

# 100 Days Mission



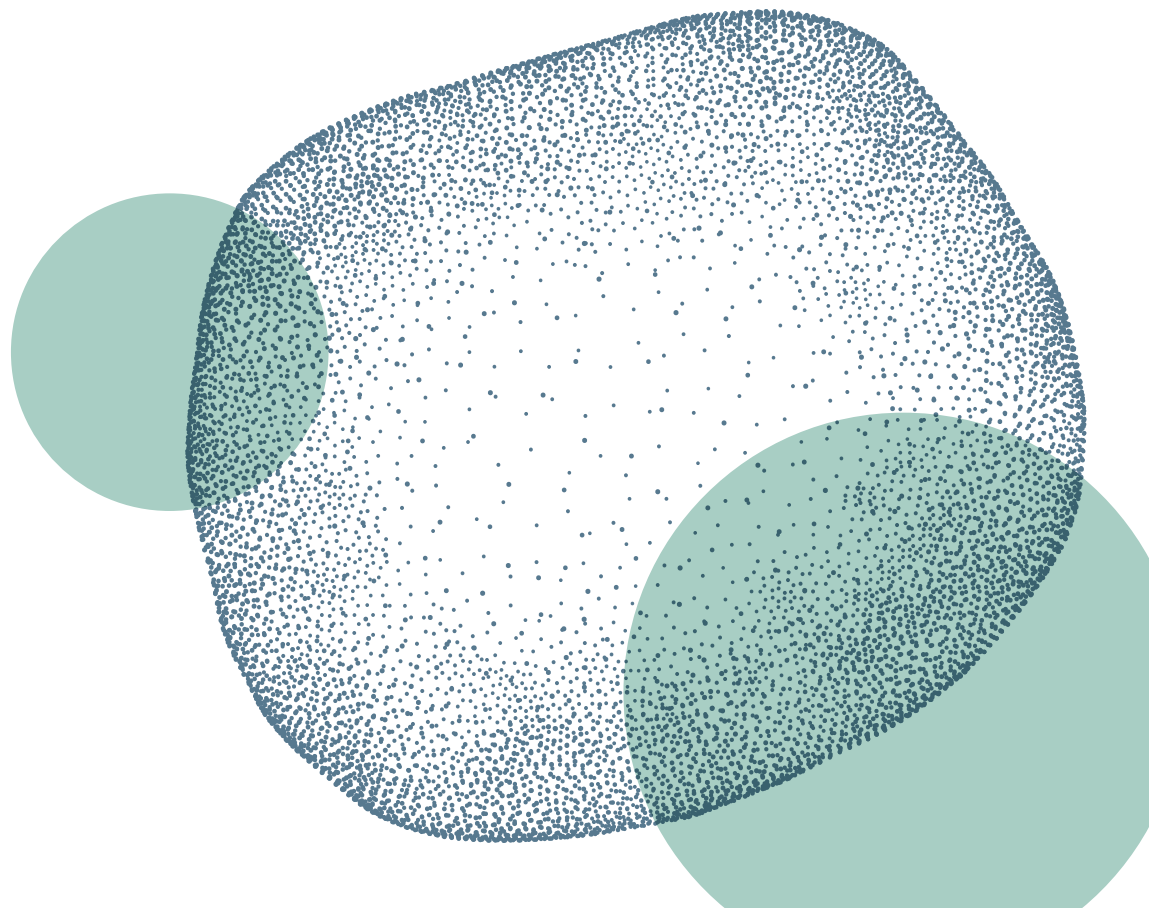
International  
Pandemic  
Preparedness  
Secretariat

## Implementation Report – 2022

Reducing the impact of future pandemics  
by making diagnostics, therapeutics,  
and vaccines available within 100 days

An independent report from the  
*International Pandemic Preparedness Secretariat*

31st January 2023



# Foreword

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Sir Patrick Vallance

# Mobilising the 100 Days Mission

This second implementation report for the 100 Days Mission comes at a critical inflection point for pandemic preparedness and response. Economic challenges and geopolitics have replaced the COVID-19 pandemic as the focal point of national and international attention. Still, outbreaks of mpox (formerly monkeypox), Sudan Ebolavirus strain, and Rift Valley Fever in 2022 provide a timely reminder of the threat and the critical necessity of global preparedness.

Progress has been made on the ambitious agenda to develop an armory of diagnostics, therapeutics, and vaccines within the first 100 days of a future pandemic threat being detected. As the initial wave of efforts have been stood up and the landscape has matured, there is now an opportunity to reflect on where progress is on track and where additional focus and effort will be needed. In some areas, including diagnostics, therapeutics, and manufacturing, the landscape looks materially different in terms of funding and players compared to 2021 when the 100 Days Mission was conceived. Notably, as encouraging evidence of the growing achievability of the 100 Days Mission, on 9 December 2022, the WHO announced the first doses of a vaccine candidate against Sudan Ebolavirus strain arrived in Uganda for safety testing 79 days after the outbreak was declared (though by that point Uganda had successfully ended the outbreak)<sup>1</sup>. Nevertheless, the 100 Days Mission for all pathogens needs to continue to move forward in pursuit of the core principles of safety, efficacy, and accessibility of Diagnostics, Therapeutics, and Vaccines (DTVs).

Continued progress relies on ongoing commitments of the G7 working with the G20 and wider international partners, the WHO, and the life sciences and biotechnology sectors. Throughout this year, leaders have reaffirmed their commitment to this ambitious 'Apollo' mission and broader pandemic preparedness – signing the G7 Pact for Pandemic Readiness in May 2022, supporting the development of a new Pandemic Instrument through the Intergovernmental Negotiating Body (INB) process, and continuing to push for effective global surveillance pathogen mechanisms. The G20 has led critical work on financing through their Joint Health and Finance Task Force and establishment of the Pandemic Fund. Global organisations have led international efforts to coalesce on regional manufacturing plans, including through the Partnerships for African Vaccine Manufacturing (PAVM)'s Framework for Action. Industry and academic partners have led on research and innovation efforts to support development of DTVs.

As preparedness efforts expand far beyond the original incubator of the G7, responsibility for tracking and supporting implementation of the 100 Days Mission has transferred to an independent Secretariat. The Secretariat

will be advised by a small Steering Group with membership from the WHO, IFPMA, current, immediate past, and incoming G7 presidencies, and supporting organisations in addition to a Science and Technology Expert Group comprising globally recognised experts.

In this second implementation report, the Secretariat continues the mission-driven approach – reporting on progress against the original 25 recommendations though focusing in on a subset of tangible actions for 2023 with clear ownership to drive delivery. As in the original 2021 report, there are three high-level goals that span the 100 Days Mission recommendations and specific areas of focus for 2023 within them:

## 1 Invest in R&D to fill the gaps in our arsenal

a. R&D should be coordinated against the WHO-endorsed priority pathogens when released in the first quarter of 2023. Diagnostics and therapeutics should receive dedicated investment and coordination needed to accelerate.

b. Programmable platform technologies should continue to be advanced and de-risked to allow rapid deployment against 'Disease X'.

## 2 Make the exceptional routine by embedding best practice between pandemics

c. Agreement to global mechanisms for pathogen sharing and integration of pathogen surveillance efforts with diagnostics R&D and usage should be explored to increase efficacy.

d. Clinical trials should continue to embed lessons learnt from COVID-19, augment global clinical trial capacity, and coordinate trial networks internationally.

e. Further effort in 2023 will be needed to build economically sustainable regional DTV manufacturing.

## 3 Establish the 'Rules of the Road'

f. Pandemic preparedness financing has advanced with the establishment of the Pandemic Fund (though this will need to be adequately replenished). However, adequate surge financing mechanisms remain a global priority for 2023.

Finally, I'll leave you with a few words of thanks to all scientific and industry leaders, international partners, and others who have adopted this 100 Days Mission and set out to deliver. There has been significant progress and momentum building around this mission and I am excited to see the progress that we can make, together, in support of future pandemic preparedness.

<sup>1</sup>WHO (2022). Ebola trial candidate vaccines arrive in Uganda in record 79 days after outbreak declared. [online] who.int. Available at: <https://www.who.int/news/item/09-12-2022-ebola-trial-candidate-vaccines-arrive-in-uganda-in-record-79-days-after-outbreak-declared>

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# Executive Summary

The 100 Days Mission was set out in 2021 to support rapid, safe, and effective development of diagnostics, therapeutics, and vaccines (DTVs) in the event of a pandemic threat. At the end of 2021, the first Implementation report was published with three ambitious roadmaps to prepare to deliver DTVs within 100 days by 2026, including clear delivery priorities for 2022. These priorities were focused on three major efforts, including gaining agreement from the global community on priority pathogens and virus families for DTV efforts, creating 'programmable' platforms for vaccines and therapeutics, and improving clinical trial and regulatory processes to support rapidly testing DTVs. Note that throughout the report 'programmable' platforms will be used to refer to technological platforms (e.g., mRNA) that can be flexibly re-deployed against various pathogens.

Since 2021, the pandemic preparedness and response (PPR) landscape has meaningfully changed. Emergency responses to COVID-19 have tapered down as populations have been vaccinated. Funding for PPR research and development (R&D) is waning, as it did in the past after outbreaks of Severe Acute Respiratory Syndrome (SARS) and Middle-East Respiratory Syndrome (MERS) (Figure 1). Economic challenges and geopolitical tensions have dominated political attention. Nevertheless, there have been positive shifts toward delivery of the 100 Days Mission. The Coalition for Epidemic Preparedness

Innovations (CEPI), national governments, and industry have made broad efforts in developing vaccine platforms and expanding their manufacturing footprint to include Africa and Latin America, strong political support was garnered for regional vaccine manufacturing, and numerous new funding channels were established for therapeutics, among numerous other initiatives.

Despite the change in context, the ambition set out in the 100 Days Mission remains an important one. By the time a vaccine was approved for COVID-19, 68.7 million cases had been reported worldwide<sup>3</sup> and the International Monetary Fund (IMF) forecasts that the world will have lost \$12.5 trillion in economic output by 2024,<sup>4</sup> underscoring the real impact that faster DTV production can have on the global community.<sup>5</sup> G7 Scientific Advisers recommended a Secretariat be established, supported by a Science and Technology Expert Group (STEG), to develop annual reviews that track progress against delivery, such as this one. The Secretariat mapped progress in 2022 against the 100 Days Mission through desk research, interviews, and written commentary from implementation partners. This effort focused on key determinants of progress, including funding, political support, and leadership. Significant progress has been made across the mission, including against the goals set out in 2021. However, there are areas where additional attention is needed in 2023:

## Clinical R&D for COVID-19

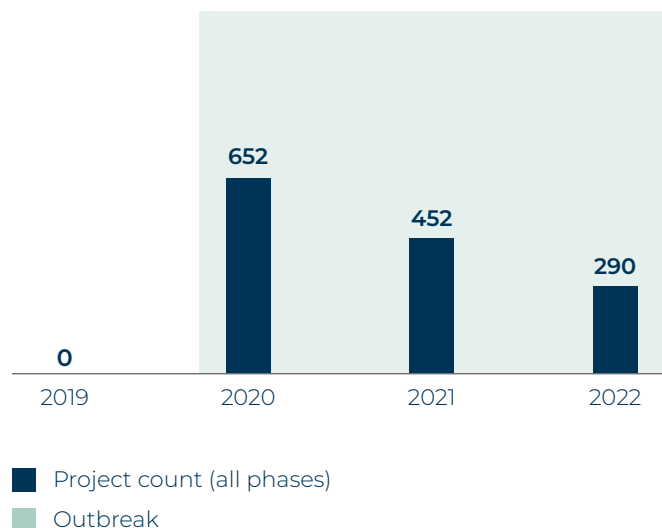


Figure 1. Clinical R&D related to COVID-19 surged in 2020 in the midst of the outbreak but has gradually reduced (count of clinical trials across all phases). This is a similar trend seen in past pandemic outbreaks, including SARS and MERS.<sup>2</sup>

*“The world will have lost \$12.5 trillion in economic output by 2024, underscoring the real impact that faster DTV production will have on the global community”*

<sup>2</sup> EvaluatePharma database (2022).

