PUBLIC HEALTH EMERGENCY **ARCHETYPES**

A framework to support equitable access to life-saving supplies in outbreaks, epidemics and pandemics

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Suggested citation: UNICEF, *Public health emergency archetypes: A framework to support equitable access to life-saving supplies in outbreaks, epidemics and pandemics*, UNICEF, Copenhagen, October 2023

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Executive summary

Public health emergencies (PHEs) and, more specifically, infectious disease outbreaks and epidemics may 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 vaccines, drugs, diagnostics and other medical countermeasures (MCMs) needed to save lives and limit the impact of disease outbreaks.

To inform decisions to support equitable access to MCMs, UNICEF has developed an analytical framework that considers strategies and tactics that international and regional agencies, including UNICEF, should prioritize in different outbreak situations. The archetypes framework analyzes features that affect the supply of MCMs to LMICs and does not focus on the biological characteristics of outbreak-prone pathogens.

The categorization of PHEs presented in this report 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, such as Sudan ebolavirus and Nipah virus, which pose little threat to high-income countries (HICs).
2. Those causing more frequent and larger outbreaks, e.g., cholera and yellow fever.
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: first, the commercial potential of markets for pathogen-specific MCMs—which influences the engagement of private sector product developers and manufacturers, and secondly, the likelihood that HICs will invest in the development and production of MCMs and whether they will monopolize the 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 research and development (R&D):

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 characteristic market challenges.

For example, in the case of pathogens causing rare and historically small outbreaks for which there are no licensed MCMs, the primary market 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.

For pathogens in the middle tier causing more frequent and larger outbreaks, demand for MCMs is higher and somewhat more predictable, including, in some cases, demand from preventative campaigns or routine use. In this outbreak category, the challenge is to make markets for MCMs sufficiently stable and attractive to support a sustainable commercial market.

At the other end of the spectrum, for global pandemics, the main market challenge for LMICs and agencies acting on their behalf is to secure access in the face of export bans and competition from HICs.

These very different market challenges are amenable to different sets of market and policy interventions or supply levers. For each of the nine archetypes, we analyze the feasibility and likely effectiveness of more than thirty supply levers, 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, summarized in a set of proposed supply playbooks for each archetype, demonstrates the importance of an approach to ensuring MCM supply in PHE preparedness and response that is explicitly differentiated according to the type of outbreak.

We emphasize that our analysis focuses on the adequate and timely supply of MCMs to countries rather than on the equally important factors that affect access and impact of MCMs after they arrive at a port of entry or national warehouse. Addressing potential barriers related to in-country distribution, cold chain, health worker training, infrastructure, appropriate use, and public attitudes toward and demand for these products requires a different set of measures that are beyond our scope.

While each pathogen and MCM is unique, we believe the archetypes framework can provide a useful starting point and structure for regional and international agencies to make informed decisions on the best approaches to ensure MCM supply in different outbreak scenarios. 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 crucial gaps in the international system. For example, no agency is currently configured to play certain critical roles at the necessary scale, such as 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 PHE preparedness and response can help to ensure that the resulting structures and partnerships are appropriate for the full range of potential outbreaks, epidemics and pandemics.

It is not the intention of this analysis to prioritize particular pathogens or provide guidance on the importance and appropriate use of particular MCMs. The archetypes framework focuses instead on how best to ensure that LMICs have access to MCMs prioritized by governments and by technical and normative agencies such as the World Health Organization (WHO) and Africa Centres for Disease Control and Prevention (Africa CDC).

Abbreviations and acronyms

Africa CDC	Africa Centres for Disease Control and Prevention
AMC	advanced market commitment
APA	advanced purchase agreement
AVAT	African Vaccine Acquisition Trust
CEPI	Coalition for Epidemic Preparedness Innovations
COGS	cost of goods sold
COVAX	COVID-19 Vaccines Global Access
DTP	diphtheria, tetanus, pertussis
FDA	Food and Drug Administration (United States)
Gavi	Gavi, The Vaccine Alliance
HERA	Health Emergency Preparedness and Response (European Commission)
HIC	high income countries
HPV	human papillomavirus
IFPMA	International Federation of Pharmaceutical Manufacturers & Associations
I&L	Indemnity and liability
IP	intellectual property
IPR	intellectual property rights
LMIC	low- and middle-income countries
LTA	long-term agreement
MCM	medical countermeasures
MERS-CoV	Middle East respiratory syndrome-related coronavirus
MR	measles rubella
mRNA	messenger RNA
NIH	National Institutes of Health (United States)
NRA	national regulatory agency
PAHO	Pan American Health Organization
PCV	pneumococcal conjugate vaccine
PPE	personal protective equipment
PHE	public health emergency
PHEIC	public health emergency of international concern
RNA	ribonucleic acid
R&D	research and development
UKVN	UK Vaccine Network (United Kingdom)
UMIC	upper-middle-income country
UNICEF	United Nations Children's Fund
WHO	World Health Organization

Glossary: Key terms

Public health emergency (PHE). The analysis focuses primarily on multi-LMIC outbreaks of infectious diseases, where UNICEF and our partners support preparedness and response. As such, this project is not primarily intended for small, single-country outbreaks that individual governments often resolve with limited support from UNICEF and our partners. This project does not focus on health emergencies caused by non-health events or non-communicable diseases. We are focused on rapidly changing, non-routine events.

While recognizing the different definitions of "outbreak", "epidemic", "PHE", "public health emergency of international concern" (PHEIC) and "pandemic", this project is not tied to any of these formal classifications.

Medical countermeasures (MCMs) are medical products, e.g., biologics, drugs and devices, that may be used in the management of a PHE. We focus on the supply of vaccines, diagnostics, therapeutics, and personal protective equipment (PPE).

Availability of MCMs refers to whether vaccines, therapeutics and PPE can reach the port of entry of LMICs. Demand-side issues, including community engagement and questions of in-country programming, delivery support, and health systems strengthening, are out of scope. However, we recognize their enormous importance to accessing in MCMs.

Market challenges, as we use the term, are market-related (as opposed to scientific or technical) barriers to the development, licensure, production or procurement of MCMs that, in turn, impede availability for LMICs. It is important to note that market challenges are not necessarily market failures in the narrower economic sense.

Supply levers are a broad range of measures that international agencies and others can use to ease market barriers and increase the availability of MCMs to LMICs. They may expedite R&D, increase supply, or ensure supply specifically for LMICs. Supply levers include, among others, grant funding, purchase commitments, regulatory and intellectual property changes, technology transfer, and treaty commitments by governments.

Introduction

Despite important successes, the international response to the COVID-19 pandemic highlighted profound inequities in access to medical countermeasures (MCMs). Many low- and middle-income countries (LMICs) received life-saving products, especially vaccines, months or years after high-income countries (HICs).[1] Efforts are underway to absorb the lessons from the COVID-19 experience and build a stronger infrastructure for ensuring fair access to MCMs in future disease outbreaks. There have been more than 30 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 in 2023.[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 a 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. LMICs are particularly vulnerable to disease outbreaks that may not meet the definition of a pandemic but, nonetheless, may impose a heavy burden on affected populations and economies. Regional and international organizations focused on LMICs, including UNICEF, need to prepare for and respond to a wide range of outbreak and epidemic scenarios.

We believe that planning for different types of disease outbreaks can be facilitated by a systematic grouping according to characteristics relevant to the availability of MCMs in LMICs. This report outlines such a framework and highlights critical implications for supply and market-shaping. After clarifying the scope of the analysis, we present the framework consisting of a set of nine 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 archetype. This analysis leads to a set of playbooks or combinations of supply interventions best suited to each type of outbreak. Finally, we summarize key insights from this work and offer recommendations.

1 Hunter, David J., et al., "Addressing Vaccine Inequity Covid-19 Vaccines as a Global Public Good", New England Journal of Medicine, vol. 386, 24 March 2022, pp. 1176-1179.
2 Independent Panel for Pandemic Preparedness and Response, Covid-19: Make it the last pandemic, May 2021.
3 Sachs, J.D., et al., "The Lancet Commission on lessons for the future from the Covid-19 pandemic", The Lancet, vol. 400, no. 10359, 8 October 2022, pp. 1224-1280.
4 Matsoso, Precious, et al., "Negotiating a pandemic accord: a promising start", The BMJ, vol 380, p. 506, 2 March 2023.
5 Kishida, Fumio, "Human security and universal health coverage: Japan's vision for the G7 Hiroshima Summit", The Lancet, vol 401, no. 10373, pp.246-247, 28 January 2023.
6 Mandaviya, Mansukh, "India plans to use its G20 presidency to build consensus on global health resilience. World Economic Forum, 10 February 2023, < https://www.weforum.org/agenda/2023/02/india-g20-presidency-consensus-global-health-resilience/> accessed, 27 March 2023.

1. The nine archetypes

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

1.1 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 the health system's capacity to respond. A number of organizations, including WHO, Africa CDC, the US National Institutes of Health (NIH), the European Commission's Health Emergency Preparedness and Response Authority (HERA), and the UK R&D Vaccine Network, have categorized and prioritized pathogens in various and valuable ways.[7,8,9,10,11]

In our work with UNICEF, 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.

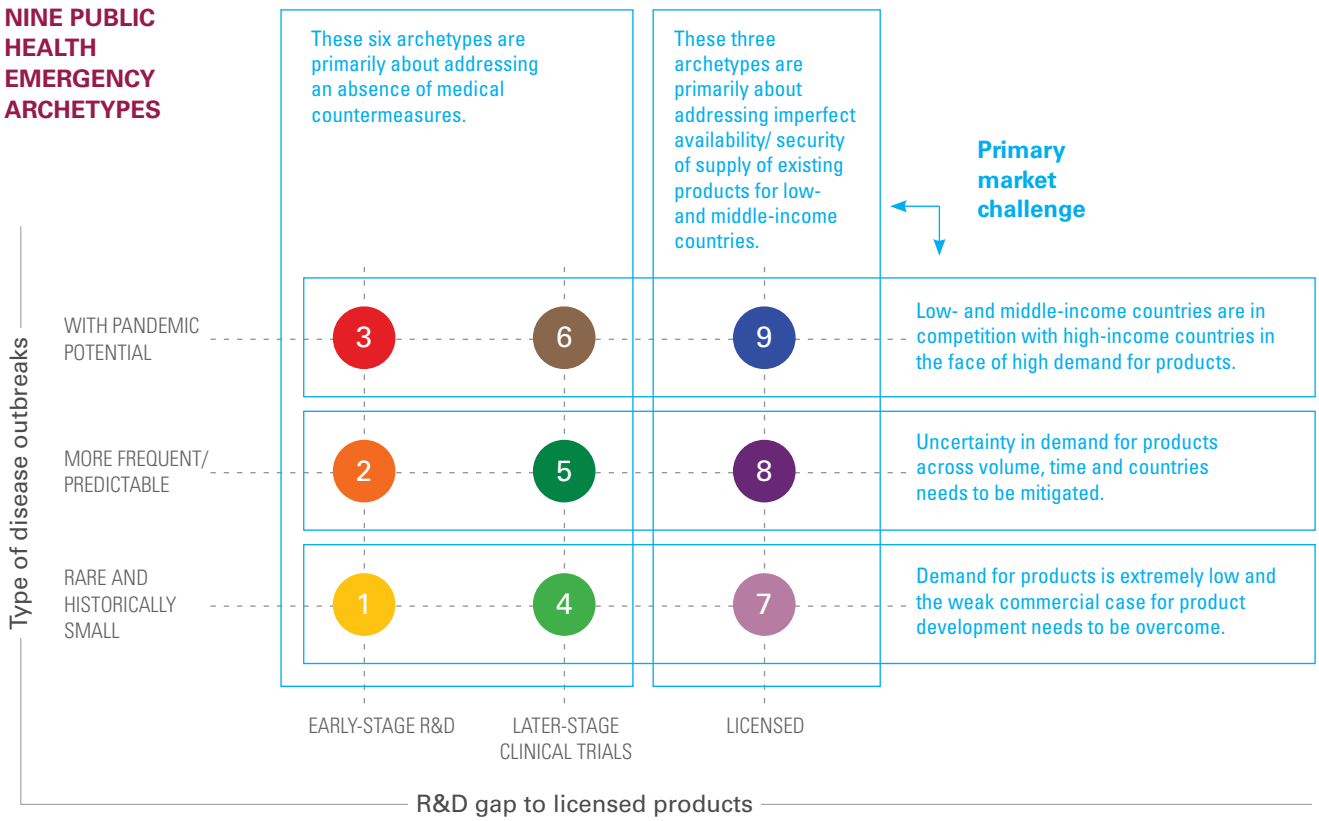
1. **Rare and historically small.** This category includes pathogens such as the Ebola, Marburg, and Nipah viruses, which, at least to date, have caused outbreaks of hundreds—or at most, thousands—of cases. Crucially, these pathogens pose little threat to HICs, either because their vectors or animal 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 is 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, dengue and chikungunya, which cause more frequent and larger outbreaks and may be endemic in some countries. Like the rare and historically small outbreaks, outbreaks in this category 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 are unpredictable, the required volumes of MCMs, averaged over year-to-year fluctuations, are 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 (MICs) can help to sustain commercial viability. Here, the main market challenge is to stabilize demand, thereby making these markets more attractive to manufacturers, which helps to ensure reliable and sufficient supply.

