

Rapid and Equitable Access to Medical Countermeasures: Lessons, Landscape, and Near-Term Recommendations

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The authors are grateful to Tristan Reed, Ruchir Agarwal, Michael Kremer, Tharman Shanmugaratnam, Adam Hacker, Nicole Lurie, Melinda Moree, Benjamin Coghlan, and Arin Dutta for inputs and discussions on the paper's issues and ideas. All views, errors, and omissions are the authors' own.

Rapid, equitable access to medical countermeasures (MCM) is essential to mitigate the health and economic consequences of future pandemic risks, which are driven by the length of time it takes to equip the world with the diagnostics, vaccines, and therapeutics to identify and combat transmission. This note takes a quick look at the lessons learned and the existing landscape of MCM manufacturing in the context of the current pandemic response and suggests eight areas for action along with near-term recommendations to the global community to both prepare and respond to future pandemic risks. The note is a first effort to make sense of the terrain and bring together ideas on what should happen in the next phase of pandemic preparedness and response, but each requires greater refinement and broader consultation and discussion.

LESSONS LEARNED AND THE CURRENT LANDSCAPE OF MCM MANUFACTURING

Low- and middle-income governments and the agencies operating on their behalf failed to make or finance “at risk” purchases of vaccines and other MCM in advance of licensure, delaying vaccine access and equity. At-risk purchases are implemented through advance purchase agreements, which typically provide the manufacturer with some prepayment and a legally binding commitment to procure the vaccine, conditional on regulatory authorization. Such contracts can secure a buyer a place in line, provide manufacturers with the certainty needed to procure inputs and other production capacity, and help manufacturers secure loans from banks. Forthcoming work from Agarwal and Reed shows that high-income countries signed advance purchase agreements for COVID-19 vaccines on average in December 2020 (with some as early as May 2020), typically before licensure, while

middle-income countries signed contracts about three months later and low-income countries five months later, typically after licensure.¹ The authors estimate that 60–75 percent of the delay in vaccine deliveries to low- and middle-income countries (LMIC) is attributable to their signing purchase agreements later than high-income countries, which placed them further behind in the delivery line (rather than factors such as export restrictions favoring deliveries to high-income countries as a group regardless of order time).

Lack of timely and sufficient financing is a major explanation for delayed vaccine orders. COVAX, the multilateral vaccine procurement agency purchasing on behalf of low- and lower-middle-income countries, executed orders later than high-income countries because it lacked cash-in-hand due to a slow trickle of donor commitments; most commitments from donors did not arrive until 2021. Multilateral development banks (MDB) also did not finance purchases before vaccines had either received emergency use authorization from a stringent regulatory authority or emergency use listing from the WHO.² This policy precluded LMIC from borrowing from MDB to make prepayments as part of advance purchase agreements, which could have secured them an earlier place in line.

A central lesson therefore is that funding must be available for MCM R&D and pre-purchases on day-zero of the next pandemic. When such demand is in place, firms, investors, and other entities can respond to ensure scale and speed. Agarwal and Reed suggest if \$10 billion had been available to the COVAX AMC in March 2020 instead of June 2021, when that financial target was met by donors, low- and lower-middle income countries could have entered the market at the same time as high-income countries, achieving vaccine equity earlier. One caveat is that if LMIC had ordered earlier, high-income countries might have still outbid them while supplies were limited. If so, an effect of earlier purchases could have been to simply increase the price paid by high-income countries—a transfer to the pharmaceutical companies—and still LMIC might not have received doses any earlier. However, this is not the only potential effect of earlier orders on prices. Earlier orders could also have incentivized firms to invest in capacity, allowing for the discovery and resolution of supply chain bottlenecks and input shortages, expanding aggregate supply, and lowering costs. Consistent with this mechanism, vaccine prices stayed steady or fell during 2021, even as orders accelerated once vaccine candidates began receiving emergency use authorization. On this basis, it is plausible prices would have remained the same, even if LMIC ordered earlier. Ahuja et al. discuss how purchase agreements could include specific clauses requiring firms to scale production capacity, providing assurance that more orders will lead to greater available production capacity and lower costs.³

However, constraints beyond financing played important roles in limiting MCM supply. There were limited incentives to repurpose and expand existing manufacturing capacity; there were shortages of trained staff and inputs; there was a lack of experienced firms; and export restrictions were put in place on critical inputs and finished vaccines. Even some of the best-known, large-scale manufacturers of vaccines pre-COVID were unable to develop and produce product in a short timeframe, emphasizing the value of a large and diversified portfolio of potential developers and suppliers.⁴ Export restrictions, over-ordering or “hoarding,” import-dependency, and lack of information also affected equitable access to vaccines.