<sup>3</sup> CEPI (2022). Delivering Vaccines in 100 Days. [online] cepi.net. Available at: [https://cepi.net/wp-content/uploads/2022/11/CEPI-100-Days-Report-Digital-Version\\_29-11-22.pdf](https://cepi.net/wp-content/uploads/2022/11/CEPI-100-Days-Report-Digital-Version_29-11-22.pdf)

<sup>4</sup> Business Standard (2022). World Economy to Lose \$12.5 Trn in Output by 2024 Due to Covid: IMF Chief. [online] business-standard.com. Available at: [https://www.business-standard.com/article/international/world-economy-to-lose-12-5-trn-in-output-by-2024-due-to-covid-imf-chief-122012100063\\_1.html](https://www.business-standard.com/article/international/world-economy-to-lose-12-5-trn-in-output-by-2024-due-to-covid-imf-chief-122012100063_1.html)

High-level goals from 2021 report	<div>1 Invest in R&amp;D to fill the gaps in our arsenal</div> <div>2 Make the exceptional routine by embedding best practice between pandemics</div> <div>3 Establish 'Rules of the Road'</div>		
	<div>a. Coordinate R&amp;D against priority virus families</div> <div>b. Advance programmable platform technologies for vaccines and therapeutics</div>	<div>c. Integrate global diagnostic R&amp;D and surveillance efforts</div> <div>d. Accelerate clinical trial and regulatory processes for data generation</div> <div>e. Build sustainable, regional DTV manufacturing capacity</div>	<div>f. Agree on 'Day 0' surge financing mechanisms</div>
2023 focus areas of additional attention			

Figure 2. 2022 priorities were used to shape detailed focus areas for 2023. 2022 priorities were detailed above in Foreword from Sir Patrick Vallance. 2023 focus areas are detailed below.

#### **a. Coordinate R&D against priority virus families**

In 2022, the global community sought agreement on priority virus families with pandemic potential. The World Health Organisation (WHO) is in the process of updating their prioritisation of pandemic pathogens, set to be released in the first quarter of 2023. Once released, these priorities can be used to direct and coordinate efforts to fast-track R&D for DTVs.

have begun and should continue to embed lessons learnt from COVID-19 to accelerate clinical trials and work toward streamlined clinical trial and regulatory processes. In 2023, additional focus on international coordination to follow disease outbreaks (including pre-approved protocols in countries with high outbreak risk), as well as strengthening regulatory capacity in LMICs will support the global community in optimising use of testing capacity to accelerate DTV development.

#### **b. Advance programmable platform technologies for vaccines and therapeutics**

In 2022, it was recommended to apply platform technologies for vaccines and therapeutics to COVID-19 and wider endemic diseases. CEPI is leading vaccines work, and many new players entered therapeutics through the support of the Antiviral Drug Discovery (AViDD) programme, the Pandemic Antiviral Discovery (PAD) initiative, and other funders. In 2023, identification of a clear 'convener' in the international Global Health architecture can help to coordinate various therapeutics efforts.

#### **e. Build sustainable, regional DTV manufacturing capacity**

Regional manufacturing capacity of essential vaccines against infectious diseases increases global supply security but should also maintain long-term cost competitiveness and avoid increased prices adversely impacting vaccine equity for routine immunisations. Numerous regional models need to be reconciled to ensure sustainable economics in the long-term. Further, sustainable manufacturing ecosystems will need to include trained workforce to cover a range of platform technologies and adequate supply of raw materials.

#### **c. Integrate global diagnostic R&D and surveillance efforts**

Diagnostics samples are inputs into a robust surveillance platform and should be shared internationally, with mechanisms that ensure reciprocity and equal benefits for all participants involved. Further, routine use of diagnostics can increase market incentives that drive diagnostics innovation for industry and affordability for low- and middle-income countries (LMICs).

#### **f. Agree on 'Day 0' surge financing mechanisms**

Response financing is critical to ensure timely access to DTVs globally. Work to date has raised significant, though still insufficient, funds for preparatory financing but have not yet agreed surge financing mechanisms.

#### **d. Accelerate clinical trial and regulatory processes for data generation**

In 2022, improvements to clinical trials and regulatory approvals were a key priority. Regulators

Achieving these priorities cannot be done by any one organisation alone; it will require partnership and division of labour, with each sector and organisation taking responsibility for their piece of the puzzle. In the current landscape, the G7 can continue to play an important political role and add significant value by leading on streamlining clinical trials and coordinating R&D funding in line with priority pathogens. The G20 presidency

<sup>5</sup> CEPI (2022). Delivering Pandemic Vaccines in 100 Days. [online] cepi.net. Available at: [https://cepi.net/wp-content/uploads/2022/11/CE-PI-100-Days-Report-Digital-Version\\_29-11-22.pdf](https://cepi.net/wp-content/uploads/2022/11/CE-PI-100-Days-Report-Digital-Version_29-11-22.pdf)

has ambitious plans to support DTV development, lead on regionalised manufacturing, and define mechanisms for surge financing that will have global benefits. The WHO will continue to play a crucial coordinating role by setting the framework for emergency preparedness, leading on global surveillance, and defining pandemic governance in a way that involves all 193 member states. Industry and academia are already leading on DTV R&D, but it is important to ensure incentives remain to continue to support pandemic DTV R&D efforts. Further, industry have committed to increasing access to DTVs through the Berlin Declaration, which should be complemented by public-private partnership throughout the R&D value chain to create libraries for priority pathogens in a sustainable and equitable manner. The Secretariat will lead on driving the mission-based approach, including developing links across stakeholders, facilitating scientific exchange via the STEG and collating progress to prepare annual Implementation reports. Most importantly, collaborative effort across all stakeholders is critical for success of the 100 Days Mission, and this report is intended to serve as a detailed baseline reference for the fast-moving and complex ecosystem of the 100 Days Mission.



# Introduction

## Background to the 100 Days Mission

In June 2021, the 100 Days Mission was endorsed by the G7 leaders to enhance preparedness and reduce the impact of future pandemic threats by making available within 100 days:

- 1** Accurate and approved rapid **Diagnostic tests**
- 2** An initial regimen of **Therapeutics**
- 3** **Vaccines** ready to be produced at scale

Development of DTVs within 100 days of an outbreak is intended to maximise the positive health impact of a rapid response and save lives. For the purposes of this report, Day 0 of the 100 Days Mission is defined as the WHO's declaration of a Public Health Emergency of International Concern (PHEIC). Organisations, including CEPI, Gavi, and others, are considering alternative triggers that could be used to define Day 0. There is outstanding work to be done to align the global community to the definition of Day 0 for diagnostics, therapeutics, and vaccines individually, given the distinct activities and development challenges for each. Nevertheless, advanced preparation to support the 100 Days Mission is critical to ensure quality, safety, and efficacy and will require significant effort. It will require streamlining processes with every outbreak, promoting regular use of accurate diagnostic tests as best practice, and developing 'programmable' platforms for vaccines and therapeutics. When the goal of the mission

is achieved – producing safe and effective DTVs within 100 Days – it still needs to be followed by effective implementation and delivery to ensure equitable access and utilisation of DTVs. In short, the 100 Day Mission is a sprint within a longer marathon.

The 100 Days Mission set out 25 actionable recommendations for governments, industry, civil society, philanthropic, and international organisations to prepare to respond to future pandemics. These recommendations can be grouped into 8 categories that comprise the necessary preparations for a successful 100 Day response, focused primarily on DTV development (centre) with key enablers to support (outside circle, as shown in Figure 4). The target for delivery of the recommendations is 2026, but many of these are complex and require significant stakeholder collaboration that may extend delivery beyond 2026.

## Global Health Equity and Resilience



COVID-19 demonstrated strengths in the world's public health ecosystem, including the ability to rapidly adopt flexible regulatory processes to approve DTVs quickly. However, the COVID-19 experience also exposed many gaps, including weak demand forecasting, insufficient market shaping and country readiness, and inadequate appreciation of barriers to uptake which affected

Non exhaustive

### Best practice in non-pandemic times

- Effective One Health surveillance system established to identify pandemic threats
- R&D for 'programmable' platforms and DTV libraries against priority pathogens
- Increased adherence to routine immunisations
- Global coordination mechanisms for international agencies to provide concerted support across DTVs
- Country-level readiness to deliver and administer DTVs

### First 100 days of a pandemic

- The WHO declares a PHEIC, which activates the Pandemic Instrument (i.e., new Rules of the Road)
- Financing is available for both research and response
- Rapid initiation of R&D by industry and others to address target pathogens using programmable platforms
- International trial network tests DTVs as they are developed

### Scale up DTVs for equitable global access

- Production capacity is scaled regionally through technology transfer
- Safe and effective DTVs are deployed equitably
- Globally coordinated post-market surveillance responds to evolving pathogen at pace with pandemic

Figure 3. The 100 Days Mission starts before and goes beyond the 100 days. The 100 Days (centre) is intended to last from outbreak declaration via PHEIC to having a first suite of safe and effective DTVs ready to be produced at scale. Efforts required in each phase will vary between diagnostics, therapeutics, and vaccines, with more significant regulatory and manufacturing efforts required for therapeutics and vaccines to achieve the 100 days target, including global vaccine manufacturing efforts.

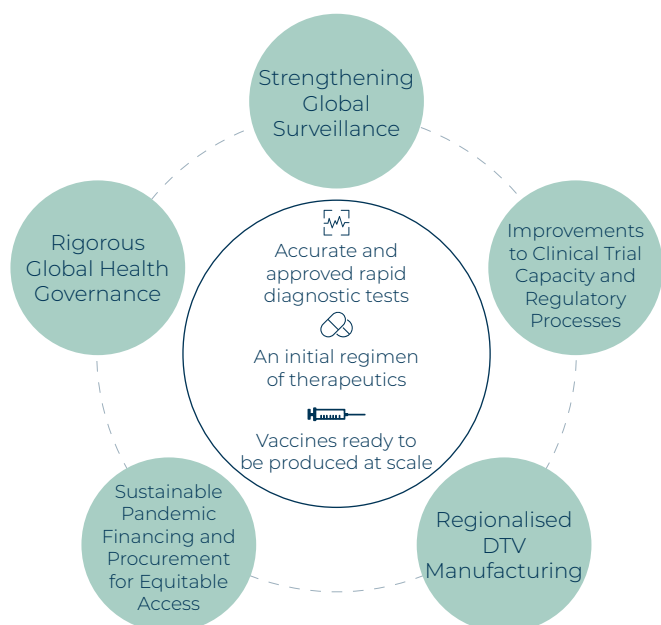


Figure 4. Various integrated PPR efforts are needed to achieve the 100DM goals. To achieve the goals of (i) accurate and approved rapid diagnostic tests; (ii) an initial regimen of therapeutics; and (iii) vaccines ready to be produced at scale for global deployment, it is important to make the exceptional routine by embedding best practice in business-as-usual activity – from cross-cutting mission enablers and improved surveillance through to routine use of rapid diagnostics and clinical trials in everyday practice. Further, the ‘rules of the road’ need to be agreed ahead of time, so no time is wasted negotiating the basics.

global equity and access to DTVs. During the height of the COVID-19 pandemic, the Access to COVID-19 Tools Accelerator (ACT-A) played a significant role in supporting R&D, accessibility, and market shaping for DTVs. ACT-A will sunset in 2023, but building on lessons from recent ACT-A reviews, there are ongoing consultations led by the WHO and within the G20 related to a future global access to medical countermeasures platform. An end-to-end platform, especially with increased attention on therapeutics and diagnostics, will provide a strong basis to prepare for future pandemic threats. Further, in addition to development of such a platform, it is key to strengthen the global infrastructure, develop regional resilience in R&D, trials, and manufacturing, improve health systems to ensure routine care services can be maintained during another pandemic, prioritise developing DTVs according to Target Product Profiles (TPPs), and establish mechanisms for rapid, at-risk funding to ensure LMICs have access to DTVs in an emergency. Importantly, the experience during COVID-19 underscored the need to build a sufficient and rapid supply of raw materials, in addition to adequate manufacturing capacity, to ensure timely access to DTVs.

There have been significant efforts to support equity, access, and resilience following the COVID-19 experi-

ence. The Global Research Collaboration for Infectious Disease Preparedness (GloPID-R) launched inaugural programmes in their first LMIC research hub in Asia-Pacific<sup>6</sup> and there was strong political attention paid to regionalised vaccine manufacturing proposals, including through the Indonesia G20 presidency's proposal to develop a network of manufacturing hubs (to be taken forward by India's presidency in 2023).<sup>7</sup> The biopharmaceutical industry committed to reserve an allocation of real-time production of DTVs for distribution to priority populations in lower income countries through the IFPMA's Berlin Declaration.<sup>8</sup>

Still, there is outstanding work to truly achieve global health equity and resilience. Looking to 2023, there is an opportunity to support an R&D ecosystem that efficiently and sustainably develops DTVs required to meet the needs of the global population in timely and affordable ways. This ecosystem should be inclusive, equitable, sustainable, and innovative. In the near-term, the Berlin Declaration will support timely access to DTVs in lower income countries. G20 governments and major funders can also contribute by including access clauses in publicly funded R&D programmes. Additionally, industry, academia, and others (including CEPI) will invest in innovation to ensure thermostability of DTVs and improve ease of delivery by directing research toward the WHO's TPPs. In the medium-term, a key priority will be to create emergency response funding mechanisms, such as automatic financing that can help to provide on-time DTV access to LMICs. Longer-term efforts can support developing market conditions for inclusive and sustainable local or regional DTV production with meaningful participation from the communities affected. These efforts include creating attractive R&D opportunities in LMICs so that they can retain key talent in-country and ensuring resilient product supply chains.