3. **True pandemics.** COVID-19 and a potential global flu pandemic are canonical examples of upper-tier outbreaks, which affect hundreds of millions or even billions of people, including those in HICs as well as LMICs. The ultimate scale and duration of pandemics are unpredictable; hence, demand for MCMs is also unpredictable. However, there is a potential for large commercial returns for product developers and manufacturers. Critically, HICs can be expected to 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 early in the pandemic demonstrated.

7 World Health Organization, "Prioritizing diseases for research and development in emergency contexts, WHO, <https://www.who.int/activities/prioritizing-diseases-for-research-and-development-in-emergency-contexts>, accessed 27 March 2023.
8 National Institute of Allergy and Infectious Diseases, "NIAID Pandemic Preparedness Plan", NIAID, December 2021.
9 Africa Centres for Disease Control and Prevention, "Risk ranking and prioritization of epidemic-prone diseases", Africa CDC, <https://africacdc.org/download/risk-ranking-and-prioritization-of-epidemic-prone-diseases/>, accessed 27 March 2023.
10 Health Emergency Preparedness and Response Authority, "HEALTH UNION: Identifying top 3 priority health threats", HERA, June 2022, <https://health.ec.europa.eu/document/download/18c127ce-da4b-4e4e-a27c-f7b93efb2980_en?filename=hera_factsheet_health-threat_mcm.pdf>, accessed on 27 March 2023.
11 The UK Department of Health and Social Care, "The UK Vaccine Network. Working Group 1- Identify and prioritise human and zoonotic diseases", DHSC, < https://www.gov.uk/government/groups/uk-vaccines-network#working-groups>, accessed on 27 March 2023.

FIGURE 1: MARKET CHALLENGES ACCORDING TO OUTBREAK TYPE AND MCM STAGE OF DEVELOPMENT



Where pathogens fall in this categorization is, of course, determined by underlying biology: animal reservoirs, vectors, modes of transmission, and so on. But, the essential point is that the market challenges associated with each archetype derive more directly from the higher-level characteristics, e.g., size and frequency. Pathogens with very different biological characteristics, 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 difficulty is that it may not always be clear in advance or in the early stages of an outbreak if HICs will be strongly affected. Easily transmissible respiratory viruses such as influenza and coronaviruses threaten all countries, but the potential for global impact is less clear for some other pathogens. Until 2022, mpox was virtually unknown in the US and Europe. Conversely, although we categorize Ebola virus disease as unlikely to strongly affect HICs, it was considered at least a theoretical threat at the time of the 2014 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 where pathogens are found can change with shifts in the reach of vector and host species and as health systems of both HICs and LMICs are exposed to new vulnerabilities. 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.

1.2 STATUS OF MCM DEVELOPMENT AND AVAILABILITY

In the archetypes framework, the division of disease outbreaks into three tiers based on the characteristics of pathogens can be complemented by a second axis based on the status of particular countermeasures, each with its own implications for market-shaping priorities.

1. For some outbreak pathogens, we have no MCMs available, and R&D is at a very early stage. For example, no specific drugs for yellow fever, dengue, or chikungunya exist. This would also be true of a previously unseen pathogen ("disease X"), especially if it did not belong to a well-understood pathogen family.

2. For other outbreak pathogens, some MCMs have advanced to clinical trials, and enough safety data is available to move to an efficacy trial when an outbreak occurs. Sudan ebolavirus vaccines are a good example of countermeasures in this category. Vaccines for pathogens from families such as influenza viruses or novel coronaviruses for which

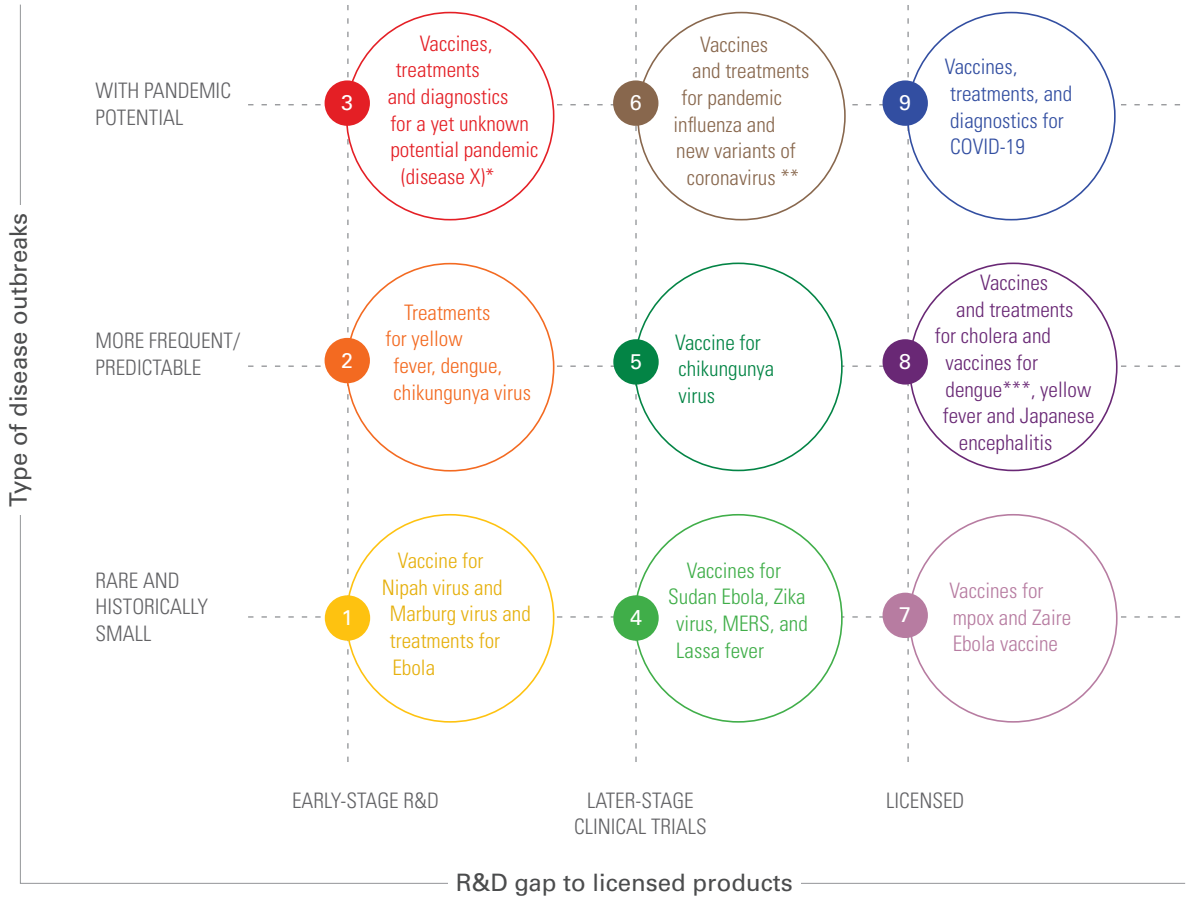
effective vaccines have already been developed could also be placed in this group.

3. Finally, in the case of pathogens where adequate MCMs already exist, the emphasis can be on ensuring sufficient supply available to LMICs.

Even when a useful drug or vaccine is available, there may be good reasons to support the development of products that are more effective, more affordable, or easier to deliver—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, the emphasis is on whether a useful product is available and, if not, on the development status of the most advanced plausible candidate or candidates.

Combining these two dimensions, we arrive at a 3 x 3 matrix of categories, which we call PHE archetypes. Figure 2 displays the nine PHE archetypes with illustrative examples of corresponding pathogen-MCM combinations.

FIGURE 2: PHE ARCHETYPES MAPPED AGAINST EXAMPLES OF PATHOGEN-MCM COMBINATIONS



* For a truly novel disease (disease X), there will be no R&D at all and 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.

** 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 categorized here.

*** 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.

2. Analysis of supply levers

The framework defines a set of nine PHE archetypes based on pathogen and MCM characteristics. Each archetype is associated with one or more market challenges that impede the timely and adequate supply of MCMs to LMICs in a disease 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 supply levers range from R&D push and pull incentives and procurement modalities to intellectual property provisions, approaches to promoting tech transfer, and support to regional manufacturing (Table 1). After defining each lever and describing how it can encourage MCM development, supply, or LMIC access, we have analyzed the circumstances in which its use is appropriate. In particular, we have assessed the feasibility and likely impact of each lever for each archetype in both preparedness and response. This analysis is presented in summary form in the two heat maps in Annex A. A 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" (Tables 2 and 3).

Finally, we have drawn out some of the higher-level findings from this analysis as a series of insights and recommendations (Section 4).

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 particular circumstances but to highlight the ways that the value of various supply levers differs across outbreak types.

TABLE 1: SUPPLY LEVERS

	R&D levers
1	R&D push funding (by LMIC-focused agency)
2	Publicly-funded intellectual property (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 a share of supply to LMICs (Berlin Declaration)
10	Putting donation infrastructure in place
11	Donations
12	Putting a resale market in place
13	Resale market
14	Pre-emptive long-term agreement (LTA) negotiation

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.

	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 – Tech transfer/licensing as a condition of APA
	Tech-transfer related levers – Bridging
22	Tech transfer and IP licensing – Patent pools and tech transfer hubs
23	Tech transfer and IP licensing – Brokering advance tech transfer 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 the 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 IP rights waiver
	Other levers
36	Publishing market information
37	Demand forecasting
38	Advocacy/soft power

3. Application of the framework to different types of MCMs

The PHE archetype framework was developed primarily based on 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, which include the lack of commercial incentives to develop products for pathogens causing small outbreaks in LMICs; the primary focus of HICs on MCMs for pathogens that they perceive to be a threat to their populations; the potential for competition with HICs to limit the supply to LMIC in pandemics.

There are differences as well, however, based on the MCM type. For example, the role of patents as barriers to expanding supply, including regional supply, varies across the MCM categories. A new diagnostic tool can generally be brought to market at a much lower expense than a new drug or vaccine, potentially creating commercially viable markets for smaller outbreaks. The roles of agencies implementing financing, R&D, procurement, delivery support, regulation and oversight are generally clearer and better developed for vaccines than for drugs or diagnostics. 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.

4. Insights and recommendations

In many ways, the following playbooks capture the main recommendations from this analysis (Tables 2 and 3). They provide detailed suggestions on approaches to driving the development and delivery of MCMs for each archetype in PHE preparedness as well as response. But the analysis also leads to a number of conclusions at a higher level (Sections 4.1, 4.2 and 4.3).