1 Agarwal, Ruchir and Tristan Reed. (forthcoming) in Oxford Review of Economic Policy, vol. 38 no. 4, October 2022.

2 See para. 42 in: <https://www.devcommittee.org/sites/dc/files/download/Documents/2021-03/DC2021-0003%20Vaccines%20final.pdf#page=25>

3 <https://www.aeaweb.org/articles?id=10.1257/pandp.20211103>

4 <https://www.cgdev.org/blog/lessons-rd-and-manufacturing-investment-equitable-covid-19-and-pandemic-response>

In addition, the choice architecture that determined which vaccines would be included in the pre-contracted portfolio by global agencies on behalf of lower-income countries had shortcomings; these countries' preferences and direct input did not feed easily into the process, highlighting the need for governance and oversight of advance procurement and manufacturing capacity that is owned by country governments and regionally representative bodies.

Ahead of the next pandemic risk, more equitable worldwide access also requires more distributed and diverse stand-by MCM manufacturing platforms, capacity, and inputs. Estimates from the Accelerating Health Technologies group⁵ led by Nobel laureate Michael Kremer suggest that investing \$60 billion upfront to expand production capacity for vaccines and supply chain inputs and \$2.2 billion thereafter to maintain capacity would be worthwhile for a future coronavirus-type risk. In the event of a pandemic, this investment could generate expected benefits of \$1.6 trillion, relative to a scenario where countries made no advance investments. Recent modeling estimates that the probability of a future zoonotic spillover event resulting in a pandemic of COVID-19 magnitude or larger is between 2.5–3.3 percent annually; this translates to a 22–28 percent chance within the next 10 years, and a 47–57 percent chance within the next 25 years.⁶ Assuming a conservative 2 percent annual risk of pandemic, the expected net benefits would be \$780 billion over the next 25 years.

In response to these challenges and the massive initial demand for MCM to combat COVID-19, regional entities such as the African Union in 2021 agreed to “ensure Africa has timely access to vaccines to protect public health security, by establishing a sustainable vaccine development and manufacturing ecosystem in Africa.”⁷ Similarly, a set of Latin America countries also pledged to accelerate manufacturing capabilities through regional political bodies such as PROSUR.⁸ ASEAN countries had targeted vaccine security and self-sufficiency even earlier, in 2019.⁹

Dozens of new manufacturing and technology transfer initiatives emerged over the last two years. These include new plants,¹⁰ continued investments by development finance institutions and multilateral development banks,¹¹ bilateral support,¹² regional partnerships,¹³ technology transfer initiatives,¹⁴ training hubs,¹⁵ and task forces.¹⁶ All merit further assessment and analysis. But for the most

5 <https://www.acceleratinght.org/academic-papers>

6 <https://www.cgdev.org/blog/the-next-pandemic-could-come-soon-and-be-deadlier>

7 <https://africacdc.org/news-item/communique-on-progress-made-on-vaccine-manufacturing-in-africa-kigali-rwanda-06-07-december-2021/>

8 <https://www.cgdev.org/publication/expanding-emergency-vaccine-manufacturing-capacity-latin-america-and-caribbean>

9 <https://cil.nus.edu.sg/databasecil/2019-asean-leaders-declaration-on-asean-vaccine-security-and-self-reliance/?msclkid=ce59a75fcfa611ecb94991600c29758b>

10 <https://english.news.cn/africa/20220330/72d438e82caa4b88a5d3a78ebdbe0b50/c.html>

11 <https://www.dfc.gov/media/press-releases/dfc-ifc-proparco-and-deg-support-south-african-covid-19-vaccine-maker-aspen>; <https://www.afdb.org/fr/news-and-events/press-releases/biovac-and-development-partners-collaborate-support-south-africas-vaccine-manufacturing-expansion-and-advance-long-term-health-security-across-africa-49641>; <https://www.reuters.com/article/us-health-coronavirus-hsbc-hldg/hsbc-and-asian-development-bank-join-forces-in-300-million-vaccine-financing-idUSKBN2BV38L>

12 https://ec.europa.eu/commission/presscorner/detail/en/IP_21_3562

13 <https://africacdc.org/download/partnerships-for-african-vaccine-manufacturing-pavm-framework-for-action/>; <https://www.paho.org/en/news/21-9-2021-paho-selects-centers-argentina-brazil-develop-covid-19-mrna-vaccines>

14 <https://www.who.int/initiatives/the-mrna-vaccine-technology-transfer-hub>; <https://medicinespatentpool.org/news-publications-post/covid-19-vaccine-technologies-mandate-expansion>

15 <https://www.who.int/news/item/23-02-2022-moving-forward-on-goal-to-boost-local-pharmaceutical-production-who-establishes-global-biomanufacturing-training-hub-in-republic-of-korea>

16 <https://www.gavi.org/vaccineswork/covax-manufacturing-task-force-tackle-vaccine-supply-challenges>

part, these investments are not coordinated. There is no assessment across the totality and viability of global or regional investments, nor a mechanism to ensure that needs are identified quickly and addressed—representing a potentially incohesive set of actions.