Global institutions and initiatives should ensure national and regional voices from all continents are heard in the decision-making processes that will affect their communities. Multilateral relations have the potential to amplify the voices of affected communities and advocate for equity and accessibility in the production of DTVs, which is crucial to the resilience of the global health architecture. Importantly, equity and resilience for pandemic preparedness is predicated on strong health systems for routine services. Efforts to strengthen health systems should include augmenting use of diagnostics in care pathways and increasing capacity for life-cycle immunisations in an effort to support the overall global health architecture. Global vaccination programmes are recommended to drive regular use and global manufacturing.

<sup>6</sup> GloPID-R (2022). Progress in the Implementation of GloPID-R's Regional Hub Strategy. [online] [glopid-r.org](https://www.glopid-r.org/articles-newsletter/progress-in-the-implementation-of-glopid-rs-regional-hub-strategy/). Available at: <https://www.glopid-r.org/articles-newsletter/progress-in-the-implementation-of-glopid-rs-regional-hub-strategy/>

<sup>7</sup> Information disclosed in proforma document or interviews with Indian government

<sup>8</sup> IFPMA (2022). Berlin Declaration. [online] [ifpma.org](https://www.ifpma.org/resource-centre/berlin-declaration-biopharmaceutical-industry-vision-for-equitable-access-in-pandemics/). Available at: <https://www.ifpma.org/resource-centre/berlin-declaration-biopharmaceutical-industry-vision-for-equitable-access-in-pandemics/>

## International Pandemic Preparedness Secretariat

A time-limited International Pandemic Preparedness Secretariat has been established to support the mission-based approach and its implementation community, aiming to complete its work by 2026. The Secretariat is not a G7 entity and will provide independent, ecosystem-wide support for the 100 Days Mission, including by:

- Catalysing scientific exchange between implementation partners
- Brokering partnerships and assisting implementation partners where necessary (e.g., states, private sector, and global health institutions)
- Delivering independent annual Implementation Reviews (in consultation with the Steering Group, the STEG, and key implementation partners)
- Supporting continuity of purpose in relation to pandemic preparedness across rotating G7 and G20 presidencies
- When invited, supporting the G7 or G20 presidencies with scientific advice and in convening non-governmental stakeholders for the purpose of driving forward the 100 Days Mission

The Secretariat is advised by a STEG and governed by a small Steering Group comprised of supporting partners (see Annex D for list of Steering Group member organisations and process for nominating members of the STEG).

*“Increasing global health equity and resilience is a key aspect of delivery across the entirety of the 100 Days Mission”*



This emphasis is visually highlighted with an icon throughout the report

# Investing in R&D to Fill the Gaps in Our Arsenal



COVID-19 has demonstrated the need to improve baseline pandemic defences and as such, R&D has been a major focus of both money and attention. In April 2020, ACT-A was launched to support R&D for an effective and equitable global response to COVID-19. Since then, there have been numerous reflections on lessons learnt from ACT-A, and as a next step, the ACT-A Facilitation Council co-chairs, in collaboration with the WHO, G7 and G20, are convening an intergovernmental discussion on a future medical countermeasures platform. The importance of a future platform is supported by principles of the European Commission (EC) Global Health Strategy.<sup>9,10,11,12</sup> Reflections from ACT-A published in 2022 highlight the need for an end-to-end solution to ensure equitable access to DTVs, from integrating diagnostics and therapeutics at the point of care to creating incentives for R&D and developing sustainable markets and procurement mechanisms that support access to DTVs. Further, it is critical to co-ordinate efforts across diagnostics, therapeutics, and vaccines in support of overall global health.

An end-to-end solution for DTVs requires extensive R&D efforts both in advance and during a future pandemic. Experiences from COVID-19 show that industry and biotechnology players have a critical role to play alongside academia, public sector, and philanthropic organisations. Applications of innovative technologies including artificial intelligence (AI) and machine learning (ML) have the potential to drive significant advances in PPR research, including predicting the folding of viral proteins and identifying the best targets for intervention. Clear commercial incentives, protection of intellectual property rights, financial de-risking, and robust voluntary collaboration structures are essential to unleashing a wave of innovation that can deliver DTVs in record time.

Given the breadth of pathogens that infect humans, PPR efforts have tried to focus on viruses with the great-

est 'pandemic potential'. At the end of 2022, the WHO together with partners (including CEPI) began convening a Prioritisation Advisory Committee to define priority pathogens of pandemic potential (including viruses and bacteria). This work will update the WHO's 2018 prioritisation and will select priority viral families, prototype pathogens within those families, as well as 'Disease X' threats. CEPI are ranking the likelihood of emergence of 'Disease X' from priority viral families<sup>13</sup> which can complement the WHO's priority pathogen list. A single endorsed list of priority pathogens can direct future development of all three DTVs and a coordinated approach across all modalities should be developed to optimise limited resources. Note that as technology advances, the lines between DTVs may blur, especially between therapeutics and vaccines (i.e., prophylactic use of a monoclonal antibodies (mAbs)), but for the purposes of this report, the classical definitions of DTVs are used.

## Diagnostics R&D

### Context and aims

Diagnostics can be seen as the 'first line of defence' for a pandemic: it is critical to identify the pathogen and its spread to initiate development of therapeutics to treat or vaccines to control it. Diagnostics are therefore a key feature of surveillance and an input to future R&D. Molecular diagnostics were successfully developed for COVID-19 in as little as 42-64 days resulting in emergency use authorisation in Korea<sup>14</sup> or emergency use listing (EUL) by the WHO,<sup>15</sup> but rapid tests did not receive EUL by the WHO for 236 days.<sup>16</sup> Though the timeline for molecular diagnostics is impressive and underscores that rapid innovation was possible during COVID-19, it is important to ensure adequate preparation in advance of another pandemic threat. As such, a five-year roadmap for Diagnostics was laid out in the 2021 Implementation report, with two key outcomes by 2026 (see end of this chapter for detailed updated Diagnostics Roadmap):

- 1** Strengthened international coordination between governments, industry, and international organisations on a sustainable diagnostics R&D ecosystem
- 2** Diagnostics developed providing broad coverage for 8-10 virus families

<sup>9</sup> Open Consultants (2022). External Evaluation of the Access To COVID-19 Tools Accelerator (ACT-A). [online] who.int. Available at: [https://www.who.int/publications/m/item/external-evaluation-of-the-access-to-covid-19-tools-accelerator-\(act-a\)](https://www.who.int/publications/m/item/external-evaluation-of-the-access-to-covid-19-tools-accelerator-(act-a))

<sup>10</sup> COVAX (2022). COVAX: Key learnings for future pandemic preparedness and response. [online] who.int. Available at: <https://www.who.int/publications/m/item/covax--key-learnings-for-future-pandemic-preparedness-and-response>

<sup>11</sup> European Commission (2022). EU Global Health Strategy. [online]. Available at: [https://health.ec.europa.eu/system/files/2022-12/international\\_ghs-report-2022\\_en.pdf](https://health.ec.europa.eu/system/files/2022-12/international_ghs-report-2022_en.pdf)

<sup>12</sup> WHO (2022). Report of ACT-A Facilitation Council Working Group on Diagnostics and Therapeutics. [online] who.int. Available at: <https://www.who.int/publications/m/item/act-accelerator-facilitation-council-working-group-report-on-diagnostics-and-therapeutics>

<sup>13</sup> UC Davis (2022). CEPI teams with UC Davis to identify viruses most likely to emerge. [online] grandchallenges.ucdavis.edu. Available at: <https://grandchallenges.ucdavis.edu/cepi-teams-up-with-uc-davis-to-identify-viruses-most-likely-to-emerge/>

# 100 Days Mission Timeline for DTV Research and Development

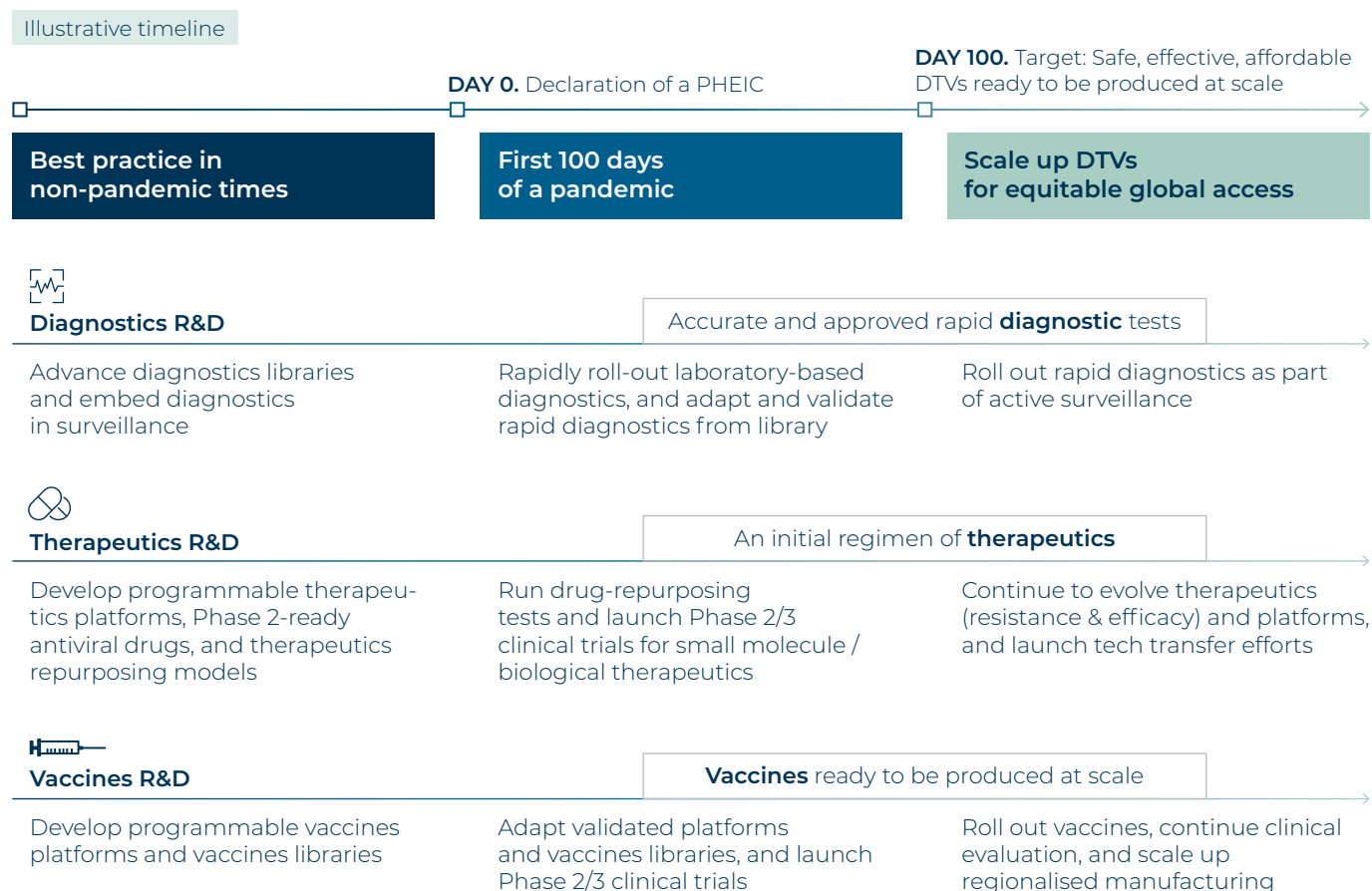


Figure 5. Research and development for pandemic DTVs involves a effort in non-pandemic times, a pivot during the first 100 days, and continued scale up and innovation. Distinct efforts are required for diagnostics, therapeutics, and vaccines R&D, but cross-DTV collaboration is key, especially to develop a joint understanding of viruses of 'pandemic potential' and the right DTVs to tackle them. (Note: Timeline is focused on DTV R&D, and does not represent a full view of broader health system preparation and response)

Beyond delivery of the diagnostics R&D roadmap, diagnostics must be used routinely in point-of-care and non-clinical settings<sup>17</sup> to establish an effective industry and integrated with surveillance efforts<sup>18</sup> [see *Chapter 3 – Strengthening Global Surveillance*]. Additionally, diagnostics must be approved for use quickly in a pandemic. For this reason, specific recommendations for diagnostics regulatory approvals were set forth in the original 100 Days Mission report [see *Chapter 4 – Improvements to Clinical Trials Capability and Regulatory Process*].