TABLE 2: PREPAREDNESS PLAYBOOKS

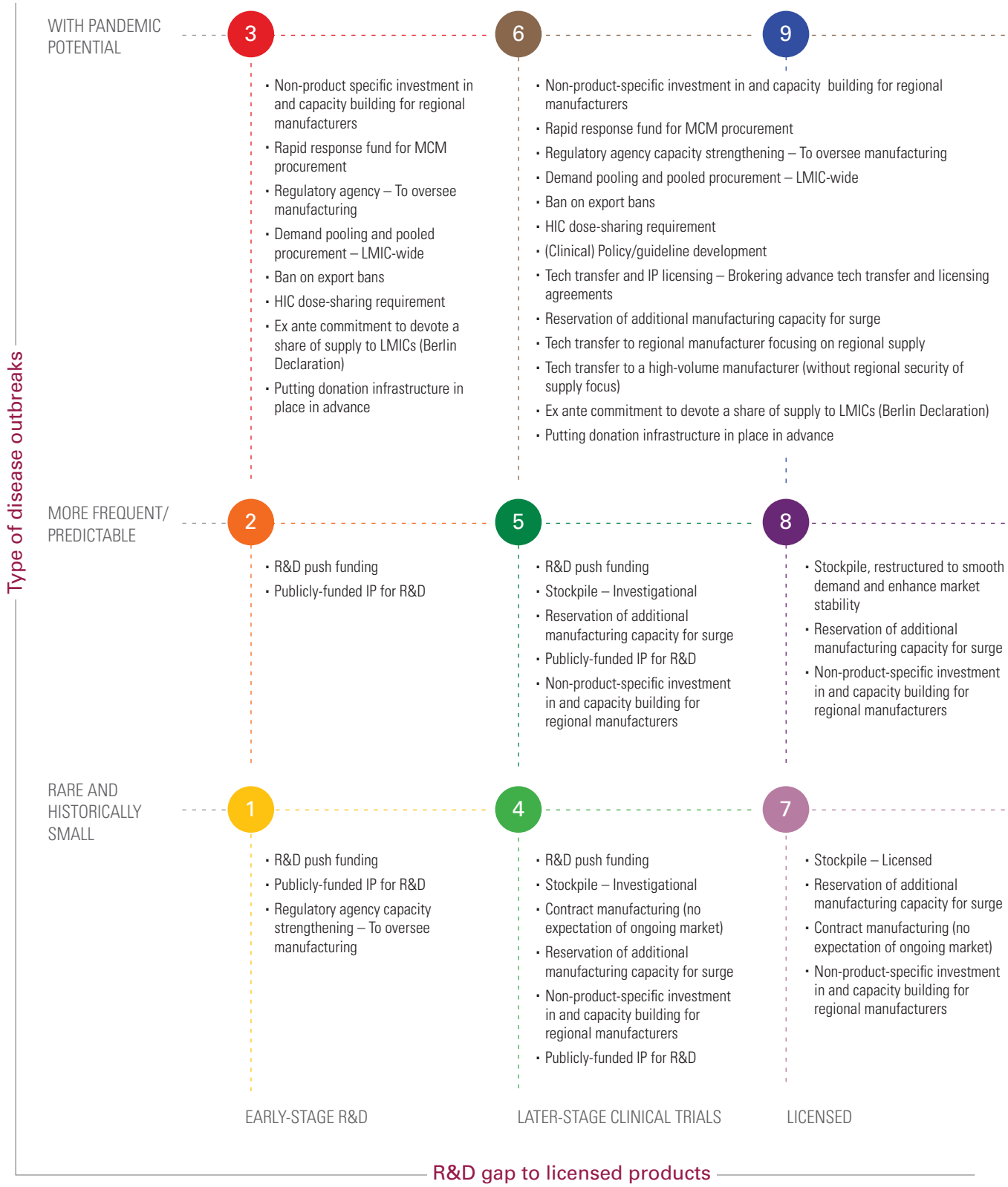
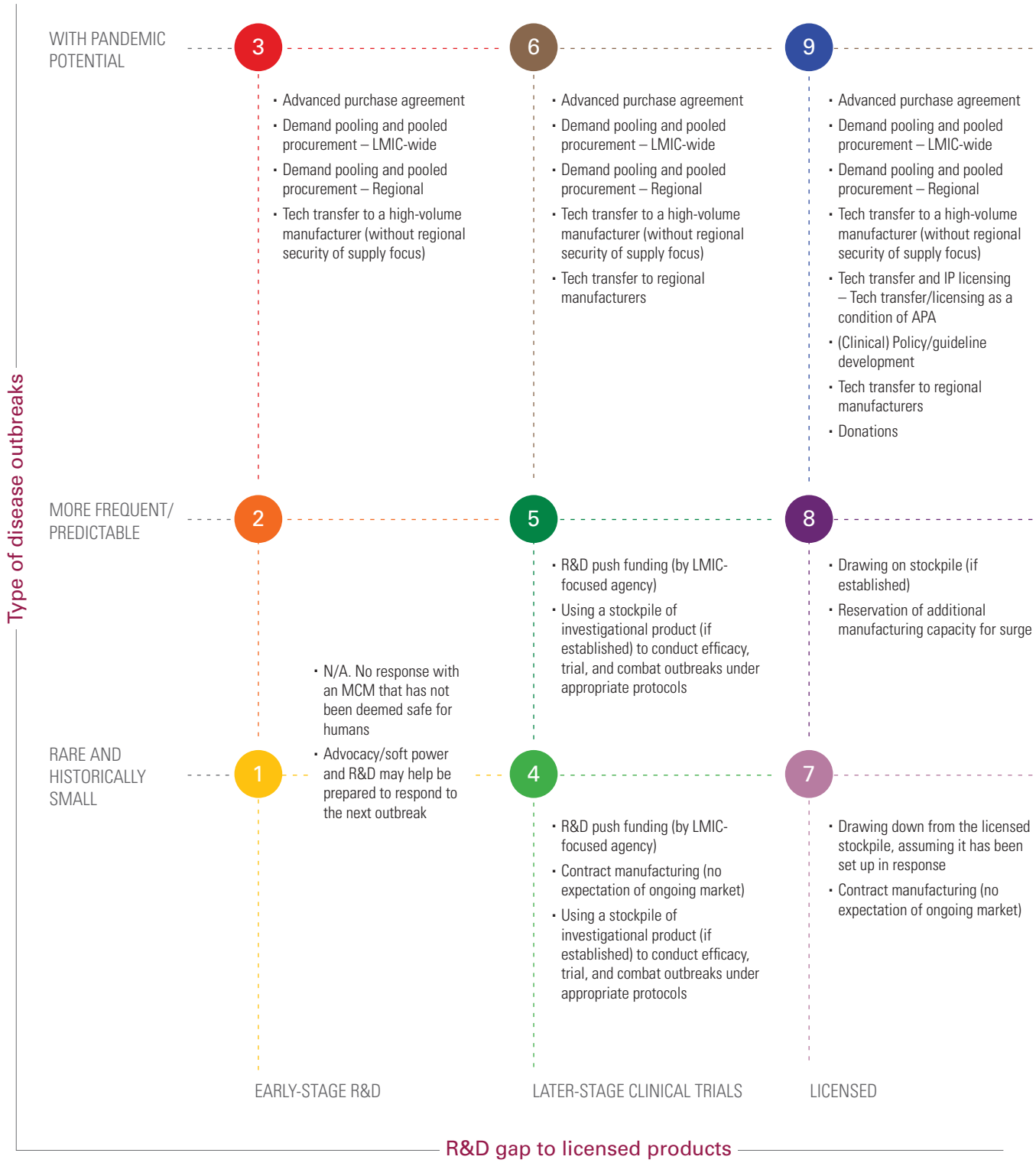


TABLE 3: RESPONSE PLAYBOOKS



4.1 HOW TO THINK ABOUT MARKETS FOR MCMS

It may be obvious, but bears repeating: We face PHEs of very different types. Outbreaks vary enormously in their scale and speed of spread. The 2022 Sudan ebolavirus outbreak in Uganda ended after only 164 reported cases. Every year, there are millions of cholera cases affecting multiple countries. And since the declaration of COVID-19 as a PHEIC in 2020, there have been billions of cases across countries of all income levels. These emergencies also differ in whom they affect: Some, like Ebola and cholera, strike only poorer countries,[13] while the COVID-19 pandemic reached every country on the planet.

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

The need for a tailored approach applies to PHEs in both preparedness and response. The market-shaping levers that will be most relevant and effective differ across PHE preparedness and response. It is too late for some preparedness investments when an outbreak is already raging. However, some actions can only be taken once the pathogen has been identified. Establishing large funds for rapid procurement is more important in preparation for pandemics than for smaller outbreaks unlikely to affect HICs, as in smaller outbreaks, LMICs are less likely to have to compete against HICs for limited supply of MCMs.[14] The type of manufacturing facilities needed to produce ready reserves of investigational vaccines are different from those required to supply a whole region in an ongoing 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. 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. By developing general strategies for each category, we can get a substantial head start on approaches to specific outbreaks when they occur.

4.2 RECOMMENDATIONS FOR PUBLIC HEALTH EMERGENCY PREPAREDNESS AND RESPONSE

We should develop playbooks, partnerships, policies and funding packages for each archetype. Playbooks such as those outlined above 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 replicating effective processes should make the international community more efficient in preparing and responding to PHEs of various types.

We 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 an outbreak's size nor duration 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 and product preferences not typically seen in conventional markets. For these and other reasons, some 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. Governments and organizations concerned with LMIC access to MCMs in outbreaks should consider whether Gavi Alliance vaccine product roadmaps[15] and UNICEF procurement strategies and market notes are fit for purpose.[16]

The range of levers we have today for ensuring an adequate and timely supply of MCMs for LMICs is too limited, and we must do more than incrementally adjust current partnerships and tactics. The current system relies too much on uncertain charity from high-income and MCM-producing countries and industry. Too little is invested in developing MCMs for pathogens that primarily threaten LMICs, and we fail to ensure a sufficient supply of established MCMs for outbreak diseases. Moreover, regionally-focused R&D, production, procurement, and delivery actors have become stronger and more assertive since COVID-19 and are progressing towards becoming a viable alternative to the global, centralized, "one-stop shop" approach in preparing for future outbreaks.

Sustained investment and new capacities are needed. The options to respond to future outbreaks depend on the decisions and actions we take now. To break out of the current paradigm, sustained investment is needed. Furthermore, some of the critically necessary initiatives to increase equitable access fall outside the core strengths of the main players in outbreak preparedness and response. New capacities and new divisions of labour are required, especially in two related areas: technology transfer, both in advance of and during outbreaks, and building the capacity of new and existing regional manufacturers to play a larger role in future

13 Outbreaks that affect only HICs are out of scope for UNICEF and therefore not part of this analysis.
14 Conditional funding for MCMs, and pooled procurement are most useful when buyer power is low or rapid deals are needed. This is more likely in situations of high competition, e.g., pandemics, rather than outbreaks of rare diseases where the international community is often the only buyer, e.g., Zaire ebolavirus.
15 https://www.gavi.org/our-alliance/market-shaping/market-shaping-roadmaps
16 https://www.unicef.org/supply/market-notes-and-updates

outbreaks. Annex C presents some preliminary analysis of the most compelling roles for regional manufacturing in PHEs, with implications for the different archetypes.

4.3 WHAT SHOULD THE INTERNATIONAL COMMUNITY AIM TO ACHIEVE IN EACH TYPE OF MARKET?

For rare and historically small outbreaks, the international community (including HIC R&D funders, foundations and international agencies) should focus on bringing at least one effective MCM product to market, relying primarily on push funding for product development and contracting production for stockpiles. Creating a "commercial"[17] 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 plays a much larger role in financing the development of these products, they are in a position, and have a responsibility, to focus investment efficiently.[18] 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 one product is "good enough", is there still a case to fund the development and trials of a second product with all the challenges of getting it to market?
- The risk of having only one product can be mitigated in various ways, including by establishing 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 product focus and business models 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. However, this will require technical capacity and either cross-subsidy from commercially viable products or ongoing national, regional, or international support.