As the pandemic evolves and time passes, the demand necessary to sustain expanded, distributed COVID vaccine production has waned. Although only 16 percent of people in low-income countries have received at least one dose, governments and international mechanisms have already purchased sufficient vaccine to cover 113 percent of the world population with two doses each.¹⁷ And despite the supply in place or on the way, vaccination rates have dropped since the start of 2022 and are currently at their lowest levels since mid-2021. Global forecasts for COVID-19 vaccine sales continue to be downgraded. This phenomenon is predictable; high initial demand and prices elicited a huge, albeit lagged, production response that led to market saturation. But more troubling is that production will now be decreased and again, this will take time to be noticed. If a new vaccine-evading, more dangerous COVID-19 variant emerged, there might be increased demand and restricted access all over again. Breaking this cycle by assuring a certain stable level of flexible manufacturing capacity with sufficient volume when needed is another lesson learned, along with the need for at-the-ready surge financing.

In addition, manufacturing capacity and technology transfer initiatives developed during this period have focused on certain vaccine types and platforms. For instance, Aspen Pharmacare's COVID-19 adeno-format vaccine production line may close imminently due to an absence of orders or demand related to pandemic dynamics, buyer vaccine type preferences, and regulator decisions. In a time where the importance of sustaining distributed, at-the-ready manufacturing of MCM should resonate widely, it will be disappointing to see the only at-scale manufacturer in sub-Saharan Africa draw down its operations. Another example is the WHO-supported mRNA hub; this is clearly a promising technology but is only one way forward. For example, there is no mRNA vaccine for seasonal influenza, which has a high probability of pandemic risk.¹⁸ Further, the cooperation underway does not comprise the only set of companies, geographies, and mechanisms of action necessary for sustained preparedness. **A key lesson then is to assure a portfolio of companies, geographies, and mechanisms of actions, and product, process, and platform flexibility,¹⁹ risk sharing, and balanced responsibilities and partnerships between buyers and producers as population demand and commercial markets inevitably shift.**

Both phenomena above illustrate **the need to shift to future preparedness and routine procurement as the overall strategy, which sustainable manufacturing capacity and technology transfer approaches can build on.** While there may be resilience benefits from more MCM manufacturing sites in general, benefits depend on their specific design and product mix. As is evident, the sustainability of new MCM manufacturing sites is not simple and depends on their ability to manufacture routine health products to remain viable during inter-pandemic periods. In addition, when there are multiple MCMs available, greater market uptake of certain products over others is driven by a range of country-specific factors (e.g., poor uptake of Moderna doses in African countries compared to J&J or preferences for Molnupiravir as compared to Paxlovid). Such considerations imply a need for medium-term national, regional and global policy and financing clarity on what to subsidize and for which populations, and how that procurement will be carried out.

17 <https://launchandscalefaster.org/covid-19/vaccinepurchases>

18 <https://www.theverge.com/2021/12/10/22828042/moderna-mrna-flu-shot>

19 <https://knowledge.insead.edu/operations/boosting-vaccine-production-needs-the-right-degree-of-flexibility-17621>

Finally, despite potential gains from trade, economies of scale lead to a home market effect: the empirical fact that countries with larger domestic markets also account for a concentrated share of exporters. The concentration of production created by the home market effect can be excessive and economically inefficient during emergencies, despite delivering lower costs in normal times. For instance, during the COVID-19 pandemic, export restrictions by India, a major vaccine producer, were a significant cause of delay in vaccine deliveries to LMIC, as COVAX concentrated orders in India to secure the lowest possible price. Smaller economies, such as the Republic of Korea and South Africa, were able to satisfy their domestic needs more quickly than India and exported substantial amounts of vaccines earlier, albeit at higher prices. Given the essentiality of MCM during pandemic, the concentration of their production in medical products in a few large economies is a kind of market failure. Economies of scale imply smaller economies will nonetheless fail to achieve a cost advantage and succeed as exporters because of the size of their home market. **Here, the lesson is that international finance can usefully subsidize the development of manufacturing capacity in smaller states to mitigate the risks of vaccine nationalism in large countries during public health emergencies.**

RECOMMENDATIONS

1. Set shared goals and principles for the “second 100 days mission” (200DM) with an underpinning regional architecture

Global leaders must align behind a global and regional “second 100 days” goal and coordinated strategy to assure speedy and equitable manufacturing and procurement of medical countermeasures in the wake of a pandemic risk.²⁰ The aim of the “second 100 days” is to build on the 100-day mission for development of vaccines and other life-saving tools such as treatment by slowing or stopping pathogen spread by deploying MCM quickly, recognizing that approaches to this challenge are needed at national, regional, and global levels. The 200DM must focus first on designing the architecture for procurement (see recommendation #3) and in-country deployment of MCMs, not just more manufacturing capacity. It is evident from COVID vaccines and antivirals that 200DM cannot be accomplished unless the MCM deployment architecture is robust. This includes procurement, regulatory, and MCM delivery channel design.

