneging on their commitments
When should the international community not use this lever?	• When stronger levers are needed e.g., guaranteed supply • When products are far from market • Where products from the regional manufacturer(s) are likely to be substantially inferior or more expensive than competing products
Examples	Proposed 'African demand compact' for African-made vaccines, being discussed by Gavi

Regulatory levers

Lever Name	**29. Strengthening regulatory agency capacity to oversee manufacturing**
Description/how it works	National regulatory agencies (NRAs) are responsible for approving products made within their borders and for ensuring that they are manufactured according to appropriate standards. Procurement by international agencies depends on confidence that this oversight is rigorous. WHO prequalification or emergency use listing, for some products a prerequisite for international procurement, specifically requires that the NRA in the producing country meet a certain standard. Weak NRAs can therefore be an obstacle to supply of MCMs from manufacturers located in certain countries. International investment in and technical assistance to NRAs can be a way to allow manufacturers in a greater range of countries to supply MCMs to international agencies and other LMICs.
Benefits	• Allowing additional regional manufacturers to supply MCMs internationally. • Very significant positive spillovers to routine product markets
Drawbacks	• Cost and time required
Implementation constraints	• Which countries to select and work with • Can be challenging, with no guarantee of success, especially where political will and agency independence are lacking
Preparedness or response (or both)?	Preparedness
When should the international community use this lever?	• When regional manufacturing is judged to be particularly important (see #26) and there are promising manufacturers in countries with weak regulators • When conditions are good for investments in NRAs to bear fruit
When should the international community not use this lever?	• In contexts where regional manufacturing is less important • Where prospects for bringing an NRA to the relevant standard are poor

Examples	• WHO regulatory strengthening programme • BMGF investments, e.g., through US Pharmacopeaia

Lever Name	**30. Expedited regulatory approvals in country of use**
Description/how it works	The use of MCMs in a particular country requires national regulatory approval. Regulatory agencies can conduct their own reviews, which can be a lengthy process, directly recognise another agency's review ("If it's good enough for you, it's good enough for me") or rely on it to varying degrees ("If you've assessed [part] of the dossier, I'll skim that and focus on [another part]"). Regulatory approval can be expedited by strengthening the capacity of NRAs to conduct reviews, helping regional NRAs to work together and harmonize requirements, or encouraging countries to "recognize" or "rely on" reviews conducted by other regulators, especially during outbreaks.
Benefits	• Recognition and reliance can dramatically accelerate licensure, bringing forward availability. • Some of the reforms catalysed by increasing use of these processes should have positive spillovers for routine approvals too.
Drawbacks	• (None)
Implementation constraints	• Strengthening regulatory agencies can be slow, difficult work, and may get into areas of fundamental state capability e.g., attraction and retention of skilled staff, political pressure etc. • Political obstacles to reliance on other national regulators
Preparedness or response (or both)?	Both
When should the international community use this lever?	Almost always. There may be nuances in focus depending on the strengths of the regulators, and/or regional PHE threats, for example, but this is almost always useful.
When should the international community not use this lever?	N/A
Examples	• AVAREF/AMA • EDCTP • CEPI work • US Pharmacopeia work

Lever Name	**31. Clinical Policy/Guideline development**
Description/how it works	Development and approval of clinical policies and guidelines for use of an MCM, often in advance of licensure of the MCM, to speed the eventual roll out of the MCM in country.
Benefits	Can prevent this from being the rate-limiting step for allocation and shipping of MCMs.[33]
Drawbacks	Can only be developed when the MCM in question is near licensure or on the market
Implementation constraints	No major concerns. Can be somewhat slower to develop clinical guidelines for groups that haven't been subject to major clinical trials e.g., women and children, immunocompromised groups
Preparedness or response (or both)?	Both
When should the international community use this lever?	In all cases this is a sensible thing to do
When should the international community not use this lever?	N/A

[33] Issues related to in-country distribution and appropriate use are generally beyond the scope of this project, but there are circumstances where available to countries, for example of donated doses, is conditional on policies being in place.