Where investigational products for pathogens causing small and rare outbreaks have been shown to be safe in humans, ready reserves should be established to allow clinical trials to start quickly at the start of an outbreak and, 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 if no outbreaks and products expire.[19] The Coalition for Epidemic Preparedness Innovations (CEPI), Gavi and UNICEF are actively looking at stockpiles of vaccines and other products in preparation for these small and rare outbreaks. 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 relatively stable market by better linking up programmatic, policy and market-shaping actions. These are a complicated and somewhat heterogeneous group of markets, as in some cases, products are used routinely 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 upper-middle-income countries (UMICs). Unlike products for rare and historically small outbreaks, demand for middle-tier PHE products is, on average, sufficient to warrant ongoing production and to support more than one supplier.

The international community could do more to smooth demand across time, countries, and different uses, using such tools as larger and differently-structured stockpiles[20], 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. As a result, manufacturers produce less or expand capacity more slowly than they otherwise might, exacerbating supply shortages.

17 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 relative to other opportunities they could pursue. We assume that buyers would have to pay a cost of goods sold (COGS) + premium to keep manufacturers in these markets.

18 International actors do fund R&D and provide target product profiles (which is engagement before prequalification), but this influence is usually small compared to industry investment. However, for MCMs aimed at small and rare outbreaks, industry investment is low, and so this paradigm is reversed. The international community needs to recognize this reality and the choices it entails.

19 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?

20 There are stockpiles for some vaccines in this category, including cholera and measles rubella (MR). 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]?

For true pandemics, the objective is to secure a 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. It also includes expanded regional manufacturing capacity and greatly accelerated technology transfer to regional and 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 a reliance on donations and other suboptimal options, as evidenced during the COVID-19 pandemic. Substantial work is underway here, with too many initiatives to list. However, it still needs to be made clear who will take responsibility for some of the most needed actions, especially concerning tech transfer and regional manufacturing, or ensuring that sufficient funding will be made available.

In preparing for pandemics, the international community must be willing to pay for flexibility, as the best balance of tools will depend in part on pathogen 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 only a few products reach the market, rapid technology transfer to additional suppliers, including regional manufacturers, will be essential. As a result, preparation for pandemic response must emphasize flexibility and readiness to deploy a variety of levers depending on how the pandemic evolves.[21]

21 This is less true of other types of outbreaks.

Acknowledgements

The PHE archetypes and supply responses project was directed by Gian Gandhi and led by Ian Thornton. Dr Paul Wilson of Columbia University was an expert advisor. We thank our colleague, Jonathan Howard-Brand, for his contributions to this work and the members of the project's Informal Advisory Group for their insightful guidance.

Dr Merawi Aragaw Tegegne of Africa Centres for Disease Control and Prevention

Dr Chikwe Ihekweazu of the WHO Hub for Pandemic and Epidemic Intelligence

Dr Aboubacar Kampo of UNICEF

Eva Kadilli of UNICEF

Dr Nicole Lurie of Coalition for Epidemic Preparedness Innovations

Paul Molinaro of WHO Operations Support and Logistics

James Platts of the Bill & Melinda Gates Foundation

Dr Amadou Sall of Institut Pasteur de Dakar

Rachel Silverman-Bonnifield of the Center for Global Development

Eloise Todd of the Pandemic Action Network

Dr Marta Tufet of Gavi, the Vaccine Alliance Secretariat

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 analyses

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 in overcoming it (which drives 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.[22]

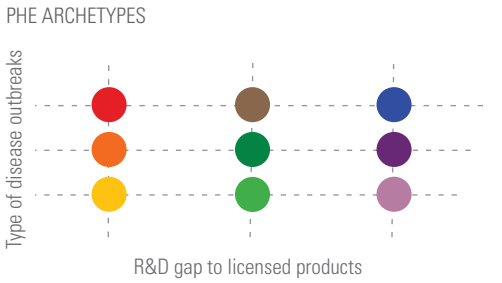
2. **Feasibility of deploying the market shaping lever in question.**

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 considered approximate—an attempt to capture significant differences. For example, an advanced purchase agreement (APA) is more complicated to put in place than a demand forecast, and negotiating a legally binding intergovernmental 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.



LEGEND

EARLY-STAGE R&D

1 RARE AND HISTORICALLY SMALL

2 MORE FREQUENT/ PREDICTABLE

3 WITH PANDEMIC POTENTIAL

LATER-STAGE CLINICAL TRIALS

4 RARE AND HISTORICALLY SMALL

5 MORE FREQUENT/ PREDICTABLE

6 WITH PANDEMIC POTENTIAL

LICENSED

7 RARE AND HISTORICALLY SMALL

8 MORE FREQUENT/ PREDICTABLE

9 WITH PANDEMIC POTENTIAL

SCORE

GOOD

OK

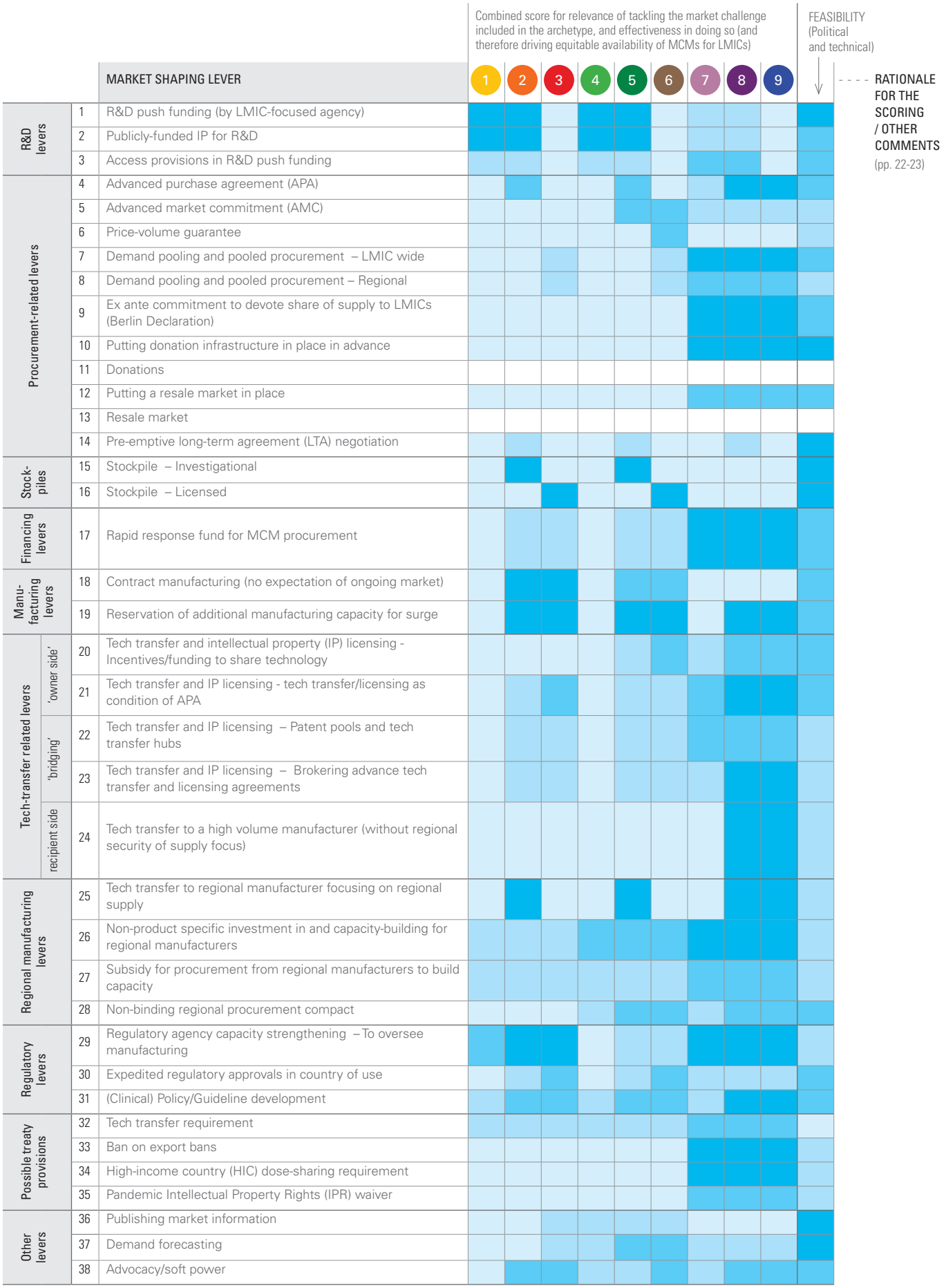
NOT GREAT

VERY POOR

N/A

22 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 that are relatively weak across all archetypes but possibly worth doing as part of a package of interventions because they are easy or quick to implement.

TABLE 4: HEATMAP FOR PREPAREDNESS (table extended to next pages)



		RATIONALE FOR THE SCORING	OTHER COMMENTS
R&D levers	1	Push funding is crucial to driving products towards licensure, especially when commercial incentives are lacking. For pandemic pathogens, commercial forces and funding from HICs mean that the incremental effect of funding by LMIC-focused agencies will be marginal in most cases, although a case can be made for some investments to help reserve supply. As a preparedness investment, R&D funding is relevant for known outbreak-prone pathogens and pathogen families, as well as relevant platform technologies.	R&D funding from sources not focused specifically on LMICs (e.g. HIC agencies) is, of course, essential in pandemics and very useful for other kinds of outbreaks if available.
	2	Publicly-funded IP, e.g., funding of university research or product development partner, is a crucial foundation for product development. For pandemic-threat pathogens, can mostly rely on HIC funding.	
	3	Access provisions are not really needed in lower-HIC-demand outbreaks. Very important for pandemics, where LMICs face competition for supply from HICs, but most impact from access provisions in HIC funding for R&D.	
Procurement-related levers	4	APA-linked to procurement for a stockpile—could play a role in preparing for lower-tier outbreaks by helping to bring a product to market. Not needed once a product is on the market; can just use contract manufacture or conventional procurement (for more frequent tier). The use case in pandemics is totally different: Security of supply in the face of competition from HICs. APAs as a preparedness tool are most relevant for known pathogens, although could perhaps put general structure and some kind of funding commitments in place for unknown pathogens, to be triggered by an outbreak meeting certain conditions.	
	5	AMCs are too complicated and expensive for rare and historically small outbreaks, where having multiple products is not a high priority; perhaps more useful for more frequent outbreaks, bringing products to market. Assumed to be less useful in pandemics because more difficult to engineer supply commitment binding on individual firms. Could be a useful form of R&D incentive in a pandemic, but this would require involvement and funding on a large scale by HICs, too large for LMIC-focused agency. As a preparedness investment, mostly relevant to known outbreak pathogens, although broad structure could possibly be put in place to include unknown pathogens.	
	6	Demand uncertainty is too high in small and rare outbreaks and in pandemics to be addressed with this instrument; could be quite useful for MCMs on the market for more frequent outbreaks, adding a floor to demand like a stockpile does. As a preparedness investment, only relevant to more frequent outbreaks with licensed MCMs, where distinction between preparedness and response is blurred.	
	7	Not considered a strong enough lever to really shape manufacturer behaviour in the rare and small or more frequent archetypes, where demand is largely pooled anyway through a proxy buyer. However, can be a useful buyer power tool in pandemics, hence useful to organize in advance.	UNICEF procurement for Gavi routine vaccines and for COVAX existing models for procurement for a large share of LMICs. These mechanisms do not include most upper middle-income countries (UMICs), however, and doing so poses important challenges.
	8	As above, but assuming weaker lever because a region is smaller than an an LMIC-whole buying pool. More difficult to organize—outside of Pan American Health Organzation (PAHO)—because no strong existing structures.	
	9	Only useful when there is HIC buying, e.g., in pandemics. Value depends on the amount and other features of the commitment, as well as on the likelihood that commitment will hold in a pandemic with severe supply shortage and the resulting pressure from high-income/producing countries. Could be established either in advance or after the onset of a pandemic, but better in advance.	Not clear who would make and enforce such a commitment: suppliers or HICs. If the expectation is that HICs would buy the doses and donate to LMICs, industry has committed little. The trade-off between feasibility and effectiveness. A modest commitment (10 per cent of doses) may be achievable but would contribute only modesly to LMICs needs; a larger commitment would more difficult to negotiate and be more vulnerable in a severe supply shortage
	10	Only useful when there is HIC buying e.g., in pandemics. Effective only when there is excess supply (and when this is clear), so likely not very timely. Benefit of doing in advance (as a preparedness investment) is in expediting flow of doses when they become available.	
	11		
	12	Only useful when there is HIC buying, e.g., in pandemics. Effective only when there is excess supply (and when this is clear), so likely not very timely. The benefit of doing this in advance (as a preparedness investment) is in expediting the flow of doses when they become available.	
	13		
	14	Potentially useful to expedite procurement if put in place before a product comes to market. Early-stage R&D too early to identify suppliers, on market not necessary. Effects modest.	
Stock-piles	15	Crucial tool for swift response at the start of an outbreak and for raising/smoothing demand. Not considered feasible for pandemics on account of the scale of the stockpile that would be needed. Most important as a preparedness investment.	
	16	Crucial tool for swift response at the start of an outbreak and for raising/smoothing demand. Not considered feasible for pandemics on account of the scale of stockpile that would be needed.	Could possible put elements of a licensed product stockpile in place before licensure (middle column of archetypes).
Financing levers	17	Most useful in pandemics, when LMICs in competition with HICs and important to get to front of queue. Useful in other kinds of outbreaks to avoid delays, but less urgent without competition. Preparedness only: Needs to be in place at start of outbreak.	
Manu-facturing levers	18	Most useful for rare and small outbreaks where market incentives are weakest and direct contracting rather than "creation of a market" is the most straightforward way to acquire necessary doses.	
	19	Most useful for frequent outbreaks where surges may exceed routine capacity, and may be more efficient than enlarging stockpile.	