## Progress

Overall progress in diagnostics was strong during the pandemic but has declined recently as reduced routine use of tests decreased demand, dedicated funding support

has waned, and coordination efforts for diagnostics R&D have been limited. The Foundation for Innovative New Diagnostics (FIND) played a central role in diagnostics throughout COVID-19, performing engagement across the value chain and with other global health entities, such as CEPI. In 2022, FIND intended to begin development of pandemic preparedness diagnostics, and to date have completed landscaping of available reagents for prototype viruses within each priority family (e.g., Lassa fever virus for the arenavirus family).<sup>19</sup> Important to note that at the time of writing, diagnostic tests only exist for 4 of the 10 existing WHO priority pathogens (though the 2018 priority list is currently being updated).<sup>20</sup>

<sup>14</sup> Information disclosed in proforma document or interviews with FIND

<sup>15</sup> WHO (2020). WHO Lists Two COVID-19 Tests for Emergency Use. [online] who.int. Available at: <https://www.who.int/news/item/07-04-2020-who-lists-two-covid-19-tests-for-emergency-use>

<sup>16</sup> FIND (2020). Antigen Rapid Tests: Country Implementation Support. [online] finddx.org. Available at: <https://www.finddx.org/covid-19/rdt-imp/>

<sup>17</sup> Initial roadmap noted 'for priority pathogens', which has since been removed as diagnostics should be for regionally-relevant pathogens

<sup>18</sup> Full outcome as outline in the 2021 report is "Diagnostics integrated into the International Pathogen Surveillance Network (IPSN) to maximise its coverage & utility", however the IPSN is set to be operationalised in 2023 and thus is not detailed in progress

<sup>19</sup> Information disclosed in proforma document or interviews with FIND

<sup>20</sup> BMJ Glob Health (2019). Kelly-Cirino CD, Nkengasong J, Kettler H, Tongio I, Gay-Andrieu F, Escadafal C, Piot P, Peeling RW, Gadde R, Boehme C. Importance of diagnostics in epidemic and pandemic preparedness. [online] ncbi.nlm.nih.gov. Available at: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6362765/>

Diagnostics R&D and innovation is supported by strong market pull created through regular use of diagnostics in high-income countries (HICs). The WHO has led efforts to reiterate the importance of diagnostics in preparing for “Pathogen X”.<sup>21</sup> The WHO R&D Blueprint team has also begun to direct R&D efforts through development of R&D roadmaps and Target Product Profiles (TPPs), which include guidelines for use of diagnostics in symptomatic and asymptomatic patients as well as ideal testing volumes required for accuracy and interpretation.<sup>22</sup> R&D for diagnostics in 2022 has been focused on improving existing tests, rather than developing new diagnostics libraries. Rapid antigen tests were released by multiple players that can simultaneously diagnose SARS-CoV-2 and influenza A/B.<sup>23</sup>

### Summary plans for 2023

Given the importance of diagnostics to bridge surveillance efforts with vaccine and therapeutic development, 2023 will need to draw sufficient funds and attention to diagnostics. Key diagnostics players, in coordination with FIND and industry, will explore mechanisms to ensure adequate funding to initiate work on diagnostics libraries, including garnering investment against FIND’s \$50-80 million proposed plan. The Indian G20 presidency has included diagnostic R&D in their list of priorities, which encourages greater funding and coordination across regions. With adequate funding, FIND is willing to coordinate diagnostics efforts across the global community, including securing key reagents and bio-banked samples for R&D, establishing partnership agreements to achieve milestones, ensuring focus on WHO-TPP compliant technologies, and aligning work with the WHO’s pandemic virus prioritisation. Further, the International Pandemic Preparedness Secretariat will support efforts to ensure diagnostics R&D receives adequate resources and political attention.

## Therapeutics R&D

### Context and aims

Therapeutics have a key role to play in the armory against future pandemics, particularly when development of vaccines is technically challenging, vaccine uptake is delayed or incomplete, for immuno-compromised individuals, and in treating break-through infections. Therapeutics against emerging infectious disease can take several forms –

direct acting anti-viral agents or ‘host-directed’ agents that modify how the body responds to viral infection and/or protects vital organs from damage. Therapeutics can be newly developed, re-purposed from an existing approved indication, or re-directed from another existing experimental indication. mAbs such as sotrovimab<sup>24</sup> and bebtelovimab<sup>25</sup> and small molecule therapeutics such as molnupiravir<sup>26</sup> and combination nirmatrelvir/ritonavir<sup>27</sup> are examples of newly developed direct acting anti-viral agents given emergency use authorisation in response to COVID-19. Dexamethasone and baricitinib are example of repurposed therapies proven to be effective as host-directed therapies (HDTs) improving the outcomes of people hospitalised with COVID-19.<sup>28</sup>

Reflecting on lessons learnt from therapeutics efforts in COVID-19, the 2021 Implementation Report for the 100 Days Mission proposed three key outcomes to be reached by 2026 (see end of this chapter for updated detailed Therapeutics Roadmap):

- 1** A sustainable R&D ecosystem and improved international coordination and funding for therapeutics R&D for infectious disease pandemic threats
- 2** 25 Phase-2 ready therapeutic assets developed against priority virus families
- 3** Readily programmable antiviral platforms (including mAbs and others) evolved towards WHO TPPs for delivery in case of a health emergency, and able to be rapidly re-purposed to ‘Disease X’<sup>29</sup>

Note that outcome #1 (above) from the 2021 Implementation Report originally named therapeutic candidates against priority respiratory virus families. Respiratory has been removed to indicate that pandemic pathogens can also be transmitted in other ways (skin-to-skin, blood-borne, vector-borne, etc.) as evidenced through the mpox outbreak this year (mpox spread through direct contact).

### Progress

Overall progress in therapeutics R&D has been accelerated by the arrival of major new efforts and funding channels, totalling over ~\$990 million, including the AVIDD programme (\$577 million)<sup>30</sup> and the Antiviral Programme

<sup>21</sup> WHO (2022). Scientific strategies from recent outbreaks to help us prepare for Pathogen X. [online] who.int. Available at: <https://www.who.int/news-room/events/detail/2022/08/29/default-calendar/save-the-date---scientific-strategies-from-recent-outbreaks-to-help-us-prepare-for-pathogen-x>

<sup>22</sup> WHO (2022). Accelerating R&D processes. [online] who.int. Available at: <https://www.who.int/activities/accelerating-r-d-processes>

<sup>23</sup> TGA (2022). First combination COVID-19 and influenza self-tests approved for Australia. [online] tga.gov.au. Available at: <https://www.tga.gov.au/news/media-releases/first-combination-covid-19-and-influenza-self-tests-approved-australia>

<sup>24</sup> US Food and Drug Administration (2022). FDA Updates Sotrovimab Emergency Use Authorisation. [online] fda.gov. Available at: <https://www.fda.gov/drugs/drug-safety-and-availability/fda-updates-sotrovimab-emergency-use-authorization#:~:text=This%20EUA%20authorizes%20sotrovimab%20for,19%2C%20including%20hospitalization%20or%20death.>

<sup>25</sup> US Food and Drug Administration (2022). Bebtelovimab Health Care Provider Fact Sheet. [online] fda.gov. Available at: <https://www.fda.gov/media/156152/download>

<sup>26</sup> US Food and Drug Administration (2022). Molnupiravir Health Care Provider Fact Sheet. [online] fda.gov. Available at: <https://www.fda.gov/media/155054/download>

<sup>27</sup> Pfizer (2021). Pfizer Receives U.S. FDA Emergency Use Authorization for Novel COVID-19 Oral Antiviral Treatment. [online] Pfizer.com. Available at: <https://www.pfizer.com/news/press-release/press-release-detail/pfizer-receives-us-fda-emergency-use-authorization-novel>

<sup>28</sup> UK Government (2022). Pharmaceutical Interventions: Therapeutics and Vaccines. [online] gov.uk. Available at: <https://www.gov.uk/government/publications/technical-report-on-the-covid-19-pandemic-in-the-uk/chapter-9-pharmaceutical-interventions-therapeutics-and-vaccines>

<sup>29</sup> Original roadmap referred to reducing the cost of producing marketable mAbs to less than \$25/gram, this has been broadened to meeting WHO TPPs

<sup>30</sup> NIAID (2022). NIAID Announces Antiviral Drug Development Awards. [online] niaid.nih.gov. Available at: <https://www.niaid.nih.gov/news-events/niaid-announces-antiviral-drug-development-awards>

## Categories of therapeutics for viruses of pandemic potential





Direct acting anti-viral	Host-directed
 <p><b>Intervention given early</b> in the course of the disease to prevent viral spread by interfering with viral entry, trafficking, or replication</p>  <p>Includes both small molecule therapeutics, and biologics (e.g. monoclonal antibodies, novel constructs), as well as blood products</p>	 <p><b>Intervention typically given later</b> in the course of the disease to modulate host response to infection or address complications</p>  <p>Pharmacologically these include, e.g, immune stimulators, immunosuppressants, anticoagulants, end organ support, and can be small molecule or biologic therapeutics</p>

Figure 6. Two main types of therapeutics can be developed for priority pathogens of pandemic potential. Different viruses will respond differently to each type of therapeutic, and some may be more applicable to specific viruses given their biology.

for Pandemics (\$12 million)<sup>31</sup> both funded by the US National Institute of Allergy and Infectious Diseases (NIAID), the PAD fund (\$90 million),<sup>32</sup> and a new programmable anti-viral programme at the Cumming Global Centre for Pandemic Therapeutics (\$226 million (AUD 250 million + AUD 75 million over 10 years)).<sup>33</sup> Additionally, the Rapidly Emerging Antiviral Drug Development Initiative (READDI, Inc.) received \$65 million (in addition to their AVIDD funding)<sup>34</sup> and AHEAD100 raised \$25 million.<sup>35</sup>

Encouragingly, many of these efforts have a focus on discovering new small molecules active against priority pathogens or viral families. Experiences from COVID-19 suggest that small molecules are more likely to meet TPPs laid out by the WHO – in particular, related to ease of distribution and cost per dose. However, given the nascency of funding detailed above and based on typical development costs and timelines, it is unlikely that the target of 25 Phase 2-ready therapeutic candidates by 2026 will be met.

Despite the success of host-directed therapies such as dexamethasone in treating hospitalised patients during COVID-19,<sup>36</sup> research in this area is relatively under-resourced with only READDI, Inc. and Drugs for Neglected Diseases initiative (DNDi) maintaining a focus on host directed therapies. READDI received \$130 million this year from AVIDD and other funders to support their work broadly across therapeutics.<sup>37</sup> However, research on host-directed therapies was out of scope for AVIDD, likely due to research challenges (i.e., lack of robust animal mod-

els) and lack of robust data for use of some COVID-19 HDTs (i.e., interferon).

Discovery efforts focused on mAbs and other new biologics have been limited. Due to funding constraints, AHEAD100 has launched a single discovery campaign aimed at one pathogen (Rift Valley Fever)<sup>38</sup> and biological therapies are in scope for one AVIDD centre. mAbs and gene editing technologies are an explicit long-term focus for the new Cumming Global Centre for Pandemic Therapeutics, launched in 2022 with a twenty-year research programme.<sup>39</sup> CEPI has expanded its mission to include biological countermeasures (i.e., vaccine-like technologies including mAbs), beginning with an initial focus on Nipah mAbs and will also fund innovation to reduce mAb costs and increase accessibility, including through collaborations with Wellcome Leap.<sup>40</sup> Industry also continues to innovate to improve potency of mAbs and reduce costs. Despite this work, current investments may not be sufficient to develop and de-risk programmable platform development through all clinical stages in support of the 100 Days Mission.

Today, there is a healthy COVID-19 therapeutics pipeline developed mostly at-risk by innovators and generics that supported the launch of multiple safe and effective therapies for COVID-19 in 2022. Pre-competitive industry collaboration is currently being planned by the International Readiness for Preventing Infectious Disease (INTREPID) group of pharmaceutical companies.<sup>41</sup> The IFPMA

<sup>31</sup> NIAID (2022). NIH Awards \$12 Million for Antiviral Therapeutic Development. [online] [niaid.nih.gov](https://www.niaid.nih.gov/news-events/nih-awards-12-million-antiviral-therapeutic-development). Available at: <https://www.niaid.nih.gov/news-events/nih-awards-12-million-antiviral-therapeutic-development>

<sup>32</sup> PAD (2022). PAD Launch as Initiative to Support New Antiviral Medicines for Future Pandemics. [online] [padinitiative.com](https://padinitiative.com). Available at: <https://padinitiative.com/pad-launch-initiative-to-support-new-antiviral-medicines-for-future-pandemics/>

<sup>33</sup> Ore, A. (2022). 'Most extraordinary': Geoffrey Cumming Wows Melbourne with \$250m Medical Donation. [online] [theguardian.com](https://www.theguardian.com/society/2022/aug/31/most-extraordinary-geoffrey-cumming-wows-melbourne-with-250m-medical-donation/). Available at: <https://www.theguardian.com/society/2022/aug/31/most-extraordinary-geoffrey-cumming-wows-melbourne-with-250m-medical-donation/>

<sup>34</sup> Information disclosed in proforma document or interviews with READDI.

<sup>35</sup> Information disclosed in proforma document or interviews with AHEAD100

<sup>36</sup> P. Horby, W.S. Lim, J.R. Emberson, et al. (2021). Dexamethasone in Hospitalised Patients with Covid-19. [online] [nejm.org](https://www.nejm.org/doi/full/10.1056/NEJMoa2021436). Available at: <https://www.nejm.org/doi/full/10.1056/NEJMoa2021436>

<sup>37</sup> Information disclosed in proforma document or interviews with READDI.