Elevating the “second 100 days” should not distract from the first-order policy imperative to make sorely needed national preparedness and health system investments to discover dangerous pathogens and stop spread before MCM are required at large scale, or from the first 100 days mission’s objective to develop and authorize a vaccine. But readiness and ability to manufacture MCM when facing a disease risk remains vitally important given the inevitability and predicted frequency of future outbreaks and pandemic risks.

To meet the 200DM goal, national, regional, and global strategies, structures, and coordinated systems must be developed that can cope with the demands of a global health emergency, should one occur, with a focus on the public interest and in consultation with relevant groups including industry and civil society. External funding will play a key role in operationalizing the shared goals and principles and delivering on the common strategy by deciding what projects to support and what conditions to include in any deal to increase and/or diversify MCM manufacturing.

²⁰ Arrangements for delivery are also essential, but outside the scope of this note.

Governments worldwide must assess the efficiency, effectiveness, and affordability of the models they pursue to achieve 200DM, as some will invest in public or parastatals for self-production while others will rely on government purchasing from private firms operating in private markets, or a mixed approach. The recommendations offered here apply (mostly) to both kinds of systems and mixed systems, as internal contracting is still likely to be required even in fully public systems.

While the world needs more distributed MCM manufacturing capacity to increase resilience, reduce geographical concentration to limit the impact of nationalism during crises, and rapidly respond to pandemic risks, it is also vital to maximally retain the benefits of global trade (specialization, economies of scale, lower prices, increased speed) for consumers and governments. Inefficient or idle manufacturing capacity is costly and buy- or produce-national policies can often be counterproductive to the public interest by increasing costs and reducing access, equity and/or quality.²¹ This is a real trade-off that needs to be minimized given huge health and development challenges and inevitably constrained public budgets, a situation that is particularly acute in lower-income countries. Such considerations also affect the current business models (high volume, low cost, just-in-time) of the global health organizations like Gavi, the Global Fund, UNICEF, and others.

In any case, it will be vital to ensure that distributed national or regional investments continue to work as part of a global system. The scale required for manufacturing means that individual regions will find it difficult to comprehensively cover all the possible platforms needed for responding to a future pandemic. Regional supply chains can also still be vulnerable to localized shocks.

- **Near-term recommendation:** Develop the vision and roadmap for 200DM with specific regional roadmaps that coordinate investments across geographies and platforms.

2. Develop better visibility and forecasting of manufacturing capacity and needs

A first step in new preparedness investments is to understand the existing manufacturing capacity of different MCM products. Multiple groups have provided and utilized different global capacity estimates, mostly focused on vaccines.²² During the pandemic, some national governments lacked insight into their own firms' capacities, as occurred in India where the government reportedly overestimated the number of vaccines that the country could produce.²³ This lack of knowledge likely contributed to the export ban on vaccines that disrupted global supply in 2020/1.

Better shared global, regional, and national visibility into and forecasting of firm capacities, products and production, and the inputs and raw materials supply chain for key MCM is critical to identify the right incentives and investments needed to assure preparedness and speed response. Recent work by McDonnell et al. (2021) highlights the need to assess capacity for whole classes of products and technology platforms, and to clearly document not only the capacity available now but also the capacity that can be reconfigured with some modest changes, and the capacity that can potentially be

21 <https://www.cgdev.org/better-health-procurement>

22 <https://www.science.org/doi/10.1126/science.abg0889>; <https://www.sciencedirect.com/science/article/pii/S0140673621003068>; <https://www.airfinity.com/products/covid-19>; https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3826499

23 <https://science.thewire.in/health/narendra-modi-government-overestimated-india-covid-vaccine-manufacturing-capacity-shortage/>

reconfigured with more sizable investments.²⁴ Some national governments already track this data, but like pandemics, market and firm capacities are global.

- **Near-term recommendation:** Set up a 200DM working group to (i) identify techniques and carry out a first-round tracking, analysis and forecast of one region's MCM manufacturing capacity and needs, and (ii) make specific recommendations on how to structure and host this work for maximal benefit at all levels of aggregation building on existing efforts.