			RATIONALE FOR THE SCORING	OTHER COMMENTS
Tech-transfer related levers	'owner side'	20	Tech transfer could be especially useful to expand total supply and secure availability in a pandemic in the face of competition, if suppliers willing to agree to offered terms. Could be put in place either in advance or after start of outbreak. Not needed in small and rare because technology specific to these diseases already developed for LMICs.	
		21	Tech transfer to a public health focused/regionally focused manufacturer may be useful in advance of potential outbreaks, to ensure continued supply. Especially true for the rare and historically small outbreaks where MNCs may be withdrawing from the market. If feasible, can be a way to scale production rapidly in the case of a pandemic	
	'bridging'	22	Most relevant to pandemics, where rapid expansion of supply and LMIC-dedicated supply are most important. Without either an enforceable treaty requirement or strong incentives, IP sharing will be challenging. Tech transfer hubs are complicated and largely unproven. Estabishment of pools especially primarily a preparedness investment, although outbreak-specific technologies could be added to existing mechanisms in a pandemic.	
		23	Setting up tech transfer agreements in advance could be a way to more rapidly expand total supply and contribute to regional supply security in a pandemic, and perhaps also to prepare for surges in other types of outbreaks. Only relevant to licensed or near-licensure products where lkely suppliers and relevant technology are understood. Besides wilingess to transfer, uncertainty about need, demand, guidance ahead of a pandemic is an obstacle to setting these agreements in advance.	
	recipient side	24	Tech transfer could be especially useful to expand total supply and secure availability in a pandemic in the face of competition, and rapid tech transfer to a high-volume producer (such as Astra Zenaca to Serum Institute of India) could dramatically increase supply to LMICs. The main challenge is obtaining the cooperation of product developers. Large volumes that these manufacturers can supply are not needed in other kinds of outbreaks. For licensed and close-to-market products for known outbreak pathogens, transfering technology ahead of an outbreak would expedite supply from recipients.	
Regional manufacturing levers		25	Regional manufacturing most useful in pandemics (to help ensure regional supply security) and in middle-tier outbreaks (as a hedge against withdrawal of other manufacturers). Regional manufacturing will in most cases require tech transfer. The main challenges are manufacturer capacity (in the short to medium term) and, for pandemics, technology owner willingness.	
		26	Generally, a good thing to do, but less useful for the rare and historically small outbreaks, where production capacity is not often the problem. Could be useful in more frequent types of outbreaks as a hedge against withdrawal of manufacturers. Useful for pandemics, driving up total supply and security of supply for that region. Investment is technically feasible, but in some cases, considerable time and investment will be needed to bring suppliers to necessary capacity.	
		27	Relatively weak lever; worth putting in place to support buyer power in the case of a pandemic, but not strong enough to drive product development for any of the categories without other levers.	
		28	Not always relevant in the rare and small category. Only one global manufacturer is really needed, but this could be a manufacturer in, e.g., Africa, where regulatory capacity tends to be weaker. More useful for frequent outbreaks and pandemics where more manufacturers/manufacturing sites and are needed, and security of supply through distributed manufacturing becomes more important. Regulatory agency strengthening is an important complement to building the capacity of manufacturers themselves.	
Regulatory levers		29	In-country approval processes can slow access in outbreaks, but usually not the main obstacle. Best as preparedness investment to put appropriate processes in place.	
		30	Can accelerate uptake of products that are near to, or on, the market, especially in cases where the product is ready, e.g., stockpiled.	
		31	Only relevant where there is HIC buying, but in those cases, could be powerful, although not clear how easy it would be to force tech transfer (as opposed to IP licensing) from an unwilling product developer Very challenging to put in place, as this would meet with fierce opposition from industry.	The compulsory nature of the lever may yield unexpected consequences, e.g., disincentivize commercial investment in R&D. Current scoring does not take this into account.
Possible treaty provisions		32	Only relevant where there is HIC buying, but in those cases, could be powerful. Main challenge is enforcement in a bad outbreak with severe supply shortage.	
		33	Most relevant in pandemics, to help expand supply and secure supply for LMICs. Impact in the absence of tech transfer depends to some extent on the technology. Blanket waiver very difficult to put in place, although agreement to share IP with geographical restrictions might be more feasible.	Trade-off between impact and difficulty: A modest dose-sharing requirement would be easier to negotiate than one that would be more likely to ensure sufficient access for LMICs.
		34	The compulsory nature of the lever may yield unexpected consequences e.g., disincentivize commercial investment in R&D	
		35	Generally weak lever—may encourage firms to fill market gaps, but likely only in combination with other levers. As a preparedness investment, most relevant to more frequent outbreaks.	
Other levers		36	Generally weak lever—PHEs are characterised by demand uncertainty, and LMICs are only part of the market, so forecasting LMIC demand on its own is unlikely to de-risk significantly.	
		37	Different advocacy use cases: in small and rare and more frequent, the advocacy would be about R&D and staying in the market. For pandemics, it would be focussed on delivering equitable access commitments.	
		38		

TABLE 5: HEATMAP FOR RESPONSE (table extended to next pages)

		MARKET SHAPING LEVER	Combined score for relevance of tackling the market challenge included in the archetype, and effectiveness in doing so (and therefore driving equitable availability of MCMs for LMICs) 1	2	3	4	5	6	7	8	9	FEASIBILITY (Political and technical)	RATIONALE FOR THE SCORING / OTHER COMMENTS (pp. 25-26)
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 Declaration)											
	10	Putting donation infrastructure in place in advance											
	11	Donations											
	12	Putting a resale market in place											
	13	Resale market											
	14	Pre-emptive long-term agreement (LTA) negotiation											
Stock-piles	15	Stockpile – Investigational											
	16	Stockpile – Licensed											
Financing levers	17	Rapid response fund for MCM procurement											
Manu-facturing 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 intellectual property (IP) licensing - Incentives/funding to share technology											
	21	Tech transfer and IP licensing - tech transfer/licensing as condition of APA											
'bridging'	22	Tech transfer and IP licensing – Patent pools and tech transfer hubs											
	23	Tech transfer and IP licensing – Brokering advance tech transfer and licensing agreements											
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	High-income country (HIC) dose-sharing requirement											
	35	Pandemic Intellectual Property Rights (IPR) waiver											
Other levers	36	Publishing market information											
	37	Demand forecasting											
	38	Advocacy/soft power											

		RATIONALE FOR THE SCORING	OTHER COMMENTS
R&D levers	1	R&D push funding is only useful in response if you have a product that is near to market, and funding can be organized and deployed quickly enough to get the trials done during the current outbreak. For pandemics, commercial forces and HIC funding should be sufficient, although there may be use cases for funding by an LMIC-focused agency in some cases.	R&D funding from sources not focused specifically on LMICs (e.g. HIC agencies) is of course essential in pandemics and very useful for other kinds of outbreaks if available.
	2	This assessment focuses on public funding of IP creation, for example, at universities. Although this kind of funding is very important for all MCM development, it is in general too far upstream to be useful in response to an outbreak.	
	3	Not needed for the lower two tiers of outbreaks, as there is little or no HIC market for these MCMs, so access provisions are not needed. Although access provisions should certainly be attached to push funding from an LMIC-focused source in pandemics, the argument for such funding is not particularly strong (see assessment of "R&D push funding"). Access provisions attached to funding from HICs could be of great value for LMICs but is beyond the scope of this assessment. The feasibility score reflects the challenge for an LMIC-focused agency in imposing access provisions on product developers who may have access to untied funding for other sources in a pandemic.	
Procurement-related levers	4	Useful for products near to market, but for very different reasons. For more frequent outbreaks, could help to de-risk development and manufacture; for pandemics, crucial to securing supply in the face of competition. No strong argument in the case of rare and historically small outbreaks, where there can be no expectation of an ongoing market and there is no competition. Push funding is more suitable.	
	5	Most useful for the more frequent outbreaks where there might be demand for multiple products. Could be used for pandemics too, but would probably have to cover HICs as well and require large funding from HIC sources. Compared to APAs, an additional drawback of AMCs for pandemics is greater difficulty in making supply commitments binding on individual firms. The feasibility score reflects the design complexity and challenge of putting such an instrument in place during a pandemic.	Some overlap between preparedness and response here, in that the basic structure of an AMC and perhaps some conditional funding commitments could be put in place in advance of a pandemic, but parameters would have to be set during the pandemic.
	6	In general, demand uncertainty in outbreaks is too great for this to be an appropriate mechanism for de-risking. May be some potential for more frequent outbreaks, in conjunction with other smoothing mechanisms.	
	7	Generally useful. Less important in small and historically small outbreaks, where at most, a small number of countries are likely to be involved, and a proxy buyer may already be unifying demand. Important in pandemics to increase LMIC market power and reduce transaction costs for suppliers.	UNICEF procurement for Gavi routine vaccines and for Covax are existing models for procurement for a large share of LMICs. These mechanisms do not include most UMICs, however, and doing so poses important challenges.
	8	Same rationale as LMIC-wide pooled procurement, although in general weaker because market power is smaller. More difficult to establish (outside of PAHO, where it is already in place).	
	9	Only useful when there is HIC buying, e.g., in pandemics. Value depends on the amount and other features of the commitment, as well as on the likelihood that commitment will hold in a pandemic with severe supply shortages and the resulting pressure from high-income/producing countries.	Not clear who would make and enforce such a commitment, suppliers or HICs. If expectation is that HICs would buy the doses and donate to LMICs, industry has committed little. Trade-off between feasibility and effectiveness. A modest commitment (10 per cent of doses) may be achievable but would contribute only modesly to LMICs needs; a larger commitment would more difficult to negotiate and be more vulnerable in a severe supply shortage
	10		Could put be important benefits from putting infrastructure in place after pandemic begins but before surplus doses are available, but for simplicity will interpret this lever as preparedness.
	11	Only useful when there is HIC buying e.g., in pandemics. Effective only when there is excess supply (and when this is clear), so likely not very timely.	
	12		Could put be important benefits from putting infrascture in place after pandemic begins but before surplus doses are available, but for simplicity will interpret this lever as preparedness.
	13	Only useful when there is HIC buying, e.g., in pandemics. Effective only when there is excess supply (and when this is clear), so likely not very timely.	
	14	Potentially useful to expedite procurement if put in place before a product comes to market. Early-stage R&D too early to identify suppliers, on market not necessary. Effects modest.	
Stock-piles	15	Having an investigational stockpile in place could be very useful in an outbreak, especially when expected duration and therefore time to conduct a trial, could be short. But needs to be set up in advance, so will interpret as a preparedness action.	
	16	Primarily a preparedness investment but can be set up in an outbreak to meet surges in demand in small and rare outbreaks and for ongoing management of more frequent outbreaks. Not appropriate for pandemics, where volumes required would in general, be very large.	Some ambiguity between preparedness and response with more frequent outbreaks, as at the global level, phases are not distinct.
Financing levers	17	Preparedness only–needs to be in place at the start of outbreak.	
Manu-facturing levers	18	Most useful for the rare and small outbreaks, where market incentives are weakest and direct contracting rather than "creation of a market" is the most straightforward way to acquire necessary doses.	
	19	Most useful for frequent outbreaks, where surges may exceed routine capacity and may be more efficient than enlarging the stockpile.	Strategies for maintaining and ensuring access to additional capacity are also very important in pandemics, but actually paying for reserve capacity is probably not the best way to do this because of the requiredsclae and cost.