<sup>38</sup> Information disclosed in proforma document or interviews with AHEAD100

<sup>39</sup> Doherty Institute (2022). Cumming Global Centre for Pandemic Therapeutics Overview. [online] [doherty.edu.au](https://www.doherty.edu.au/cumming-global-centre-for-pandemic-therapeutics/about-cgcpt/overview). Available at: <https://www.doherty.edu.au/cumming-global-centre-for-pandemic-therapeutics/about-cgcpt/overview>

<sup>40</sup> CEPI (2021). 2022-2026 Strategy. [online] [cepi.net](https://cepi.net/wp-content/uploads/2021/03/20211201-CEPI-2022-2026-Strategy.pdf). Available at: <https://cepi.net/wp-content/uploads/2021/03/20211201-CEPI-2022-2026-Strategy.pdf>

<sup>41</sup> Information disclosed in proforma document or interviews with INTREPID

has played a key advocacy role for therapeutics R&D in 2022 through policy briefs and supporting critical multi-lateral efforts.<sup>42</sup> Still, therapeutics is a challenging space for individual companies given it is anchored on developing products that will only be needed in the case of an outbreak (similar to the field of antimicrobial resistance). The most attractive niche in therapeutics is viral families with seasonal profiles and existing commercial markets (i.e., influenza), but that leaves a major gap in the pandemic repertoire. In the near-term, it is important to consider how therapeutics investment is directed toward therapeutics for WHO-prioritised pathogens that do not currently have high political attention or investment.

Coordination has emerged as a major challenge in therapeutics. The ecosystem is nascent and there is no 'CEPI for therapeutics' playing a convening role to date. Prioritisation of pathogens of pandemic potential is underway by the WHO, but in the interim, groups have no internationally endorsed framework for directing R&D efforts.

### [Summary plans for 2023](#)

Key to maintaining positive momentum in therapeutics will be identifying organisations that are willing to play a role in convening, information sharing, and collaborating. The WHO's updated list of priority pathogens of pandemic potential will provide an opportunity to take stock of global efforts, foster collaboration, and identify gaps in early 2023. This can be actioned as key funders such as the Biomedical Advanced Research and Development Authority (BARDA), the Health Emergency Preparedness and Response Authority (HERA), and the Cumming Global Centre for Pandemic Therapeutics develop and communicate detailed plans for their therapeutics research programmes. It will be critical for industry to demonstrate continued engagement and leadership in this space as well, including through private-public collaborations and by advancing their own internal programmes. Given the volume of stakeholders, it is essential for key therapeutics players to come together as early as possible to jointly identify a body, or bodies, to act as a global therapeutics convener for information sharing and technical collaboration, to minimise duplication and support broad coverage of priority pathogens. The International Pandemic Preparedness Secretariat can support these efforts as requested (e.g., through global mapping of research across therapeutic type, viral target, and stage of development).

One area where additional focus is needed is biological therapies, including mAbs and other rapidly programmable antiviral platforms to complement mAbs. Groups with an expressed interest in this modality such as AHEAD100, CEPI, Wellcome Leap, the Cumming Centre, and select AViDD centres should participate in coordination efforts. Given the criticality of programmable platforms to PPR, there is a need to define a clear blueprint for developing multiple programmable platforms in line with WHO TPPs for delivery in a health emergency. This blueprint should lead to cheaper and more easily distributed mAbs as well as identify and prioritise other promising platform approaches.

Despite a strong funding climate for therapeutics in 2021, there has been a decline in funding interest for therapeutics R&D in 2022 and therapeutics would benefit from additional resources. To meet the 100 Day Mission goals of ~25 Phase 2-ready antivirals by 2026, R&D centres across industry and academia need to advance discovery efforts, conduct candidate selections on 60-100 programmes, and prepare to progress 40-60 programmes through Investigational New Drug (IND)-enabling studies in 2024/25. Attrition rates will vary by pathogen and viral family, but significant additional resources are needed to explore new programmable therapeutic modalities and to advance compounds to the clinic. The development of partnership models to enable industry to take forward de-risked candidates and progress them through clinical development will be important in this period as clinical development is currently beyond the remit of many ongoing efforts.

## **Vaccines R&D**

### [Context and aims](#)

The success of vaccines developed in response to COVID-19 is well documented but cannot be taken for granted in the event of a future pandemic. To date, nearly 16 billion COVID-19 vaccine doses have delivered globally.<sup>43</sup> Even if the COVID-19 experience were repeated, a step-change in performance is required to deliver vaccines within 100 Days. Key to rapid delivery is extensive preparation and experience with implementing platform technologies in terms of securing approval for new vaccines and the data required for each platform. A library of vaccines developed against pathogens with the greatest pandemic potential should allow rapid efficacy testing – and ideally – help contain the initial outbreak. Recognising that pandemics will not always arise from known pathogens, a programmable platform technology that is robust, stable, and easy to deliver globally is critical to respond rapidly to future unknown threats. Messenger RNA (mRNA) and adenovirus vector technology played this role in COVID-19. Finally, rapid scale-up of manufacturing globally and equitable distribution must be a core plank of future response efforts [see Chapter 3 – Regionalised Manufacturing of DTVs].

Reflecting these themes and the recommendations of analyses conducted by CEPI and other key partners, there are three key outcomes to be reached by 2026 (see end of this chapter for detailed updated Vaccine Roadmap):

- 1** Vaccine libraries developed for 10 high priority virus families
- 2** Readily programmable vaccine platform technology available, able to be rapidly re-purposed to an emerging 'Disease X' threat
- 3** Vaccine platforms optimised for large scale production and simplified routes of administration and storage (i.e., to comply with the WHO TPPs)

<sup>42</sup> IFPMA (2022). Open Letter on ACT-A Therapeutics and Ongoing Roadblocks to Enhancing Access. [online] ifpma.org. Available at: <https://www.ifpma.org/resource-centre/open-letter-on-act-a-therapeutics-and-ongoing-roadblocks-to-enhancing-access/>

<sup>43</sup> UNICEF (2022). COVID-19 Market Dashboard. [online] unicef.org. Available at: <https://www.unicef.org/supply/covid-19-market-dashboard>

## Illustrative pipeline for PPR antiviral development

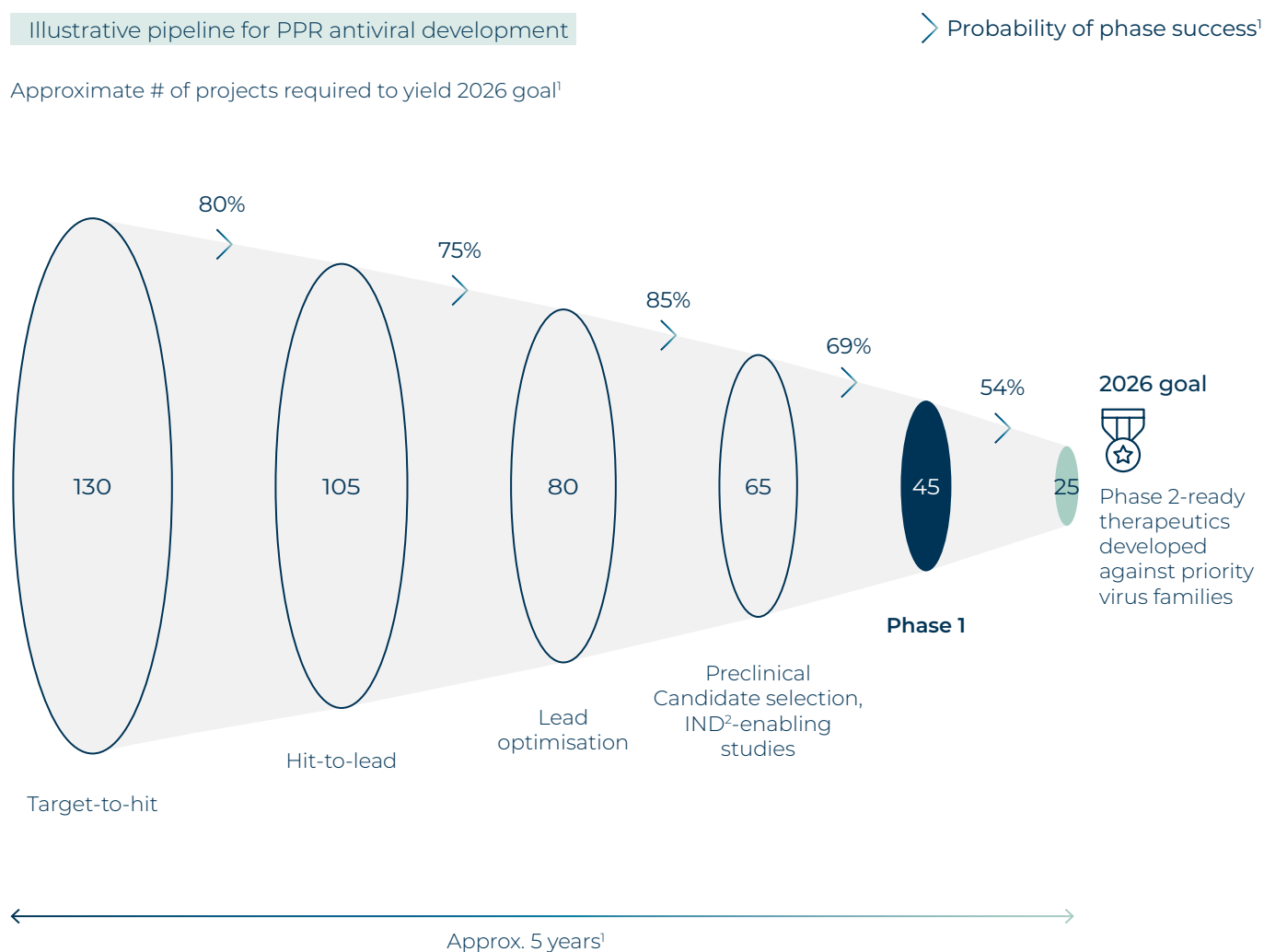


Figure 7. Evolving therapeutic assets to Phase 2 readiness is a multi-year process. There are significant drop-out rates along key steps of the discovery and development process, but attrition rates and timelines will vary depending on the type of therapeutic (e.g., mAb, small molecule antiviral), virus (family) and target.

Note: Illustrative process and project numbers portrayed. Attrition rates and timelines will vary.

1. Based on READDI Inc analysis of Paul, S., Mytelka, D., Dunwiddie, C. et al. How to improve R&D productivity: the pharmaceutical industry's grand challenge. Nat Rev Drug Discov 9, 203–214 (2010). <https://doi.org/10.1038/nrd3078>; 2. IND = Indication

Note that this section is focused specifically on vaccine R&D; manufacturing capacity and supply chain to produce vaccines will be covered in Chapter 3.

### Progress

Vaccines are unique amongst DTVs in having CEPI as a single clear 'convener' of efforts recognised by the international community. A major milestone for vaccines was CEPI's planned funding replenishment that took place in 2022. CEPI secured \$2 billion (total post-replenishment) of a \$3.5 billion target to "accelerate the development of

vaccines and other biologic countermeasures against epidemic and pandemic threats so they can be accessible to all people in need".<sup>44</sup> CEPI since launched calls for proposals to complete phase 1/2 clinical testing of vaccines for Rift Valley Fever, develop protective approaches to SARS-CoV-2 and betacoronaviruses, develop virus family vaccine libraries, optimise mRNA platform technologies for rapid responses, and address broader cross-cutting innovation topics.<sup>45</sup> CEPI also continues to play a coordinating role in the vaccine ecosystem, and has published a recent report on "What Will it Take" that outlines five areas of innova-

<sup>44</sup> CEPI (2022). Global Community Comes Together in Support of 100 Days Mission and Pledges Over \$1.5 Billion for CEPI's Pandemic-Busting Plan. [online] cepi.net. Available at: [https://cepi.net/news\\_cepi/global-community-comes-together-in-support-of-100-days-mission-and-pledges-over-1-5-billion-for-cepi-pandemic-busting-plan/](https://cepi.net/news_cepi/global-community-comes-together-in-support-of-100-days-mission-and-pledges-over-1-5-billion-for-cepi-pandemic-busting-plan/)

<sup>45</sup> CEPI (2022). Call for Proposals. [online] cepi.net. Available at: [https://cepi.net/wp-content/uploads/2022/09/16092022\\_RVF-Funding-Call\\_Call-Text.pdf](https://cepi.net/wp-content/uploads/2022/09/16092022_RVF-Funding-Call_Call-Text.pdf)

tion required to make the 100 Days target achievable for vaccines, including a library of prototype vaccines, clinical trial networks, identification of immune response markers, global manufacturing capacity, and disease surveillance.<sup>46</sup>

National governments are another major focus of vaccine efforts. BARDA recently published their 2022-26 Strategic Plan which includes a commitment to invest in at least five different vaccine platforms across an array of virus families with pandemic potential.<sup>47</sup> The National Institutes of Health (NIH) 2021-2025 strategic plan has a dedicated focus on influenza research including developing a pan-influenza vaccine<sup>48</sup> while NIAID is investing in pan-coronavirus vaccine candidates,<sup>49</sup> using innovative vaccine and adjuvant platforms. Japan launched SCARDA with \$1.2 billion of funding over 5 years (JPY 150.4 billion), for basic research in vaccine science and early-stage trials for vaccine candidates. The centre will initially invest in vaccine research for eight pathogens, including coronaviruses, mpox, Dengue, and Zika, using a range of technologies including mRNA, viral vectors, and recombinant proteins.<sup>50</sup> The EC (through HERA) will invest up to \$84 million (€80 million) in their “COVID-19 Vaccines 2.0” projects to foster the development of next generation vaccines, with the aim of finding promising technologies that can be used beyond COVID-19.<sup>51</sup>

Industry continues to play an important role in developing programmable vaccine platforms. In September 2022, Pfizer began dosing patients in a Phase 3 trial for its quadrivalent mRNA influenza vaccine candidate, the first Phase 3 efficacy study for an mRNA influenza vaccine.<sup>52</sup> Moderna<sup>53</sup> and BioNTech<sup>54</sup> are advancing a programme of vaccine candidates through clinical development, based on their experience developing mRNA vaccines for COVID-19. Other industry-sponsored programmes include vaccines for Zika, Nipah, and multiple efforts targeting influenza.