3. Establish global, prepositioned “day-zero financing” that can be rapidly released to jumpstart R&D and global and regional MCM manufacturing investments

To **enable adequate surge manufacturing**, institutional, financial, and budgetary arrangements should be established to enable rapid, large-scale, and at-risk surge financing to procure and produce MCM on behalf of lower-income countries when pandemic risks emerge.

While specific design elements merit further consideration, Agarwal and Reed (forthcoming) propose a credit line for a \$20 billion Advance Commitment Facility (about the amount raised by ACT-A to date) that could serve as the financing component to a successor to ACT-A or, alternatively, to regional ACT-A equivalents focusing on distributed manufacturing investments that are connected to R&D investments.

The authors lay out three steps that would govern the operations of the Fund:

1. **Countries establish a pandemic Advance Commitment Facility.** The role of the Facility will be the pooled purchase of vaccines, tests, treatments, and PPE on behalf of LMIC during pandemics. The defining feature of the Facility is that, unlike ACT-A, it would have access to resources on day-zero, which we define as the date when the WHO declares a global pandemic (March 11, 2020, for COVID-19) and/or when a pre-agreed number of deaths from a pathogen are recorded in multiple countries. The Facility would have an independent management team, with oversight from a Board with representatives from participating countries. When there is no ongoing global pandemic, operations would be minimal, with the Board holding annual meetings, and management consulting periodically with civil society, global health agencies, and national health authorities. The Facility would be activated during global pandemics, following rules agreed ahead of time.
2. **A financier establishes a credit line to the Facility.** Any financier could provide the credit line, including a commercial bank, consortium of development banks, private foundation, or a newly established global health financing agency. The credit line could be backed by commitments by participating countries made in advance of the next pandemic.
3. **The Facility rapidly responds to pandemics on day-zero.** Once a pandemic risk is triggered by the WHO, the Facility is activated, and its management can draw on the credit line to execute its mission to purchase a portfolio of health products for LMIC. Free or subsidized health products are then allocated to eligible countries according to an agreed rule. The allocation of investment across products would be determined based on the nature of the pathogen and guided by an

²⁴ <https://www.cgdev.org/blog/we-should-track-global-vaccine-manufacturing-better-here-why-and-how>

independent, inclusive panel of experts. For instance, if the timeline to develop a vaccine is slower than during COVID-19, early access to tests and treatments would be useful. An (optional) feature could be that LMIC would have the option to buy directly from the Facility at cost, like the COVAX Self-Financing Participant (SFP) Facility. Funds from these sales would be used to repay loans made by the credit line.

During a pandemic, the operations of the Facility need not follow the exact model of the COVAX AMC, which as implemented had some shortcomings (e.g., excessive reliance on a single large vaccine producing country that restricted exports; allocation of scarce funds for free vaccines away from low-income countries towards middle-income countries that could potentially afford to purchase them on their own). The facility could also be operated regionally, for instance by the Africa Vaccine Acquisition Task Team, or the Pan American Health Organization's Revolving Fund.

The key question is how the financier can manage its exposure to the credit risk. When the Facility draws a loan from the credit line to purchase health products, who can the financier count on to pay back the loan? According to Agarwal and Reed (forthcoming), there are four options to manage the credit risk, which could be used either separately or in combination. Under Option A, donors (e.g., high-income countries, foundations) make a legally binding commitment to repay the loan after the next pandemic. This option would be equivalent to donors pledging in advance of COVID-19 to fully fund the ACT-A and a financier lending against this commitment. Under Option B, a group of LMICs make a legally binding commitment to repay the loan, without involvement from high-income countries. This option would be akin to LMIC forming their own Facility to make purchases on their behalf. Under Option C, the private sector assumes the risk by buying pandemic-linked bonds. The financier would issue these bonds and repay the principal only if no pandemic is declared before its maturity. Donors and/or LMICs themselves would have to provide the financier with funds annually to service interest on the bonds if a pandemic is not declared (akin to paying an insurance premium). The World Bank's pilot Emergency Financing Facility provides proof of concept: bonds issued by the facility paid out during COVID-19, generating a net transfer from the private sector to the public sector.²⁵ Under Option D, no advance commitments are made by anyone, but the financier is empowered by its shareholders to retain the full risk of loans drawn from the credit line on its balance sheet. In this case, the financier's shareholders may have to replenish its capital after the pandemic (if no grants are raised ex-post). In addition, ahead of the pandemic, carrying such risk may impact lending activities if the financier's capital constraint is binding.

Of course, the political economy could constrain a financier's ability to manage risk in these ways. LMICs may lack the fiscal space to guarantee the credit line themselves (Option B). High-income countries may be unwilling to commit in advance to fund a Facility that would compete with them to buy health supplies for their own populations in the next pandemic (Option A). Further, donor countries backing the Facility may nudge its management to make purchases from their own developers, potentially trading off speed of delivery or quality of health products to promote national interests. Options C and D may help in part overcome these challenges, though if the financier is an international financial institution owned by national governments, political economy constraints would still be relevant.