			RATIONALE FOR THE SCORING	OTHER COMMENTS
Tech-transfer related levers	'owner side'	20	Tech transfer could be especially useful to expand total supply and secure availability in a pandemic in the face of competition, if suppliers willing to agree to offered terms. Largely too late as a reponse investment, apart from the more frequent outbreaks, and in the case of pandemics. Not needed in small and rare because technology specific to these diseases already developed for LMICs.	Trade-off between effectiveness and feasibility/cost: incentives might have to be large to induce participation by suppliers in a pandemic, or when platform technologies are involved.
		21	Tech transfer could be especially useful to expand total supply and secure availability in a pandemic in the face of competition. The ability to impose these conditions in APAs depends on buyers' market power. This will, in most cases, be challenging for LMICs or proxy buyers. In general, this lever is not needed for smaller outbreaks because the products used in these are specifically developed for LMICs.	
	'bridging'	22	Establishment of pools is really a preparedness investment, but outbreak-specific technologies could be added to existing mechanisms in a pandemic. Most relevant to pandemics, where rapid expansion of supply and LMIC-dedicated supply are most important. Without either an enforceable treaty requirement or strong incentives, IP sharing will be challenging. Tech transfer hubs are complicated and largely unproven.	
		23	Preparedness investment only.	
	recipient side	24	Tech transfer could be especially useful to expand total supply and secure availability in a pandemic in the face of competition, and rapid tech transfer to a high-volume producer (e.g., Astra Zeneca, Serum Institute of India) could dramatically increase supply to LMICs, although doing so after an outbreak begins means substantial delays. The main challenge is obtaining the cooperation of product developers. Large volumes that these manufacturers can supply are not needed in other kinds of outbreaks.	
Regional manufacturing levers		25	Regional manufacturing most useful in pandemics (to help ensure regional supply security) and in middle-tier outbreaks (as a hedge against withdrawal of other manufacturers). Regional manufacturing will in most cases require tech transfer. The main challenges are manufacturer capacity (in the short to medium term) and, for pandemics, technology owner willingness.	Technology owners will probably be more willing to transfer to regional manufacturers than to high-volume manufacturers, who may be seen as greater potential competitors for lucrative markets.
		26	Preparedness investment only.	
		27	Preparedness investment only.	
		28	Could be set up either in advance (preparedness or in a pandemic if regional suppliers are expected to bring products to market). Could help to assure prospective suppliers of the market. Generally weaker lever, as compact is not binding–most applicable to routine markets.	
Regulatory levers		29	Slow and hard to do, so most likely a preparedness investment. In reality, a workaround seems more likely even during a pandemic.	
		30	In-country approval processes can slow access in outbreaks, but usually not the main obstacle.	
		31	Very useful as soon as there are products near to market, and an outbreak happens.	
Possible treaty provisions		32	Implementing this and other mandatory measures as part of a treaty requires years of negotiation, so will consider this as a preparedness investment, although certain measures could possibly be negotiated individually during a pandemic.	
		33	Implementing this as part of a treaty requires years of negotiation, but these could possibly be negotiated individually during a pandemic.	
		34	Implementing this as part of a treaty requires years of negotiation, but these could possibly be negotiated individually during a pandemic.	
		35	Implementing this as part of a treaty requires years of negotiation, but these could possibly be negotiated individually during a pandemic.	
Other levers		36	Generally weak lever; may enourage firms to fill market gaps, but likely only in combination with other levers.	
		37	Generally weak lever; public health emergencies are characterized by demand uncertainty, and LMICs are only part of the market, so forecasting LMIC demand on its own is unlikely to de-risk significantly	
		38	Advocacy could be useful in different ways in different types of outbreak: for LMIC-limited diseases, could help to push pharma and funders to contribute to product development; in pandemics, to push for equity of access.	

B. Market health considerations for PHEs

The Gavi-UNICEF Healthy Markets Framework[23] 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 different routine vaccine market elements. It has become the dominant framework for market shaping for MCMs for LMICs.

FIGURE 3: THE GAVI-UNICEF HEALTHY MARKETS FRAMEWORK

Demand health	Materialization of demand	The degree to which country introductions and campaigns materialize
	Predictability of demand	The degree to which both the quantity and timing of demand can be accurately predicted and sustained by countries
	Balanced demand of appropriate products & timely uptake of new innovative products	The degree to which country product choices are data-driven, value-based; leading to balanced demand for appropriate products & timely uptake of new innovative products
Supply dynamics	Supply meets demand	The degree to which overall supply availability of antigen meets demand
	Meeting country product preference	The degree to which available supplies will be able to meet countries' product choices
	Supplier base risk	The magnitude of risk that the supplier base will be unable to supply expected doses (considering supplier buffer capacity, sustainability, technical risks, diversity and portfolio viability)
	Geopolitical & regulatory risk	The magnitude of risk that doses cannot be released or exported from the country of production
	Market sustainability & attractiveness	The degree to which the market remains sufficiently attractive for incumbent suppliers to be competitive or for new suppliers to enter
Innovation	Incentivizing & scaling up innovations	The degree to which ongoing innovations address countries' unmet needs and may be adopted by countries in the future

This project sought to interrogate whether the Gavi-UNICEF Health Markets Framework was fit for the purpose of analyzing and managing MCM markets for PHEs. Table 6 below compares PHE MCM markets with MCM markets in the context of endemic pathogens using the same pillars of market health as the Gavi-UNICEF Framework.

TABLE 6: MARKET HEALTH CONSIDERATIONS FOR PHEs

Characteristic	PHE MCM markets	Markets for MCMs for endemic pathogens	Implications for PHE MCM 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 birth cohorts for diphtheria, tetanus, pertussis (DTP) and pneumococcal conjugate vaccine (PCV).	Even when there is some potential for high demand, demand risk for the producer is very high.

23 https://www.gavi.org/our-alliance/market-shaping

Characteristic	PHE MCM markets	Markets for MCMs for endemic pathogens	Implications for PHE MCM market shaping
Market size	Many PHEs are relatively small-scale, with correspondingly small volumes of MCMs needed. For example, in 2023, only 19,000 doses have been drawn down from the Zaire ebolavirus vaccine stockpile, with 6,500 doses for outbreak response, some for vaccination or health care workers and some to replace expiring doses. There are three exceptions: • True pandemics. • Products used in preventative campaigns and outbreak response, e.g., cholera vaccine. • Diagnostics, where some products could be used for surveillance and response.	There tend to be many orders of a bigger magnitude than PHE markets, e.g., global demand for DTP or human papillomavirus (HPV) vaccines.	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, innovation, etc.
Frequency of outbreaks	Outbreaks of some pathogens are infrequent, while others are more common and may have a seasonal pattern.	Some outbreak pathogens are endemic in some countries. As a result, markets for MCMs for these pathogens may be larger and somewhat more stable.	The low frequency of outbreaks contributes to market uncertainty and creates challenges in sustaining supply. In addition, the infrequency of outbreaks makes it difficult to plan and conduct efficacy trials, creating a barrier to product development and new entrants.
Urgency	PHEs are, by definition, emergencies, and the need for MCMs is urgent. Getting to market and scaling up supply quickly are very high priorities. It may also entail some increased tolerance for suboptimal products, e.g., efficacy may be less than desired or not as fully demonstrated.	Although speed to market may be important commercially in these markets, it is not the priority as it is in PHEs. There is minimal willingness to relax standards or licensing norms, especially for vaccines given to healthy 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 typically be. There are at least two reasons for this: fear of and desire to avert a worst-case scenario and overvaluing of epidemic deaths as opposed to deaths from routine causes that have been normalized. Price insensitivity is substantially driven by the perception of threat to HICs, even when an outbreak initially affects only LMICs.	Price/cost to country 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, e.g., perceived risk to HICs (see left).	This 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.

Characteristic	PHE MCM markets	Markets for MCMs for endemic pathogens	Implications for PHE MCM market shaping
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 rare 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 agencies acting on their behalf.
Trade and export bans	When there are shortages of PHE MCMs, producing countries may impose export bans on key inputs and finished products.	Export bans are very unlikely.	The 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 the allocation of scarce supplies in an emergency.
Political pressure not to maximize profit	Suppliers could face public scrutiny and political pressure to prioritize the public good in an outbreak, with calls for them to donate products or sell them at cost and share IP and technology.	Though there are notable exceptions, there are much lower levels of public scrutiny in most markets, e.g., HIV and hepatitis C.	This political scrutiny can support availability and affordability in the short term but may send negative signals to manufacturers and, in the worst case, discourage involvement in PHE MCM markets.

As mentioned in Section 4, the table above reaffirms that unique characteristics across different PHE MCM markets render an analysis using the currently available Healthy Market Framework neither appropriate. Figures 4 and 5 below summarize how PHE MCM market health should diverge from the fuller conception of market health relevant to routine vaccine markets.