Notably, many of the efforts listed above are based on programmable platforms such as mRNA. Recognising some of the current challenges around this platform, CEPI and partners have reviewed the current technology landscape for mRNA vaccines and are currently assessing applications for efforts to further enhance mRNA platform technology.<sup>55</sup> To support enhancements in mRNA vaccines, CEPI is partnering with SK bioscience to develop mRNA

vaccines for Japanese encephalitis and Lassa Fever,<sup>56</sup> as both a means to establish additional experience in technical and regulatory processes required to bring mRNA products to market and to develop effective vaccines for these pathogens.

### Summary plans for 2023

A key goal set out in the first Implementation report is the development of 10 vaccine libraries for high priority viral families by 2026. CEPI will work toward the target of clinical proof of concept (PoC) for four virus family vaccine libraries and pre-clinical PoC for an additional six virus family vaccine libraries. Based on typical development timelines, including discovery, PoC, and clinical trials, an initial wave of vaccine candidates would likely need to enter pre-clinical PoC testing in 2023 to reach 10 libraries by 2026.

As mentioned above, the publication of priority pathogens by the WHO in 2023 coupled with the work led by CEPI and the University of California Davis to rank the potential of ‘Disease X’ emergence from key viral families will provide an opportunity to focus future R&D efforts. Further, these prioritisations offer an opportunity for collaboration between key players including national efforts such as those led by BARDA, SCARDA, HERA, and others. Besides targeting R&D toward specific pathogens or virus families, industry, academia, and public-private partnerships including Gavi and the Vaccine Innovation Prioritisation Strategy (VIPS) alliance should continue collaborative efforts to evolve vaccines toward WHO TPPs. This should include needle-free and other accessible vaccine delivery mechanisms as well as increasing thermostability.

International collaboration and coordination will be critical in the coming years to meet the goals of the 100 Days Mission in vaccines. CEPI’s 2022 replenishment was the start of a resource mobilisation effort to reach the 5-year target of \$3.5 billion, but there remains a gap to date of ~\$1.5 billion in unfunded investment. As with therapeutics and diagnostics, the International Pandemic Preparedness Secretariat is willing to work with global R&D funders to map ongoing research against priority pathogens, to identify gaps and support plans to address them.

<sup>46</sup> CEPI (2022). What will it take? Global coalition outlines how to beat the next Disease X pandemic in 100 days. [online] cept.net. Available at: [https://cepi.net/news\\_cepi/what-will-it-take-global-coalition-outlines-how-to-beat-the-next-disease-x-pandemic-in-100-days/](https://cepi.net/news_cepi/what-will-it-take-global-coalition-outlines-how-to-beat-the-next-disease-x-pandemic-in-100-days/)

<sup>47</sup> BARDA (2022). BARDA’s Strategic Plan 2022-2026. [online] medicalcountermeasures.gov. Available at: <https://www.medicalcountermeasures.gov/barda/strategic-plan/>

<sup>48</sup> NIH (2021). NIH-Wide Strategic Plan 2021-2025. [online] nih.gov. Available at: <https://www.nih.gov/sites/default/files/about-nih/strategic-plan-fy2021-2025-508.pdf>

<sup>49</sup> NIAID (2022). Coronavirus Vaccines and Prevention. [online] niaid.nih.gov. Available at: <https://www.niaid.nih.gov/diseases-conditions/coronavirus-vaccines-prevention>

<sup>50</sup> Mallapaty S, (2022). Japan’s \$2-billion initiative to prep pandemic vaccines in 100 days. [online] nature.com. Available at: <https://www.nature.com/articles/d41586-022-03000-3>

<sup>51</sup> EC (2022). European Health Union: first State of Health Preparedness Report shows EU’s strong progress. [online] ec.europa.eu. Available at: [https://ec.europa.eu/commission/presscorner/detail/en/ip\\_22\\_7154](https://ec.europa.eu/commission/presscorner/detail/en/ip_22_7154)

<sup>52</sup> Pfizer (2022). Pfizer <https://www.pfizer.com/news/press-release/press-release-detail/pfizer-initiates-phase-3-study-mrna-based-influenza-vaccine>

<sup>53</sup> Moderna (2022). Product Pipeline. [online] modernatx.com. Available at: <https://www.modernatx.com/en-US/research/product-pipeline>

<sup>54</sup> BioNTech (2022). Pipeline & Products. [online] biontech.com. Available at: <https://www.biontech.com/int/en/home/pipeline-and-products/pipeline.html>

<sup>55</sup> Information disclosed in proforma document or interviews with CEPI

<sup>56</sup> CEPI (2022). CEPI and SK bioscience Partner to Advance mRNA Vaccine Technology to Build Vaccine Library, Enable Rapid Response Against Disease X. [online] cepi.net. Available at: [https://cepi.net/news\\_cepi/cepi-and-sk-bioscience-partner-to-advance-mrna-vaccine-technology-to-build-vaccine-library-enable-rapid-response-against-disease-x/#:~:text=CEPI's%20partnerships%20with%20SK%20bioscience,now%20mRNA%2Dbased%20vaccine%20technologies.](https://cepi.net/news_cepi/cepi-and-sk-bioscience-partner-to-advance-mrna-vaccine-technology-to-build-vaccine-library-enable-rapid-response-against-disease-x/#:~:text=CEPI's%20partnerships%20with%20SK%20bioscience,now%20mRNA%2Dbased%20vaccine%20technologies.)



# Detailed DTV Roadmaps I/III

## Diagnostics R&D

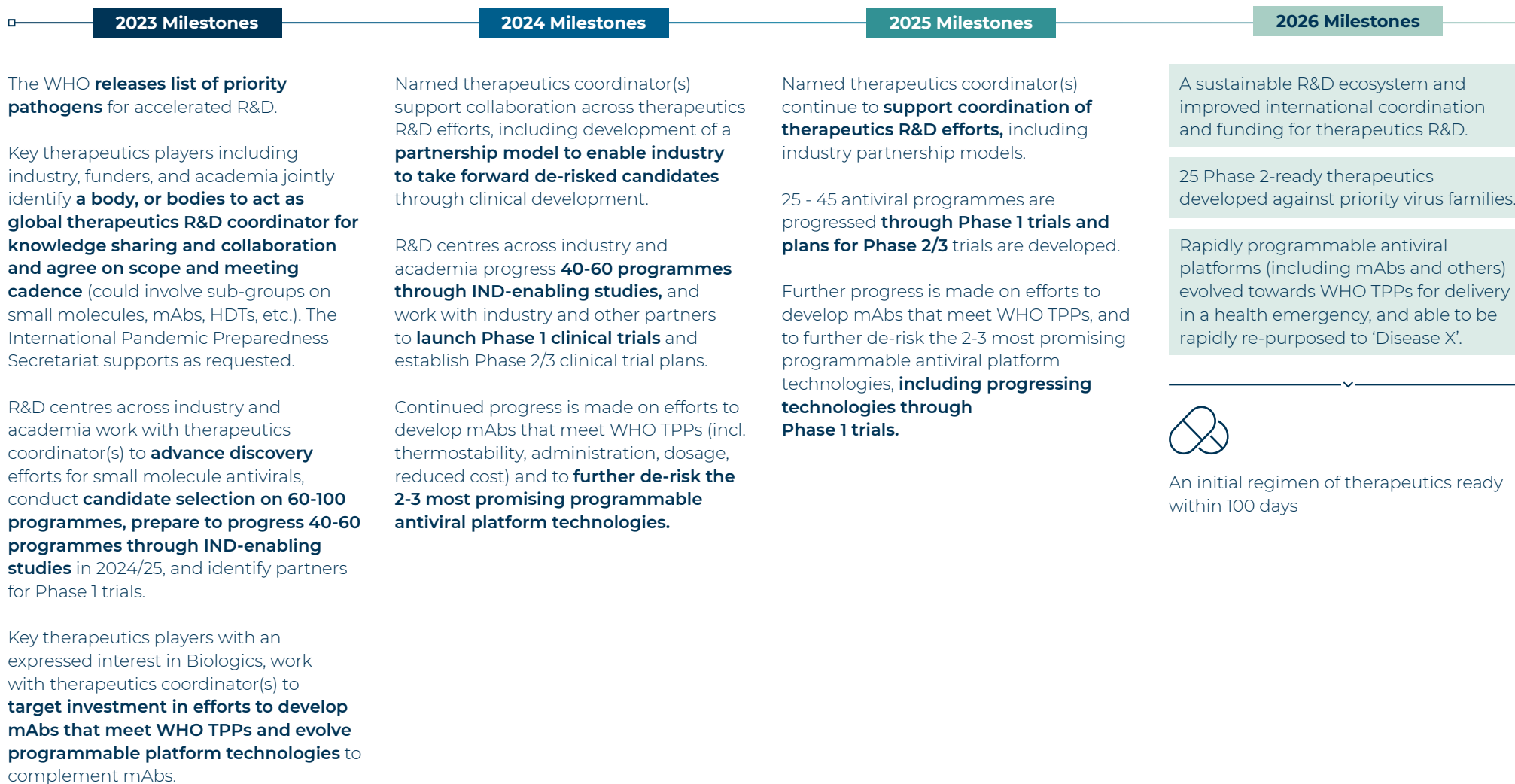


Note: Yearly milestones and 2026 outcomes have been updated since the 2021 Implementation Report given progress made and current landscape.

Roadmap is intended to deliver on diagnostics R&D. Complementary work related to surveillance and use in point-of-care settings has been removed to maintain focus

# Detailed DTV Roadmaps II/III

## Therapeutics R&D



1 IND = Investigational New Drug; Note: Yearly milestones and 2026 outcomes have been updated since the 2021 Implementation Report given progress made and current landscape. Recommendation #3 originally named therapeutic candidates against priority respiratory virus families. Respiratory has been removed given that pandemic pathogens can also be transmitted skin-to-skin, by blood, vector-borne etc. as evidenced through the mpox outbreak this year 2021 implementation report for recommendation #5 referred to reducing the cost of producing marketable mAbs to less than \$25/gram, this has been broadened to meeting WHO TPPs and cost reduction more generally

# Detailed DTV Roadmaps III/III

## Vaccines R&D



Note: Yearly milestones and 2026 outcomes have been updated since the 2021 Implementation Report given progress made and current landscape. Roadmap is intended to deliver on vaccines R&D. Complementary work related to vaccines manufacturing surveillance link to vaccines R&D has been removed to maintain focus.

# Making the Exceptional Routine by Embedding Best Practices

## Strengthening Global Surveillance

### Context and aims



The COVID-19 pandemic highlighted gaps in the way epidemiological information is collected, processed, shared, and accessed. Effective global surveillance is critical for global health as the first line of defence against pandemic threats (with critical input from diagnostics). When pathogens can be accurately and consistently identified, the 100 Days Mission can start to develop and deploy DTVs at pace. There are four key components of robust global pandemic surveillance:

- 1** An international network of local surveillance systems, able to identify and characterise local outbreaks for rapid responses
- 2** A global ecosystem of interoperable data analytics platforms to enable rapid data sharing that can identify emerging patterns and trends
- 3** Mechanisms for rapid exchange of pathogen samples to enable global R&D efforts for DTVs (including reciprocity with sample providers)
- 4** Routine use of diagnostics, especially in high-income settings where it has a key role in underpinning global affordability and promoting innovation

### Progress

The WHO is leading efforts on surveillance network capacity, interoperable data, and sample exchange processes. The WHO Hub for Pandemic and Epidemic Intelligence (Pandemic Hub) is the focal point of surveillance network efforts, having convened a series of successful discussions in 2022 on key surveillance topics.<sup>57</sup> Further, the Pandemic Hub took ownership of the Epidemic Intelligence from

Open Sources (EIOS) platform which consolidates 35,000 data feeds into a single, useable platform. The WHO BioHub launched a pilot effort in Switzerland to test global pathogen sharing protocols using SARS-CoV-2 variants.<sup>58</sup> Through this pilot, the BioHub is defining a system of incentives for global access and benefits sharing, which should minimise delays in pathogen accessibility to promote rapid development of DTVs. Additionally, the WHO announced plans to expand the Global Influenza Surveillance and Response System (GISRS) to GISRS+, to monitor additional respiratory pathogens.<sup>59</sup> In collaboration with the WHO's work, other partners have made significant progress in data sharing and interoperable analytics. data.org's Epiverse,<sup>60</sup> released an open-source software package for epidemiological analysis called Epiverse-TRACE,<sup>61</sup> that can support assessment of pandemic threats. HERA committed \$26.5 million (€25 million) to establish a laboratory network called DURABLE, which aims to exchange real-time data and early signals of biological health threats to inform decision-making at the global level. Finally, consolidating efforts across surveillance, the Pandemic Hub<sup>62</sup> and CEPI<sup>63</sup> each independently led international simulation workshops to assess collaborative surveillance and coordinated response protocols.