Examples	Donations of COVID-19 vaccines through COVAX were only approved when the receiving country had put in place clinical guidelines. Sometimes this was not done sufficiently far in advance of the donations' potential arrival, and so delayed access.

Possible Treaty provisions

The WHO has begun negotiations on a pandemic treaty or accord. Neither the final content of such an accord, its prospects for ratification, or the likelihood of enforcement in a pandemic is yet clear, but this section profiles some potential elements that might be included and could be thought of as supply levers. We have focused on potential mandatory actions, as these would require a treaty or some other binding mechanism.

Lever Name	**32. Tech transfer requirement**
Description/how it works	If a certain trigger is met, such as the WHO declaration of a PHEIC, suppliers of MCMs would be required to make the relevant technologies available to other producers in order to expand supply as rapidly as possible. Similar but stronger than a pandemic IPR waiver. Such a requirement would presumably have to be imposed on firms and enforced by the governments of the countries in which the firms are based.
Benefits	If such a requirement could be enforced, it could (see levers #20-25) • Expand total supply by allowing additional manufacturers to produce a product that has already come to market (or is in development). • Be less expensive and less risky than expanding supply through independent R&D • Reduce costs if new suppliers have lower costs than originators. This is often the case with generic drug suppliers. • Improve access for LMICs or specific regions if tech transfer recipients target supply to LMICs or specific regions. This objective may also be furthered by transfer to manufacturers located in LMICs or underserved regions. • Build capacity for future products/technology platforms and outbreaks.
Drawbacks	The same drawbacks as tech transfer more generally: • Can be slow and expensive, depending in part on the preexisting capacity of recipient. • Depending on the cost structure of recipient, unit costs may be higher than originator cost or cost of contracted low-cost producers. • Typically requires separate regulatory approval, in manufacturing country and by WHO/countries where the products are being used • In addition, the prospect of mandatory tech transfer could deter some firms from developing outbreak MCMs, either by reducing the potential profit from these products or by loosening control over a technology used for other products. • Could hinder or confuse processes of voluntary tech transfer.
Implementation constraints	• Difficult to enforce on firms, as foot-dragging may be difficult to distinguish from legitimate sources of delay. How would compliance be measured? Would expression of willingness be sufficient? • Might also be difficult to enforce on producing countries, who may want to protect the interest of their manufacturers • Who would decide to whom tech should be transferred? Would it have to be share with all potential recipients expressing an interest?

Preparedness or response (or both)?	Requirement could be put in place before or during a pandemic, to be used during an outbreak. If international treaty required, almost certainly only feasible if done in advance, for example through current WHO-led process.
When should the international community use this lever?	In (anticipation of) pandemics, especially when there are products on the market but supply is highly constrained, and there are willing and able manufacturers who are not being engaged by current producers.
When should the international community not use this lever?	In smaller outbreaks not affecting HICs, where rapid expansion of supply is less important and where suppliers and product developers are already focusing on LMIC markets. A tech transfer requirement in a treaty should specify the conditions under which the requirement would be triggered.
Examples	N/A