²⁵ Holders of the Class A bond earned 3.57% compared to the 6.9% promised if a pandemic did not occur. Holders of the Class B bond (which was higher risk and unlike the Class A bond would also have paid out for pandemics of filovirus, Lassa fever, Rift Valley fever, and Crimean Congo Hemorrhagic fevers) earned a -32.96% return compared to the 11.5% promised if a pandemic did not occur.

There are issues related to the risk of repayment that require further examination. For example, it is possible that no or few MCM candidates meet regulatory requirements, or do not substantially slow the transmission of a novel pathogen. At-risk investments will not always deliver successful products, as evidenced by CureVac's shelved vaccine, or they may lead to excess purchases, as evidenced by the COVAX AMC. But investors must be willing to tolerate these losses in pursuit of the tools necessary to curb pandemic threats. The AMC Fund would require a guarantee of repayment by Bank shareholders to cover losses or the Bank's credit rating could be affected. Plus, if well-designed with strong risk assessment capabilities and adequate flexibility, a global mechanism for surge financing can help the world better manage some of the risks associated with future pandemic R&D and manufacturing and decrease future losses.

- **Near-term recommendation:** Alongside the FIF, invite a proposal from the international financial institutions (IMF, MDB) for the design and establishment of a pandemic Advance Commitment Facility with access to finance to make advance purchases of MCM as early as day-zero of the next pandemic, with concrete options for management of the credit risk and governance of the Facility. Further request that MDB review policies that restrict advance purchases of MCM in advance of licensure.

4. Assure R&D investments facilitate global access and distributed manufacturing

Given their extensive investment in R&D, high-income and emerging market economies also have an important direct role to play in assuring the preconditions for distributed manufacturing of MCM. Future government funding for medical research and development, for example, should attach clearer conditions if successful discoveries are made, e.g., commitments to provide affordable medical countermeasures with cost-plus pricing for LICs and LMICs, treatment of intellectual property, and requirements for technology transfers to third-party manufacturers. CEPI already includes such clauses in its agreements but could expand the requirements and obtain greater leverage in connection with an Advance Commitment Facility.

- **Near-term recommendation:** Prepare guidance for BARDA, HERA and other preparedness agencies investments on clauses and conditions that will facilitate rapid global access and distributed manufacturing of key MCM.

5. Sustain demand for MCM capacity in the interpandemic period

Advance contracts for manufacturing of classes of pandemic-potential vaccines, treatments and other technologies should be developed. This would mean linking R&D investments to manufacturing capacity and advance purchase agreements for small volumes of vaccines against pathogen diseases or families with pandemic potential, as they are developed. A hub of know-how for technology transfer and advance purchase contracting could also be established to support regional and global entities like CEPI in technology transfer and advance contracting. Establishing guaranteed surge financing via the Advance Commitment Facility could enable a special program of supply-side manufacturer investments by development finance institution or government investments with long-term, concessional terms. Knowing the probability of outbreaks and needed volumes of MCM along with a guaranteed revenue stream might reduce uncertainties for investors on the supply side. Feasibility

would need to be assessed given the uncertainties. In parallel, capacity for sufficient and rapid supply of inputs to MCM—critical commodities and raw materials—must be assured.

The adoption and scale of flexible, modular regional technology platforms should be supported to serve a range of infectious disease product manufacturing needs (dual+ use). To this end, a partnership—potentially supported by a new pandemic fund (FIF)—could be developed to invest in a portfolio of regional technology processes and platforms, to be awarded competitively to firms and consortia in LMIC. This would build on successful voluntary licensing initiatives for therapeutics, diagnostics, and vaccines. Licensing should not be restricted to low-income countries or sub-Saharan Africa only; partnerships should also be built across middle-income countries. Flexibility and fungibility in production networks will allow recourse and hedging capabilities against the specific MCM required for a given pathogen. It will also help create the opportunity to pool demand for routine health products and MCMs and help integrate disease verticals.

Greater routine demand for MCM to address existing infectious disease threats should be created, which can be repurposed in a pandemic to target specific pathogens and help keep efficient firms engaged, seek new partnerships in different parts of the world, and produce under different platforms. Attention on COVID-19 response and its requirements should be maintained to increase COVID-19 vaccine coverage levels around the world, determine the cost-effectiveness of primary doses and boosters in different country contexts²⁶ and act on the procurement implications. As relevant, governments should help manufacturers increase production of products that support pandemic response, reach new suppliers or markets, recover from workforce and supply chain interruptions, and achieve greater resilience. New sites also offer the opportunity to innovate, introduce and test new manufacturing technologies such as new fill and finish technology, modular production, and other innovations.