FIGURE 4: THE GAVI-UNICEF HEALTHY MARKET FRAMEWORK: SUPPLY SIDE

Supply meets demand	The degree to which overall supply availability of antigen meets demand	ABSOLUTELY CRUCIAL, BUT WHAT THIS 'ROUTINE' FRAMEWORK DOES NOT INCLUDE IS THE TIMELINESS OF THIS SUPPLY
Meeting country product preference	The degree to which available supplies will be able to meet countries' product choices	PERHAPS LESS IMPORTANT IN A PHE CONTEXT, WHERE ACCESS TO AN EFFECTIVE PRODUCT IS THE PRIORITY (AND THERE MAY BE ONLY ONE PRODUCT)
Supplier base risk	The magnitude of risk that the supplier base will be unable to supply expected doses (considering supplier buffer capacity, sustainability, technical risks, diversity and portfolio viability)	VERY CHALLENGING FOR MOST (SMALL) PHEs, WHERE HAVING MORE THAN ONE SUPPLIER MAY BE UNREALISTIC AND UNECONOMICAL
Geopolitical & regulatory risk	The magnitude of risk that doses cannot be released or exported from the country of production	HUGELY IMPORTANT FOR PANDEMICS (EXPORT BANS), AS A ROUTE TO SECURING SUPPLY, BUT HARDER TO ACHIEVE FOR SMALLER, SINGLE SUPPLIER PHEs
Market sustainability & attractiveness	The degree to which the market remains sufficiently attractive for incumbent suppliers to be competitive or for new suppliers to enter	VERY CHALLENGING FOR MOST PHEs. SOME MARKETS MAY MOVE TOWARDS A MORE STABLE AND SUSTAINABLE STATE, BUT NOT MANY. ARGUABLY MORE IMPORTANT IS HAVING THE KNOW-HOW AND CAPACITY TO RAPIDLY SCALE UP PRODUCTION WHEN NEEDED

FIGURE 5: THE GAVI-UNICEF HEALTHY MARKET FRAMEWORK: DEMAND SIDE

Materialization of demand	The degree to which country introductions and campaigns materialize	HUGELY IMPORTANT, BUT OUTSIDE OF OUR SCOPE FOR THIS PROJECT
Predictability of demand	The degree to which both the quantity and timing of demand can be accurately predicted and sustained by countries	PREDICTABLE DEMAND IS BY DEFINITION NOT FEASIBLE FOR PHEs
Balanced demand of appropriate products & timely uptake of new innovative products	The degree to which country product choices are data-driven, value-based; leading to balanced demand for appropriate products and timely uptake of new innovative products	VERY CHALLENGING FOR PHEs, WITH RAPIDLY CHANGING DATA ON EFFECTIVENESS, AND POTENTIALLY EVOLVING PATHOGENS TOO
Incentivizing & scaling up innovations	The degree to which ongoing innovations address countries' unmet needs and may be adopted by countries in the future	AS IMPORTANT FOR PHEs AS OTHER MARKETS, BUT MADE CHALLENGING BY THE DIFFICULTY OF CONDUCING EFFICACY TRIALS (IN SMALL OUTBREAKS) AND GREAT ADVANTAGE THAT URGENCY GIVES TO PRODUCTS ALREADY ON THE MARKET

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 that 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[24] · Product-specific tech transfer to regional manufacturers[25]	Rare and historically small outbreaks 4 7 and more frequent outbreaks 5 8
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 · 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] · Non-binding regional procurement compact	Pandemic potential pathogens and outbreaks 6 9

24 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)
25 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
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

D. Market shaping levers: Descriptions and analyses

This annex provides more detail on the 38 market shaping levers UNICEF has analyzed to inform the PHE archetypes. In the following tables, 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 heatmaps (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 MCMs to LMICs. An analysis that prioritized other market objectives such as affordability, sustainability, or ongoing innovation might lead to different conclusions.

	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 Declaration)
10	Putting donation infrastructure in place
11	Donations
12	Putting a resale market in place
13	Resale market
14	Pre-emptive long-term agreement (LTA) 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 – Tech transfer/licensing as condition of APA
	Tech-transfer related levers – Bridging
22	Tech transfer and IP licensing – Patent pools and tech transfer hubs
23	Tech transfer and IP licensing – Brokering advance tech transfer 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 intellectual property rights (IPR) waiver
	Other levers
36	Publishing market information
37	Demand forecasting
38	Advocacy/soft power

R&D levers

Lever 1 - R&D push funding (by LMIC-focused agency)

Description/how it works	Direct financial support to an MCM developer to support R&D to incentivize or accelerate product development or make the product more suitable for LMICs. In theory, it could include other mechanisms for reducing R&D costs to product developers, such as tax breaks. In this project, the focus is on push funding from agencies concerned with LMIC access. 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 the 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 the development/adaptation of products needed by LMICs.
Drawbacks	· Transfers R&D risk entirely or in part to funders and requires funders to "pick winners". · Does not offer developers a return comparable to commercial markets. · By itself, it 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)?	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 the supply of available products cannot be expanded sufficiently, market forces and funding from HICs are inadequate to drive R&D. · When the existing MCMs are suboptimal for LMICs because of presentation, cold chain requirements, dose regimen, or delivery model. · As a way to secure access to supply through access provisions (Lever 2).
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 the 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 fever and MERS-CoV vaccines.

Lever 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 developing 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 the benefits of IP access against potential disincentives and choose which circumstances and for which kinds of R&D 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, rare, and more frequent outbreaks to avoid trapping and 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 the main source of funding. · For commercially borderline products, where the 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	Licensing of conjugation technology by the US National Institutes of Health (NIH) or US Food and Drug Administration (FDA), used in meningitis A vaccine.

Lever 3 - Access conditions in R&D push funding

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 developing 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 the benefits of IP access against potential disincentives and choose which circumstances and for which kinds of R&D 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, rare, and more frequent outbreaks to avoid trapping and 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 the main source of funding. • For commercially borderline products, where the 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	Licensing of conjugation technology by the US National Institutes of Health (NIH) or US Food and Drug Administration (FDA), used in meningitis A vaccine.

Procurement-related levers

Lever 4 - Advanced purchase agreement (APA)

Description/how it works	An APA is a 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 the 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. It is also noted: • 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	• 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 to invest in additional production capacity—in this sense, they are a classic pull mechanism. Importantly, unlike advanced market commitments (Lever 5), APAs insulate suppliers from aggregate demand risk (e.g., if the outbreak is smaller or ends sooner than expected) and competitive risk (e.g., if users will prefer other products). • In the 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 they end up obligated to buy more than they need, either of a class of products (e.g., COVID-19 vaccines) or 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, using APAs by all buyers, especially HICs, can result in a bidding war, driving up prices for everyone. • The use of APAs by HICs can be a grave threat to LMIC access, as neither they nor their proxy buyers are likely to be able to win a bidding war with HICs. • Requires buyers to "pick winners" 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 into these commitments early in a pandemic (Lever 17). • 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 be put in place for existing or close-to-market products for pandemics, with purchase contingent on an outbreak. • APAs 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 the development or production of a product needed for an outbreak primarily affecting LMICs (but also weigh 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 periods 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. 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 is too fierce. In these circumstances, LMIC buyers will likely lose an APA bidding war and resources may be better spent on expanding supply through tech transfer and other means. • Towards the middle or end of a large outbreak, if HICs have overbought, donations or resale markets will likely provide an adequate supply for LMICs. • When there is an adequate supply of appropriate products in this situation (e.g., the case of COVID-19 vaccines in late 2022) and there is no rationale for buyers assuming all demand risk.
Examples	• COVAX APAs, especially those signed in advance of product approval. • Gavi's commitment to buy Merck's Ebola vaccine after the West Africa trial.

Lever 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 specific requirements regardless of who makes them. Two entirely different types of AMCs are worth distinguishing. · In a "classic" Type 1 AMC, price is specified, but volume is not guaranteed. Instead, demand or need from eligible recipient countries triggers purchase at the agreed price. In this way, the AMC sponsor commits to subsidizing these purchases and ensures that if demand materializes, it will translate 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. · In a Type 2 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 the 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 the purchase of its product. This difference may be decisive in outbreaks. A consequence is that an AMC may have trouble attracting suppliers in competition with APAs (firm commitments to particular suppliers) offered by other buyers. An AMC may be most appropriate where it is 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. However, 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?	• It is not clear if AMC is ever the best strategy, but could be used. • For R&D, especially when the scientific obstacles are modest (i.e., later stages). • When multiple suppliers are desirable and feasible (i.e., for more frequent and larger outbreaks but not for small and rare outbreaks). • When large volumes are desired, justifying multiple suppliers. • When all or most important buyers join. • If 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 are 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 vaccine AMC (modified Type 1). • UNICEF's Zika virus diagnostics APA (Type 2). • Proposed (not implemented) COVID-19 vaccine AMCs (Type 2).

Lever 6 - Price-volume guarantee

Description/how it works	A third party guarantees demand for an MCM if the demand does not materialize from the agreed buyer(s) to reduce demand uncertainty for suppliers and incentivize their participation in R&D or manufacturing. For example, a guarantor promises that if 10 specified countries buy less than 1 million 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(s) does not need to put up capital themselves because 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 the cost to the guarantor is very high. • As with APA, risk of paying for a product that is not needed. Here, this risk is borne by the guarantor.
Implementation constraints	• Complex to design. • Requires a willing guarantor.
Preparedness or response (or both)?	In theory, both. However: • 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 LTA for rotavirus vaccines.

Lever 7 - Demand pooling and pooled procurement – LMIC-wide

Description/how it works	A group of potential buyers join together to signal demand for an MCM and buy/procure that MCM together or through a proxy buyer. There is 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, e.g., price, delivery commitments and flexibility.[28] · Can help buyers mitigate R&D risk, e.g., 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.
Implementation constraints	· 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. · Buyers have to agree on products and terms and, in certain types of pooling, on mechanisms for sharing
Preparedness or response (or both)?	Response, but: · Pooling arrangements are best agreed in advance.
When should the international community use this lever?	· In outbreaks where there are few or 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 pandemic-level outbreaks, where LMIC buyers are struggling with buyer power vs. HICs, e.g., COVAX or African Vaccine Acquisition Trust (AVAT) procuring COVID-19 MCMs. · When demand is very varied and uncertain across buyers, where pooling can help to smooth demand for suppliers. · To reduce transaction costs for both buyers and suppliers when there are large numbers of potential buyers.
When should the international community not use this lever?	· When participants have not harmonized requirements and preferences · When there is insufficient trust, especially if pooling involves sharing.
Examples	· COVAX, UNICEF procurement of routine vaccines for Gavi.

28 Except for the "aligned" model

Lever 8 - Demand pooling and pooled procurement – Regional

Description/how it works	As in LMIC-wide pooled procurement (Lever 7), but regional.
Benefits	• Same as broader pooling (Lever 7), although market power will generally be weaker. • Could be a vehicle for joint procurement from regional suppliers.
Drawbacks	• Same as broader pooling (Lever 7). • Weakens potential buying power of LMIC-wide procurement mechanism; invites competition among regions
Implementation constraints	As in Lever 7.
Preparedness or response (or both)?	Response, but: • Best if an arrangement is 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 player perceives that its 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	• European Union COVID-19 vaccine procurement. • AVAT COVID-19 vaccine procurement. • Pan American Health Organization's (PAHO's) Revolving Fund.

Lever 9 - Advance commitment to devote share of supply to LMICs (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. [29] This lever concerns voluntary commitments by suppliers. Mandatory sharing, imposed on HICs by a pandemic treaty, is considered separately (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 indemnity and liability (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 catalyzing production capacity increases, LMICs also have access to a share of this expanded supply.

29 The Berlin Declaration does not state the proportion of production capacity, but some sources have mentioned 10 per cent. 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 the model depends on HIC purchase of unshared doses (and perhaps of LMIC share as well) and because in outbreaks not affecting HICs, 100 per cent 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 are 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, (i.e., share of production), country eligibility, allocation rules, delivery timelines, price, and other terms, along with penalties for non-compliance. · 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 ensure access.
Examples	International Federation of Pharmaceutical Manufacturers and Association's (IFPMA's) Berlin Declaration, 2022.

Lever 10 - Donations infrastructure established in advance

Description/how it works	Donation of surplus MCMs from HICs and other producing countries to LMICs can be a useful tool in certain contexts (Lever 11), and 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, e.g., Africa CDC, PAHO and others, as well as the 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. 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	Although some precedent has been established through COVAX, this supply lever has not yet been deployed ex ante

Lever 11 - Donations

Description/how it works	Donation of surplus MCMs from HICs and 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 the 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 is excess supply/HIC 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, and 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 the R&D success rate is high. • Most important in cases where LMICs are struggling to obtain supply through other means, either by competing successfully with HICs in markets or through regional supply.
When should the international community not use this lever?	• Not useful for outbreaks not affecting HICs. • In outbreaks when supply is insufficient, even for HICs. • When HIC-favoured products are not appropriate for LMICs.
Examples	COVID-19 vaccines through COVAX and bilaterally.

Lever 12 - Putting a resale market in place

Description/how it works	Resale markets could be another way, in addition to donations, to facilitate the flow of MCMs from HICs or other countries with excess supply to LMICs or other countries that need and want them (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, and regional entities, e.g., 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 arrangements in place in advance could speed the access of MCMs to LMICs in the event of HIC over-buying and surplus.[30] • 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 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.
Examples	US-led MCM clearing house

Lever 13- Resale markets

Description/how it works	Resale markets could be another way, in addition to donations, to facilitate the flow of MCMs from HICs or other countries with excess supply to LMICs or other countries that need and want them (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.