Lever Name	**33. Ban on export bans**
Description/how it works	If a certain trigger is met, such as the WHO declaration of a PHEIC, all countries would be prohibited from banning the export of medical countermeasures and key inputs to those products e.g., bioreactor bags, glass etc.
Benefits	• If successfully enforced, could increase access for LMICs, particularly those without their own production capacity and especially in a pandemic. • Might/should also increase the rate of production of MCMs by mitigating shortages of inputs.
Drawbacks	• Does not protect LMICs from market imbalances: better-resourced countries could still monopolise supply through their buying power. • Could reduce supply for producing LMICs, who would now be obliged to export even if domestic needs had not been met.
Implementation constraints	• Very hard to enforce: this is probably the main drawback of such a proposal • Might be difficult to define, as producing countries could use a range of strategies for constraining exports.
Preparedness or response (or both)?	Negotiated as part of preparedness for use in pandemic response.
When should the international community use this lever?	Pandemics, or at least multi-country outbreaks affecting one or more producing countries, as export bans are only relevant if a product is in short supply and there is tension between use in a producing country to protect is own population and export to other affected countries.
When should the international community not use this lever?	• Not necessary when producing countries are not affected or at risk, or when supply is adequate or can be scaled up quickly to meet needs. • Uncertainty about enforceability suggests that the international community should not rely too heavily on such a provision, even if it is successfully enshrined in a treaty, and should focus on measures to allow rapid scale-up of supply or to disperse supply sufficiently to reduce vulnerability to export bans.
Examples	N/A

Lever Name	**34. HIC dose-sharing requirement**

Description/how it works	If a certain trigger were met, such as the WHO declaration of a PHEIC, all buying countries would have to donate a certain percentage or quantity of doses/courses/tests to LMICs/countries that need them, in real time, either directly or through an international body. Similar to the Berlin Declaration proposed by IFPMA, but mandatory rather than voluntary and imposed on HICs rather than producers.
Benefits	Potentially provides some (free) supply for LMICs
Drawbacks	• See below on implementation constraints – would be very hard to negotiate ex ante an agreement that would be specific enough for LMICs/their buyers to rely on it as a source of reliable, timely supply. • May be inadequate for LMIC needs, if donation requirement is too small, or if HICs buy few doses in an outbreak primarily affecting LMICs.
Implementation constraints	Could be very difficult to enforce if HICs were having difficulty meeting their own needs in a pandemic.
Preparedness or response (or both)?	Requirement put in place in advance for use in response
When should the international community use this lever?	Pandemics primarily, or PHE's that met the trigger and where HICs are buying up supply e.g., Monkeypox. If this could be negotiated and enforced, it would be a useful complement to other levers, but likely never a primary channel for supply
When should the international community not use this lever?	Non-pandemics/PHEs that do not meet the pre-agreed trigger; outbreaks not affecting HICs
Examples	N/A

Lever Name	**35. Pandemic IPR waiver**
Description/how it works	If a certain trigger were met, such as the WHO declaration of a PHEIC, all countries would have the ability to access relevant IP for development or production of medical countermeasures
Benefits	• Should accelerate R&D for products pre-licensure • Should accelerate tech transfer to enable additional manufacturers to make licensed products. For small molecule drugs in particular, IP is often the main barrier to production. For vaccines, IP is an important barrier, but tech transfer is usually needed too.
Drawbacks	• Potential for disincentivizing commercial R&D on PHE-relevant products • Could also disrupt R&D/pharmaceutical business models for non-PHE products, because of shared technology platforms. • For some classes of products, traditionally including vaccines, access to IP may not be sufficient to enable manufacture by additional suppliers.
Implementation constraints	• Unlikely that a sweeping commitment can be negotiated. • Would need to agree on whether and how IP holders would be compensated and possibly also limitations on geographic scope.
Preparedness or response (or both)?	Response
When should the international community use this lever?	Pandemics
When should the international community not use this lever?	Smaller outbreaks, where IP is much less of a barrier to product development and manufacture
Examples	Proposed IP waiver for COVID-19 drugs