A share of routine procurement by existing regional and global purchasing pools to vaccines, diagnostics and treatments (such as antivirals) should be reserved for suppliers based in LMIC—both as a supply security measure and as an investment in manufacturing capacity. Retaining a distributed share will require payment of a “regional premium” that will likely reduce over time.

Routine test-and-treat programs could also be expanded to include new delivery approaches that are cost-effective (or would become cost-effective with external support). For example, a massive expansion of HIV test-and-treat programs could build on the new infrastructure and firms created by the COVID-19 market and help with continued distributed manufacturing of diagnostics and antivirals.²⁷ Seasonal influenza and HPV vaccines should also be introduced and scaled-up where cost-effective, expanding adult immunization programs (which would involve listing the vaccine, paying for the vaccine, and vaccine confidence interventions).

Direct contracts or incentives should be created for new technologies or expanded manufacturing capacity, with an eye on efficiency and trade-offs. Governments that wish to support capacity can provide incentives, tax waivers, and procurement for small volumes or stockpiles of those MCM that are approved. For existing technologies, global health organizations can invest in new or expanded stockpiles based at Gavi,²⁸ the Global Fund (COVID-19 antivirals and diagnostics, for example), and re-

²⁶ <https://www.cgdev.org/blog/price-priorities-pace-three-factors-drive-cost-effectiveness-covid-19-vaccination-strategies>

²⁷ <https://www.cgdev.org/publication/policy-actions-us-government-accelerate-access-oral-antivirals-covid-19-low-and-middle>

²⁸ Gavi operates stockpiles for vaccines against cholera, yellow fever, and other vaccine-preventable, outbreak-prone disease for which there are existing vaccines.

gional procurement bodies, or enable inventory reserves by suppliers. They can also provide expertise to help manufacturers reduce costs, create new products, develop the next-generation workforce, find new markets, and achieve business success. Some scholars have proposed directly contracting for manufacturing capacity via capacity subsidies, as the returns if pandemic occurs are enormous.²⁹

Near-term recommendations:

- Develop a hub of know-how at CEPI on technology transfer and advance procurement contracting to support regional and global entities in technology transfer and advance contracting for MCM.
- Design and set up a partnership—potentially supported by a new pandemic fund (FIF)—to invest in a portfolio of regional technology processes and platforms, to be awarded competitively to firms and consortia, with preference to smaller countries.
- Generate greater routine demand for MCM to address existing infectious disease threats via the Global Fund to Fight AIDS, TB and Malaria, for example—first dealing with cost-effective control of COVID-19, but also taking the opportunity to improve the scope and effectiveness of existing disease control programs that can use the same manufacturing facilities and procurement strategies.
- Invite WTO and regional trade groups (e.g., AfCFTA, RCEP) to review policies on state aid in medical goods. The judicious use of subsidies and tariffs to develop diverse production capacities specifically in smaller countries benefits these countries' own populations, and the world, since countries with smaller populations can meet domestic demand quickly and will be less likely to restrict exports during emergencies.
- Development finance institutions, such as US DFC, Proparco, and British International Investment, should further promote the development of manufacturing capacity in LMIC (while balancing the need for surge capacity versus viability outside of pandemics), developing a broader production and distribution network for MCM.

6. Expand regulatory capacity and harmonization processes towards greater convergence and alignment in preparation for pandemic periods

Regulators should establish mechanisms to enable joint scientific advice and align key elements of license-enabling trials including agreement on the design and utility of platform trials as well as optimal use of adaptive, real-world observational and effectiveness trials. Such convergence will avoid fragmentation in clinical research for example by assuring common endpoints, and guarantee robust, reliable, and comparable results. Regulators from MCM-producing countries should agree and establish clear guidance on the essential elements needed to issue emergency use authorization to MCM, including trial design, efficacy and performance thresholds, and length of follow up. Guidance should also be issued on post-license evaluation and monitoring requirements.

²⁹ <https://scholar.harvard.edu/brandonjoeltan/research>

Regulators from MCM-producing countries should also institutionalize rolling reviews of leading MCM during pandemic periods. This will enable regulators to quickly analyze results as they become available, rather than wait for full applications. Last, these regulators should establish clear procedures to exchange and publish data, conduct joint dossier reviews and evaluations of potential safety signals, and actively contribute to the WHO emergency listing and prequalification procedures

Regulators from non-MCM-producing countries should establish clear legal frameworks to facilitate emergency use regulatory mechanisms and good reliance practices in line with the WHO Emergency Use Listing (EUL).

Finally, regulators can establish clear strategies for public outreach and communication during pandemic periods through strong, effective, open, and transparent engagement with stakeholders and the public, ideally assuring maximal alignment between the science as reviewed by regulators and the decisions taken by political authorities for public health policy and practice. This is vital to communicate rapidly evolving scientific knowledge, while counteracting misinformation and minimizing confusion.