<sup>57</sup> Pandemic Hub (2022). Latest from the WHO Hub for Pandemic and Epidemic Intelligence. [online] pandemicandepidemicintel.substack.com. Available at: <https://pandemicandepidemicintel.substack.com/p/latest-from-the-who-hub-for-pandemic>

<sup>58</sup> WHO (2022). 1 Year Progress Report. [online] who.int. Available at: [https://cdn.who.int/media/docs/default-source/campaigns-and-initiatives/biohub/who\\_biohub-system\\_1\\_year\\_progress\\_report\\_may\\_2021\\_may\\_2022.pdf?sfvrsn=9477ff0c\\_1&download=true](https://cdn.who.int/media/docs/default-source/campaigns-and-initiatives/biohub/who_biohub-system_1_year_progress_report_may_2021_may_2022.pdf?sfvrsn=9477ff0c_1&download=true)

<sup>59</sup> WHO (2021). Surveillance of Influenza and SARS-CoV-2 and the Development of GISRS Plus. [online] who.int. Available at: <https://www.who.int/news-room/events/detail/2021/10/12/default-calendar/2nd-who-global-e-consultation-on-the-integrated-sentinel-surveillance-of-influenza-and-sars-cov-2-and-the-development-of-gisrs-plus>

<sup>60</sup> Data.org (2021). Wellcome and The Rockefeller Foundation Fund new data.org Initiative Epiverse. [online] data.org. Available at: <https://data.org/news/wellcome-rockefeller-fund-new-data-org-initiative-epiverse-analyzing-emergence-and-spread-of-pandemics/>

<sup>61</sup> Github (2022). Epiverse-Trace. [online] github.com. Available at: <https://github.com/epiverse-trace>

<sup>62</sup> Global Health Hub (2022). Results of the G7 Health Ministers' Meeting in Berlin. [online] globalhealthhub.de. Available at: <https://www.globalhealthhub.de/en/news/detail/g7-health-ministers-unite-to-secure-a-healthy-future-results-of-the-g7-health-ministers-meeting-in-berlin-may-19-20-2022>

<sup>63</sup> Information disclosed in proforma document or interviews with CEPI



Despite progress, there remains an outstanding gap in the routine use of diagnostics. Consistent use of diagnostics outside of global health emergencies has multiple advantages: it provides necessary data inputs into the surveillance network, promotes affordability of diagnostics for LMICs, and drives incentives for diagnostics R&D [see *Chapter 2 – Diagnostics*]. This year, COVID-19 testing waned as governments eased mandatory testing policies,<sup>64</sup> causing the diagnostics market to recalibrate. There have been some efforts to increase diagnostics usage for regional pathogens, including expanding tuberculosis testing in nine LMIC countries.<sup>65</sup> Nevertheless, it is important to ensure diagnostics are regularly used globally to support surveillance both in routine clinical care and during an emergency. Further, as discussed above in *Chapter 2 – Diagnostics*, it is critical to ensure accurate and standardised diagnostics are approved for use across geographies and therefore international regulators are encouraged to coordinate and collaborate in support of these efforts.

In addition to clinical diagnostics discussed above, as part of a One Health approach, environmental samples can be a key input to surveillance efforts. Wastewater surveillance increased in usage during COVID-19 as a cost-effective tool to provide early community-level detection<sup>66</sup> and has been used to detect mpox, flu, and respiratory syncytial virus as well.<sup>67</sup>

#### Summary plans for 2023

Key to supporting global surveillance efforts in 2023 is accelerating existing momentum, increasing routine use of diagnostics, and ensuring collaboration between surveillance and diagnostics R&D. Surveillance will continue to be driven primarily by the WHO but will require political support of the G7 and G20 by leading national diagnostic testing programmes and actively participating in global surveillance efforts.

The WHO will continue to support global surveillance priorities, including through the Pandemic Hub, GISRS+, and the Global Initiative on Sharing Avian Influenza Database (GISAID). The WHO and HERA will develop a partnership that funds epidemic and pandemic intelligence efforts, including sharing of data in collaboration with the Pandemic Hub.<sup>68</sup> Implementation plans to support GISRS+ expansion will continue to be developed to support

non-influenza respiratory pathogens. In collaboration with the Aids Healthcare Foundation (AHF), GISAID will launch efforts to increase genomic sequencing in LMICs. Further, the WHO's International Pandemic Surveillance Network (IPSN) will publish an investment case for sustaining national funding for pathogen surveillance.

The BioHub will apply learnings from the Switzerland sample exchange pilot to propose mechanisms for reciprocity. It is important to note here that learnings from COVID-19 demonstrate that unhindered and rapid access to pathogen sequence information fuels R&D efforts, which should be considered in development of future pathogen sharing models. There are concerns related to transactional models of pathogen sharing (such as those that apply to the Nagoya Protocol) that would not facilitate sufficiently rapid pathogen sharing. Therefore, it would be worthwhile to further discuss the development of a system coordinated and operated internationally. Key to effective sample sharing is streamlined processes that allow for quick and unhindered access to pathogens to collect and share biological samples rapidly. This could take the form of pre-agreed exchange protocols and / or an international specimen bank that would have the dual purpose of supporting surveillance and testing of diagnostics in development. Still, pathogen exchange protocols are complex and should be covered in negotiations of the Pandemic Instrument that will set guidance for “rules of the road” during the response to future pandemics [see *Chapter 4 – Rigorous Global Health Governance*]. Additional environmental surveillance efforts will be supported by the WHO, especially in areas with high risk of zoonotic crossover.

There is significant potential in organisations such as data.org and the Global Pandemic Data Alliance (GPDA) to lead meaningful contributions to surveillance. For these initiatives to grow, they will require continued funding and political support from successive G7 and G20 presidencies. Subject to this funding and support, in 2023, Epiverse will begin testing and deploying the Epiverse-TRACE suite of tools with country partners and will publish a global maturity assessment of data capabilities.

#### **Improvements to Clinical Trials Capability and Regulatory Processes**

##### Context and aims

Clinical trials and regulatory processes were areas of exceptional innovation during the COVID-19 response. The success and impact of platform trials such as the UK's RECOVERY trials demonstrated a new paradigm for clinical trials at-scale that is applicable well beyond a

<sup>64</sup> Our World in Data (2022). Daily COVID-19 tests per thousand people, based on a 7-day rolling average. [online] ourworldindata.org. Available at: <https://ourworldindata.org/grapher/daily-tests-per-thousand-people-smoothed-7-day>

<sup>65</sup> Unitaaid (2022). Unitaaid Launches Major New Investment to Increase Tuberculosis Detection and Find the Missing Millions. [online] unitaid.org. Available at: <https://unitaid.org/news-blog/unitaid-launches-major-new-investment-to-increase-tuberculosis-detection-and-find-the-missing-millions/#en>

<sup>66</sup> BMJ (2022). What poo tells us: Wastewater surveillance comes of age amid covid, monkeypox and polio. [online] bmj.com. Available at: <https://www.bmj.com/content/378/bmj.o1869>

<sup>67</sup> WastewaterSCAN (2022). Partnership across academia, industry, public leaders and philanthropic organisations to monitor disease through municipal wastewater systems to inform public health responses locally and nationally. [online] wastewaterscan.org. Available at: <https://wastewaterscan.org/about/>

<sup>68</sup> European Commission (2022). Global Health: HERA and WHO launch new €15 million partnership for stronger pandemic preparedness and response. [online] ec.europa.eu. Available at: [https://ec.europa.eu/commission/presscorner/detail/en/mex\\_22\\_7591](https://ec.europa.eu/commission/presscorner/detail/en/mex_22_7591)

pandemic response. RECOVERY was able to set up and recruit over 10,000 patients in less than 2 months. However, platform trials like RECOVERY, PANORAMIC, Solidarity Therapeutics,<sup>69</sup> and RECAM-CAP were the exception, not the rule, and much of the evidence generation during COVID-19 was characterised by duplication, poor quality study design, and chronic underpowering. For example, more than 250 trials between February 2020-2021 studied hydroxychloroquine,<sup>70</sup> but only 5% met the WHO criteria for actionable data.<sup>71</sup> Additionally, there was little to no international coordination of trial efforts and trials run across countries used different endpoints, assays, and inclusion criteria which made post-hoc meta-analyses across trials difficult.

Beyond rapid and efficient execution of trials, regulators also worked to achieve accelerated review timelines and demonstrated unprecedented levels of engagement with innovators to provide guidance and review data rapidly during COVID-19.

Still, clear challenges remain to accelerate clinical trials and shorten regulatory timelines in peacetime to prepare for a future pandemic. Adherence to timelines, reliability of regulatory processes, and mutual recognition can be improved, especially in some LMICs, to support building a strong R&D environment that can support clinical trials and regulatory review in a future pandemic.

To combat these challenges and prepare to accelerate and streamline clinical trial processes, there are four outcomes proposed by 2026:

- 1** Sufficient clinical trial capacity and capability, especially in areas where outbreaks are likely
- 2** Coordinated clinical pipelines for this global network of trials
- 3** Best practices on trial design embedded across global efforts
- 4** Flexible regulatory procedures, including pre-agreed emergency regulatory procedures during a PHEIC

## Progress

Overall progress in accelerating clinical trials and regulatory processes has centred upon a resolution adopted by WHO member states at the 75th WHA, led by the UK and Argentina and supported by the WHO Secretariat titled, 'Strengthening clinical trials to provide high-quality evidence on health interventions and to improve research quality and coordination'.<sup>72</sup> This resolution sets out a series of recommendations that will continue to strengthen clinical trial capacity globally, coordinate research priorities based on funding and needs, enable clinical governance processes in line with risk, streamline regulatory procedures in peacetime and during a PHEIC, and increase sharing of clinical trial methodologies, results, and regulatory assessments. Further, the WHO announced that the medical products regulatory agencies of China, Egypt, Nigeria, and South Africa reached maturity level 3<sup>73,74</sup> and Korea and Singapore reached level 4<sup>75</sup> indicating that the overall regulatory system is "stable, well-functioning, and integrated",<sup>76</sup> and is contributing to improving global clinical trial capacity in those countries.