30 Like donations, producing countries could resell products whilst still having insufficient supply for their own populations, but this seems unlikely

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 it is possible that some countries will have excess supply. • Could also be relevant in some mid-tier outbreaks, especially where the 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 14 - Pre-emptive long-term agreement (LTA) 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 up the 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 reduce administrative time and costs required to place a purchase order and support the availability of MCMs.
Drawbacks	• Putting an LTA in place entails significant transaction costs. As the agreement may never be used, products would have to be 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?	• FIf 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, since the cost of negotiating the LTA is probably not worth it.
Examples	

Stockpiles

Lever 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 and it is 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, available supply can be put to use immediately in a trial or outbreak control. · When factors other than supply availability are likely to be rate-limiting.
Examples	Sudan ebolavirus vaccines.

Lever 16 - Stockpile – Licensed

Description/how it works	A store of a licensed MCM, ready for rapid deployment in the 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.
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 unused 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 health care workers, 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 doses. • Most pandemic-potential pathogens for which the MCM is unlikely to be able to prevent the 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. • Meningitis A vaccine. • Cholera vaccine. • Zaire ebolavirus vaccine.

Financing levers

Lever 17 - Rapid response fund for MCM procurement

Description/how it works	Governments and/or donors set aside money for the 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 favourable 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 the trigger for releasing the funds and conditions for use when so many aspects of a future pandemic are difficult 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 is 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	Not yet developed.

Manufacturing levers

Lever 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	Recognizes that some MCM 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 the incentive to produce more cheaply.
Implementation constraints	Ascertaining cost of goods, if the 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	Analogous to contract manufacture of trial lots.

Lever 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 that has been reserved—and paid for—may not be used.
Implementation constraints	Decisions on which products, how much capacity and price.
Preparedness or response (or both)?	Primarily preparedness: • Could also be useful for more frequent outbreaks, where the 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 in the next five years[31].

Tech transfer and IP licensing

Lever 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.

31 See: https://cepi.net/news_cepi/cepi-invites-vaccine-developers-and-manufacturers-to-join-global-outbreak-response-network/

Drawbacks	• Can be slow and expensive, depending in part on the pre-existing 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 transfers 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 the 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. • Monopolization of supply by HICs or producing countries is not an issue or not likely to be an issue. • No recipient with the necessary capacity to begin production in a timely manner is available. • 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 the transfer of Oxford-AstraZeneca and Sinovac-CoronaVac COVID-19 vaccine technology to domestic producers during the pandemic.

Lever 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, most 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 the 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. For example, discerning between valid instances of technological transfer delays and deliberate procrastination can pose challenges. The appropriate course of action in the event of the firm's non-compliance may be unclear. • 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 tech transfer/licensing is thought to be needed and voluntary measures are not working.
When should the international community not use this lever?	• When tech transfer and additional manufacturers are not a high priority. • When requirement might deter sellers to LMICs/proxy buyers.
Examples	None for international buyers.

Tech transfer-related levers – Bridging

Lever 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 the 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 the transfer is needed and feasible to multiple 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's Medicines Patent Pool, licensing to pool of Merck and Pfizer COVID-19 drugs. • WHO's mRNA vaccine technology transfer hub.

Lever 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 the 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 of 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 Serum Institute of India partnering on a Sudan ebolavirus 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 more than one manufacturer. • Also not very relevant for the more frequent outbreaks, where there is less urgency to rapidly expand production.
Examples	

Tech transfer-related levers – Recipient side

Lever 24 - Tech transfer to a high-volume manufacturer (without regional security of supply focus)

Description/how it works	Transfer of the know-how and IP required to manufacture an MCM from the product developer or other current producer to another manufacturer, enabling that manufacturer to 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 (Lever 20). This lever focuses, in particular, on transfer to high-volume suppliers, who may also be low-cost. This 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 it involves platform technologies useful for other products and markets. • Willingness of the recipient to accept a transfer in the absence of additional incentives if the market is small, uncertain, or likely to be short-lived. • Capacity of the recipient. • Capacity of regulatory authority in the 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 the COVID-19 pandemic.
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 a 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 25 - Tech transfer to a regional manufacturer focusing on the security of regional supply

Description/how it works	As tech transfer to a high-volume producer (Lever 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 the willingness and ability of the supplier to supply beyond the home country and on the 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 the country of recipient. · Willingness of originator to transfer technology and IP, especially if it 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 the 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 the COVID-19 pandemic.
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, the main advantage of regional supply could be insurance against the 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 a good chance of success.
When should the international community not use this lever?	· For early-stage products. · For more frequent outbreaks, where non-regional supply is secure and more affordable. · Less important in pandemics if ample and secure supply from originator manufacturers or high-volume, non-regional suppliers.

Examples	· COVID-19 vaccine tech transfers from AstraZeneca to Bio-Manguinhos and Sinovac to Instituto 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 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, e.g., 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 the total supply of MCMs, providing greater regional security of supply, and, for small and rare outbreak MCMs, insuring against supply interruption caused by the 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 authority (NRA) 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, 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 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 the capacity of African vaccine manufacturers.

Lever 27 - Subsidy for procurement from regional manufacturers

Description/how it works	Like other suppliers, regional 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 Levers 25 and 26). • Could make the supply of some non-outbreak products more secure both globally and regionally by increasing the number of suppliers.
Drawbacks	• Expense: Subsidy might have to be considerable and sustained over time. • Subsidy could be difficult to withdraw once put in place and could create long-term dependence and 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, this 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 (Lever 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 (Lever 26). • Where no regional suppliers are ready to participate in non-outbreak markets even with a subsidy. • Where regulatory agencies are not strong enough (to allow WHO prequalification). • 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 28 - Non-binding regional procurement compact

Description/how it works	A group of buyers/potential buyers, e.g., countries in a geographical region pledge to purchase products from specific suppliers, e.g., suppliers in their region. This could help de-risk demand for those suppliers and may encourage R&D investment and production capacity scale-up. It 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, it could help to justify international investment by building assurance that products will find buyers. • Builds regional solidarity.
Drawbacks	• Relatively weak, as compact is non-binding: 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 and delivery conditions, complicating the 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 the 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 (Lever 26), yet a risk that countries will not choose the resulting products. · When other, stronger levers are not available. · When regional solidarity and capacity for concerted action are 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 the 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 29 - Strengthening regulatory agency capacity – To oversee manufacturing

Description/how it works	NRAs are responsible for approving products made within their borders and ensuring that they are manufactured according to appropriate standards. Procurement by international agencies depends on confidence that this oversight is rigorous. For some products, WHO prequalification or emergency use listing is a prerequisite for international procurement, specifically requiring that the NRA in the producing country meet a certain standard. Weak NRAs can, therefore, be an obstacle to the supply of MCMs from manufacturers 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	· Identifying 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 (Lever 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. · Bill & Melinda Gates Foundation investments, e.g., through US Pharmacopoeia.

Lever 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 recognize 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 reforms catalyzed by the increasing use of these processes should also have positive spillovers for routine approvals.
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 regional PHE threats, for example, but this is almost always useful.
When should the international community not use this lever?	N/A
Examples	• Organizations currently engaged in initiatives to expedite regulatory approvals in country of use include: • African Vaccine Regulatory Forum/ African Medicines Agency • European & Developing Countries Clinical Trials Partnership • CEPI • US Pharmacopeia

Lever 31 - Clinical policy/guideline development

Description/how it works	Development and approval of clinical policies and guidelines for the use of an MCM, often in advance of licensure of the MCM, to speed the eventual rollout of the MCM in the country.
Benefits	This can prevent this from being the rate-limiting step for the allocation and shipping of MCMs.[32]
Drawbacks	It can only be developed when the MCM in question is near licensure or on the market
Implementation constraints	No major concerns. It 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.

32 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.

When should the international community use this lever?	Clinical policies and guidelines may be a legal/regulatory requirement, and in all cases, this is a sensible thing to start on as early as feasible.
When should the international community not use this lever?	N/A
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, resulting in delayed access.

Possible Treaty provisions

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, which would require a treaty or some other binding mechanism.

Lever 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 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 where the firms are based.
Benefits	If such a requirement could be enforced, it could (Levers 20 to 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 the recipient. • Depending on the cost structure of the recipient, unit costs may be higher than the originator cost or cost of contracted low-cost producers. • Typically requires separate regulatory approval in the 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 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. Concerns that would need to be addressed, e.g., How would compliance be measured? Would expression of willingness be sufficient? · Might also be difficult to enforce on producing countries, e.g., Who may want to protect the interest of their manufacturers? · Other concerns would include: Who would decide to whom tech should be transferred? Would it have to be shared with all potential recipients expressing an interest?
Preparedness or response (or both)?	Requirements could be put in place before or during a pandemic to be used during an outbreak. · If an international treaty is required, it is almost certainly only feasible if agreed in advance, for example, through the 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 the 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 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 MCMs and key inputs to those products, e.g., bioreactors, bags, glass etc.
Benefits	· If successfully enforced, it could increase access for LMICs, particularly those without their production capacity, 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 monopolize supply through their buying power. · Could reduce supply for producing LMICs, who would now be obliged to export even if domestic needs were unmet.
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 us in a producing country to protect its 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 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 and tests to LMICs and other 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) supplies or LMICs.
Drawbacks	• See below on implementation constraints—it would be very hard to negotiate ex ante an agreement specific enough for LMICs/their buyers to rely on it as a reliable, timely supply source. • May be inadequate for LMIC needs if the donation requirement is too small or if HICs buy few doses in an outbreak primarily affecting LMICs.
Implementation constraints	It could be very difficult to enforce if HICs were having difficulty meeting their own needs in a pandemic.
Preparedness or response (or both)?	Requirements put in place in advance for use in response.
When should the international community use this lever?	• Pandemics primarily, or PHEs that met the trigger and where HICs are buying up supply, e.g., mpox vaccine. • If this could be negotiated and enforced, it would be a valuable 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 35 - Pandemic IPR waiver

Description/how it works	A WHO declaration of a PHEIC or other trigger would ensure that all countries can access relevant IP for the development or production of MCMs.
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 36 - Publishing market information

Description/how it works	A global health actor or initiative, e.g., UNICEF monitors the availability and status of relevant MCMs; this information could cover both the supply side, e.g., the status of medical countermeasures, production capacity, etc., and the demand side, e.g., current major buyers, forecast future demand etc. It could also include price information and other contractual terms if suppliers and buyers allow 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 supplier agreements. • 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, it can help bring in new suppliers to fill the gap.
Drawbacks	• The insight is influenced by the quality of the underlying data. • 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, any forecast could create false expectations.
Examples	• UNICEF COVID-19 market dashboard. • GAVI Secretariat biannual vaccine demand forecasts. • UNICEF Supply Division annual forecast exercise.

Lever 37 - Demand forecasting

Description/how it works	Similar to Lever 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 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 manufacturers produce too much product on the basis of an inaccurate forecast, they still take all the demand risk.
Implementation constraints	It 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 the 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 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 catalyzing public pressure. Objectives could include increasing investment in needed R&D, increasing 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 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, civil society organization coalitions, etc.
Preparedness or response (or both)?	Both preparedness and response.
When should the international community use this lever?	• When targets of advocacy, e.g. industry, 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. • To be applied in parallel with other levers. • When there is a strong public sentiment to build on, e.g., if the PHE primarily impacted LMICs and MCM developers were perceived as unhelpful, this context might be ripe for media and advocacy approaches.
When should the international community not use this lever?	As a frontline lever. Closed-door advocacy is acceptable as part of manufacturer engagement, but combative advocacy should be deployed carefully, given the international community's dependence on manufacturers.
Examples	• Médecins Sans Frontières Access Campaign. • People's Vaccine Initiative.

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