For national regulatory initiatives, there should be increased agility in the issuance of guidance by the WHO; the second 100 days is a good timeframe within which to assure issuance of guidance on MCM particularly around treatments. It is unclear why the WHO treatment guidelines for antivirals to combat COVID-19 came out several months after several national stringent regulatory authorities had issued their recommendations. As member states discuss WHO funding and other issues like the roles of the FIF and WHO, there should be an ask for clear targets from the WHO, and any related resource requirement needs.

Near-term recommendations:

- Launch a consortium of regulators from MCM-producing countries to define and move forward on a regulatory agenda around pandemic and epidemic MCM, with support from WHO and CEPI. Leverage CEPI's Regulatory Advisory Group to facilitate effective collaboration between broad networks of regulators and ensuring progress in vaccine regulation.
- Promote and expand the use of joint scientific advice procedures, for example, expanding the joint US FDA-EMA advice procedure to involve additional MCM-producing countries.
- Ensure Stringent Regulatory Authorities develop aligned guidance regarding the optimal use of platform and adaptive trials that can be deployed in case of outbreak.
- Promote and expand use of regulatory reliance and work-sharing procedures such as that performed by ACCESS countries or in oncology Project Orbis, for example.
- Advocate for greater use of WHO EUL with even greater country recognition of WHO EUL with minimal additional regulatory requirements.
- Regulators from MCM-producing countries and the WHO should establish harmonized requirements and set timeframe targets for rapid reviews and recommendations around MCM during public health emergencies as part of 200DM.

7. Develop global and regional governance and coordination to underpin the system as a “mission control approach” to implementation

National experiences in the US and UK around R&D, manufacturing, and procurement of MCM during COVID-19 suggest that unified, cross-agency mission control with flexibility and know-how to take rapid, risky decisions is necessary to meet goals. Such an approach was also recommended as part of the G7 100DM commitment, along with a dedicated secretariat involving stakeholders from each country.³⁰

Yet a key lesson of the COVID-19 response is the importance of deep and early engagement with emerging market economies and developing countries; their know-how, institutions, and government budgets must be in the mix if there is to be success. There are dilemmas and tensions between fully representative and consultative approaches and the speed, flexibility and risk-taking that is necessary for a 200DM mission. Governments will need to agree on goals, principles, and the rules governing the process in consultative and representative ways but should also assure that the implementation is structured to allow for speed and agility. Regional mission approaches for the 200DM—backed by global resources and financing arrangements—are probably the best and only feasible way forward. G20 task forces have also been proposed. Regardless of next steps, this effort will be a medium- to long-term undertaking.

- **Near-term recommendation:** Establish regional mission control task forces for 200DM with the aim of preparing investment roadmaps, hosted by existing regional authorities in cooperation with external funders and with input from stakeholders.

8. Assess progress, uncertainties, and unknowns to continually maximize impact while minimizing risks and trade-offs

In addition to the near-term recommendations explored in this paper, there are unanswered technical and policy questions that merit ongoing analysis. For example: How much total subsidy is needed to sustain a portfolio of pandemic-ready manufacturing capacity? How should governments, regional and global entities size the overall investment required, needed where, and with what method? Modeled estimates of required capacity in the case of different pandemic risks are needed by type of product and associated platform, building on work by Kremer and colleagues.³¹ More information is needed on how much money has been spent so far and where it has been used. And finally, if international financing for peacetime MCM manufacturing is limited, how should scarce resources available for 200DM be allocated, especially considering trade-offs with other uses of funding. Another area of inquiry should seek to understand whether “leapfrog technologies” like mRNA genuinely change markets and thus the calculus of private firms in lower-income countries given the competitive outlook. There are also questions about how to deal or price in uncertainty and unpredictable timelines in pandemic risks.

³⁰ https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1038969/100_Days_Mission_-_First_Implementation_Report_L.pdf

³¹ <https://www.acceleratinght.org/academic-papers>

A final, related question is how to structure the investments in manufacturing capacity; how much push versus pull financing is closest to optimal? Push contracts during R&D provide the greatest opportunity to secure significant access commitments because of the higher risk involved in the early stages of developing vaccines and other medical countermeasures, and the resulting willingness of the developer to accept access conditions in exchange for investment. The appropriate mix of push and pull funding will necessarily vary for products with different risk levels; the mix would change for prototype vaccines and therapeutics. Analysis and modeling of the alternative approaches are needed and implemented models can be evaluated prospectively.

- **Near-term recommendation:** Support a consortium of organizations to conduct ongoing policy research and testing of innovations as part of MCM initiatives, enabling learning across borders and regions.



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