Other levers

Lever Name	36. Publishing market information
Description/how it works	A global health actor or initiative e.g., UNICEF, monitors the availability and status of relevant medical countermeasures. This information could cover both the supply side (status of medical countermeasures, production capacity etc.) and demand side (current major buyers, forecast future demand etc.). Potentially could also include information on prices and other contractual terms, if suppliers and buyers allowed it. This information is synthesized and published so all stakeholders can access it.
Benefits	• Gives LMICs or those buying on their behalf an up-to-date understanding of potential/existing products, reducing the risk of entering into unnecessary/poorly advised agreements with suppliers • Should help buyers to make deals more quickly in an outbreak • Can help manufacturers scale production to meet LMIC needs (if the forecast is credible) • When market gaps are identified, can help bring in new suppliers to fill the gap
Drawbacks	• The insight is only as good as the data from which it's drawn • Very weak lever on its own
Implementation constraints	• Minor challenges around managing confidential information e.g., production capacity, but these can be solved. • Unwillingness of some suppliers and buyers to share potentially useful information.
Preparedness or response (or both)?	Both
When should the international community use this lever?	In almost all cases, with a particular focus on fast-moving markets, unless the forecast is so uncertain as to have no value
When should the international community not use this lever?	For demand forecasts in particular, when there is so much uncertainty that any forecast could create false expectations.
Examples	• IMB MarketScan database, • UNICEF's COVID-19 Market Dashboard • GAVI Secretariat biannual vaccine demand forecasts; • UNICEF Supply Division Annual Forecast Exercise

Lever Name	37. Demand forecasting
Description/how it works	Similar to #36, A global health actor or initiative e.g., UNICEF, produces and publishes a demand forecast to inform relevant manufacturers (current and future) of likely demand. This information is synthesized and published for all relevant players to be able to use.
Benefits	Low-cost lever, based on data gathered as part of business as usual, that can shape the capacity investment and maintenance of manufacturers (in combination with other levers)
Drawbacks	Is a fundamentally weak lever – the forecast is only as good as the data and methodology used, and has no real de-risking effect for manufacturers. If they produce too much product on the basis of an inaccurate forecast, they still take all the demand risk.
Implementation constraints	Can be very challenging to forecast for one channel or product in multi-channel markets e.g., pandemics, where there are bilateral deals, regional deals, LMIC-wide deals, and donations, all of different products, as well as the 'normal' epidemiological uncertainty inherent in a PHE

Preparedness or response (or both)?	Response
When should the international community use this lever?	• Always
When should the international community not use this lever?	• N/A
Examples	• UNICEF COVID-19 vaccine demand forecasts, and Oral Cholera Vaccine forecasts

Lever Name	**38. Advocacy/soft power**
Description/how it works	International agencies soft power which could be used to increase MCM availability and affordability to LMIC through a range of tactics, including leveraging existing relationships with producers and HICs, the media, and catalysing public pressure. Objectives could include increasing investment in needed R&D, increase supply, making supply available to LMICs on a timely basis and on reasonable terms, reducing hoarding (on the part of HICs), or eliminating export bans.
Benefits	These levers do not require significant funding or formal legal agreements. They can complement other levers, and can be effective, as advocacy around HIV drug prices demonstrated.
Drawbacks	• Potential impact is probably limited in the fact of compelling profit considerations or domestic political considerations • Risk of eroding goodwill with suppliers, on whom international agencies depend for both outbreak and routine products, and with donor nations
Implementation constraints	Good advocacy requires pre-emptive investment in relationships e.g., media contacts, CSO coalitions etc. You cannot expect to just put out a press release and see impact.
Preparedness or response (or both)?	Both preparedness and response
When should the international community use this lever?	• When targets of advocacy (e.g. big pharma or national governments) are sensitive to political pressure or public opinion • When the potential gains in availability are worth the risk of damage to the relationship with the manufacturer or donor • As a complement to other levers • When there is a strong public sentiment to build on e.g., if the PHE primarily impacted LMICs, and medical countermeasure developers were seen to be less than helpful, this context might be ripe for media work, for example
When should the international community not use this lever?	• As a frontline lever. Closed-door advocacy is fine, as part of manufacturer engagement, but combative advocacy should be deployed carefully, given the international community's dependence on manufacturers
Examples	• MSF Access Campaign • People's Vaccine Initiative NB COVAX deliberately chose not to use this set of tools