Encouragingly, additional global efforts have sought to progress individual elements of the vision for clinical trials laid out at the 75th WHA. GloPID-R,<sup>77</sup> CEPI,<sup>78</sup> the WHO,<sup>79</sup> and Bill and Melinda Gates Foundation (BMGF)<sup>80</sup> have initiated work to build clinical trial capacity and capability in geographies most at risk from emerging infectious diseases. Notably, it is key to retain clinical trial capacity globally through testing of routine products in diverse populations. As global clinical trial capacity is developed, coordination becomes increasingly important. New governance models have been proposed in the US and Europe to support international coordination of research. The European Clinical Trial Network for Infectious Disease

<sup>69</sup> Solidarity Therapeutics trial initially covered remdesivir, lopinavir, hydroxychloroquine, and interferon

<sup>70</sup> Pearson H. (2021). How COVID broke the evidence pipeline. [online] nature.com. Available at: <https://www.nature.com/articles/d41586-021-01246-x>

<sup>71</sup> WHO (2021). Coordination between WHO Living Guidelines and WHO EUL and PQ. [online] extranet.who.int. Available at: [https://extranet.who.int/pqweb/sites/default/files/documents/Determining\\_eligibility\\_criteria\\_PQ\\_EUL\\_ERP\\_medicines\\_14April2021.pdf](https://extranet.who.int/pqweb/sites/default/files/documents/Determining_eligibility_criteria_PQ_EUL_ERP_medicines_14April2021.pdf)

<sup>72</sup> WHO (2022). New WHO Resolution on Clinical Trials. [online] who.int. Available at: <https://www.who.int/news/item/12-09-2022-new-wha-resolution-on-clinical-trials>

<sup>73</sup> WHO (2022). Egypt and Nigeria medicines regulators achieve high maturity level in WHO classification and WHO launches list of regulatory authorities that meet international standards. [online] who.int. Available at: <https://www.who.int/news/item/30-03-2022-egypt-and-nigeria-medicines-regulators-achieve-high-maturity-level-in-who-classification-and-who-launches-list-of-regulatory-authorities-that-meet-international-standards>

<sup>74</sup> WHO (2022). South Africa's vaccine regulator reaches new WHO level to ensure safety, quality and effectiveness. [online] who.int. Available at: <https://www.who.int/news/item/05-10-2022-south-africa-s-vaccine-regulator-reaches-new-who-level-to-ensure-safety-quality-effectiveness>

<sup>75</sup> CDC (2022). List of National Regulatory Authorities (NRAs) operating at maturity level 3 (ML3) and maturity level 4 (ML4). [online] cdn.who.int. Available at: [https://cdn.who.int/media/docs/default-source/medicines/regulatory-systems/list-of-nras-operating-at-ml3-and-ml4.v2.pdf?sfvrsn=ee93064f\\_9&download=true](https://cdn.who.int/media/docs/default-source/medicines/regulatory-systems/list-of-nras-operating-at-ml3-and-ml4.v2.pdf?sfvrsn=ee93064f_9&download=true)

<sup>76</sup> According to the WHA resolution 67.20

<sup>77</sup> GloPID-R (2022). Progress in the implementation of GloPID-R's regional hub strategy. [online] glop-id-r.org. Available at: <https://www.glop-id-r.org/articles-newsletter/progress-in-the-implementation-of-glop-id-rs-regional-hub-strategy/>

<sup>78</sup> CEPI (2021). CEPI Results Framework. [online] cepi.net. Available at: <https://cepi.net/wp-content/uploads/2022/01/20211126-CEPI-2.0-Results-Framework-v1.0-jan-21.pdf>

<sup>79</sup> WHO (2022). Solidarity Vaccine Trials. [online] who.int. Available at: <https://www.who.int/emergencies/diseases/novel-coronavirus-2019/global-research-on-novel-coronavirus-2019-ncov/solidarity-trial-of-covid-19-vaccines>

<sup>80</sup> Clemens, S.A.C., Sekine, A.K., Tovar-Moll, F., Clemens, R. (2022). Building clinical trial capacity for vaccine efficacy trials in Latin America in response to the pandemic. [online] sciencedirect.com. Available at: <https://doi.org/10.1016/j.jvax.2022.100238>

(ECRAID)<sup>81</sup> was established as a pan-European network of clinical trial platforms to offer a single point of access to initiate clinical trials in 2000+ sites across 40 countries. Coordination of global research funding initiatives have been led by GloPID-R with engagement from the UK Department of Health and Social Care (DHSC), who co-hosted a Funding Roundtable event with global research funders, the WHO, and the G7.<sup>82</sup>

Learnings from COVID-19 provide an opportunity to embed best practices for clinical trial and regulatory processes overall, including in routine and emergency settings. These opportunities ideally would be embraced by all parties, including through updates currently being drafted to the International Council for Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH)'s 'Good Clinical Practice' guidelines.<sup>83</sup> The ICH guidelines are a set of internationally recognised ethical and scientific quality requirements that must be followed for clinical trials with human subjects. The Good Clinical Trials Collaborative (GCTC) also published draft guidelines in 2022 for execution of well-planned, well-run, and clinically relevant trials.<sup>84</sup> Further, learnings from this year's Ebola outbreak highlight the need for pre-approved clinical trial protocols in countries with high risk of outbreaks in order to execute at speed.

Globally, regulators have made efforts to revise processes, incorporating lessons and flexible regulatory procedures used during COVID-19 into business-as-usual. Regulatory authorities in countries such as the UK<sup>85</sup> and Canada<sup>86</sup> are proposing the use of risk-based frameworks to accelerate approvals that would allow some clinical trials (e.g., for medicines that have been approved for human use elsewhere in the world) to be conducted without prior regula-

tory review. Input collected on these proposals should be shared with international stakeholders to support successful implementation across countries. Risk-based frameworks are critical for a rapid response especially in light of the potential impact of emerging viruses and viral variants. With this in mind, it will be important to advance these types of frameworks globally in the near-term while maintaining safety at the forefront. Risk assessments should balance the uncertainty of human use with the urgent need for a new vaccine. Uncertainty can be overcome with baseline knowledge of the new construct, including through platform or animal data, immune responses to similar vaccines, safety profiles, and knowledge of the virus (including transmission patterns such as RO). Importantly, the International Coalition of Medicines Regulatory Authorities (ICMRA) supports risk-based and other flexible regulatory initiatives and have recommended permanent structures across Stringent Regulatory Authorities (SRAs) for international alignment and cooperation on regulatory processes, including coordinating clinical evaluations for expedited market approval.<sup>87</sup>

### Summary plans for 2023

As DTVs are developed over the next few years, it will be increasingly important to continue to ensure adequate clinical trial capacity for rapid testing. Despite major successes in clinical trial and regulatory processes during COVID-19, there remains significant outstanding effort required to develop clinical trial capabilities globally, coordinate and prioritise capacity, and accelerate regulatory procedures.

*"[Regulatory] risk assessments should balance uncertainty of human use with the urgent need for a new vaccine"*



<sup>81</sup> ECRAID (2022). Ecraid Kick-Off and Launch. [online] ecraid.eu. Available at: <https://www.ecraid.eu/ecraid-launch>

<sup>82</sup> GloPID-R (2022). GloPID-R and UK DHSC Organise Funders' Roundtable to Strengthen the Clinical Trial Ecosystem. [online] glopid-r.org. Available at: <https://www.glopid-r.org/glopid-r-and-uk-dhsc-organise-funders-roundtable-to-strengthen-the-clinical-trials-ecosystem/>

<sup>83</sup> ICH (2022). 2023 Annual Workplan includes updates to Good Clinical Practice (E6 R3). [online] ich.org. Available at: [https://admin.ich.org/sites/default/files/inline-files/ICHAssociation\\_WorkPlan\\_2023\\_Approved\\_2022\\_1018.pdf](https://admin.ich.org/sites/default/files/inline-files/ICHAssociation_WorkPlan_2023_Approved_2022_1018.pdf)

<sup>84</sup> Good Clinical Trials (2022). Guidance. [online] goodtrials.org. Available at: <https://www.goodtrials.org/resources/guidance-in-world-languages/>

<sup>85</sup> UK MHRA (2022). Proposals for legislative changes for clinical trials. [online] gov.uk. Available at: <https://www.gov.uk/government/consultations/consultation-on-proposals-for-legislative-changes-for-clinical-trials/proposals-for-legislative-changes-for-clinical-trials>

<sup>86</sup> Health Canada (2022). Forward Regulatory Plan 2022-2024 (Modernisation of the Regulation of Clinical Trials). [online] canada.ca. Available at: <https://www.canada.ca/en/health-canada/corporate/about-health-canada/legislation-guidelines/acts-regulations/forward-regulatory-plan/plan/modernization-regulation-clinical-trials.html>

<sup>87</sup> ICMRA (2022). Updated Framework for the Involvement of Health Regulatory Authorities in the Management of Global Health Crises, Version 2. [online] icmra.info. Available at: [https://www.icmra.info/drupal/sites/default/files/2022-10/icmra\\_framework\\_for\\_crisis\\_management.pdf](https://www.icmra.info/drupal/sites/default/files/2022-10/icmra_framework_for_crisis_management.pdf)

## Regulators used cumulative evidence from three closely related Pfizer-BioNTech platform vaccines to reduce need for new trials

**CASE STUDY:** Accelerated regulatory approval in COVID-19 with risk-based approach

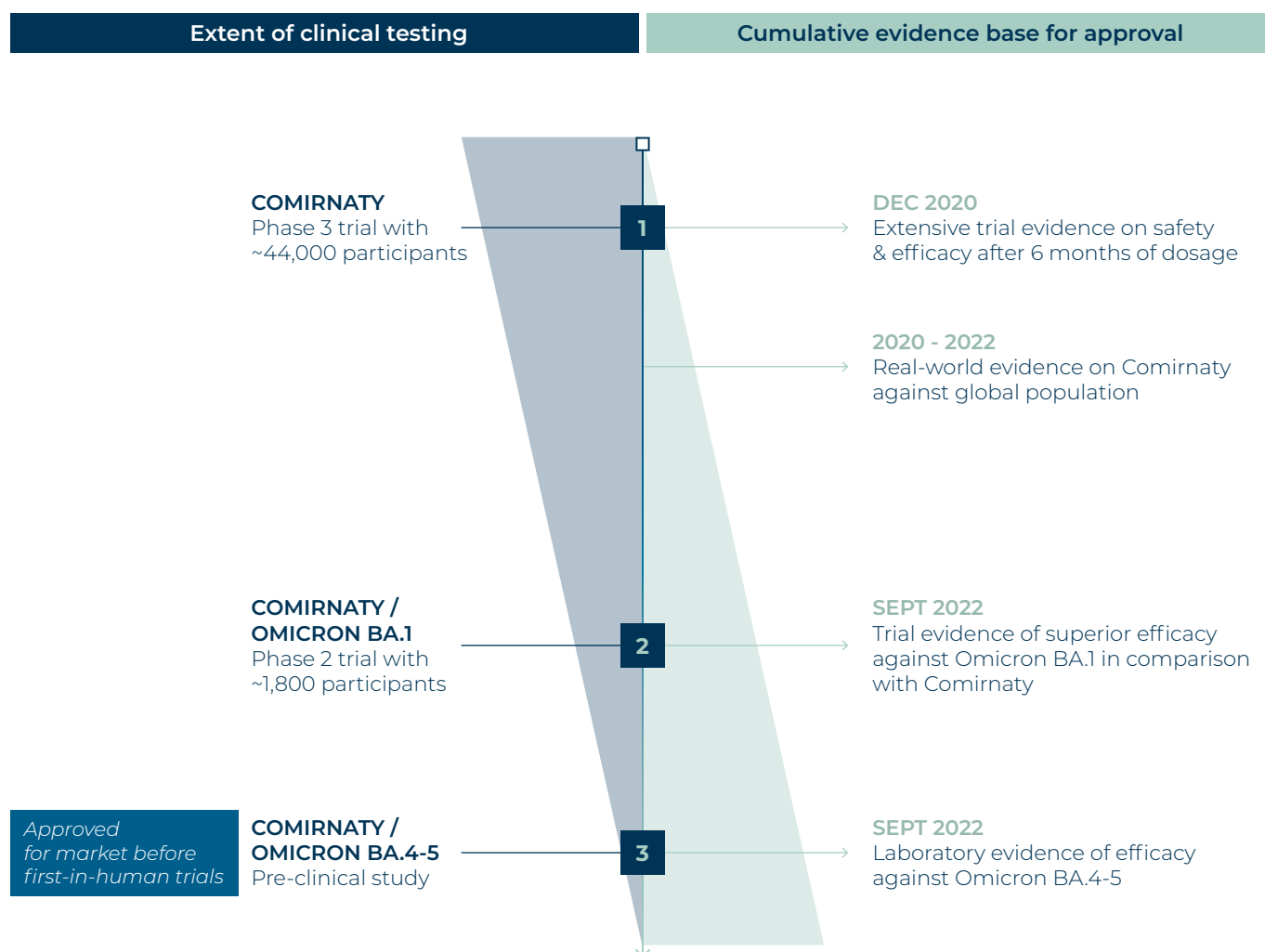


Figure 8. Example of accelerated regulatory approval of three Pfizer-BioNTech platform vaccines through risk-based approach. The 2022 Comirnaty/Omicron BA.4-5 vaccine was approved at pre-clinical stage by using safety and efficacy clinical data of the previously approved, closely related 2022 Comirnaty/Omicron BA.1 vaccine.<sup>88, 89, 90</sup>

To advance these aims in 2023, the WHO will continue to support implementation of the clinical trials resolution from the 75th WHA, reporting on progress at the 76th WHA in 2023. Underscoring the importance of clinical trials to DTVs, CEPI's latest paper<sup>91</sup> noted that establishing global clinical trial networks is one of the five key areas of innovation required to make the 100 Days Mission a reality. As a first step, the WHO's capacity building efforts should

ensure that Emergency Use Procedures are implemented globally.

GloPID-R will launch another regional clinical trial hub in Africa (the first hub was in Asia-Pacific) and continue to develop plans for other hubs. The Pandemic Preparedness Platform for Health and Emerging Infection Response (PANTHER) will create a flexible clinical research platform

<sup>88</sup> European Medicines Agency (2022). First adapted COVID-19 booster vaccines recommended for approval in the EU. [online] ema.europa.eu. Available at: <https://www.ema.europa.eu/en/news/first-adapted-covid-19-booster-vaccines-recommended-approval-eu>

<sup>89</sup> Pfizer (2021). Pfizer-BioNTech COVID-19 Vaccine COMIRNATY® Receives Full U.S. FDA Approval for Individuals 16 Years and Older. [online] pfizer.com. Available at: <https://www.pfizer.com/news/press-release/press-release-detail/pfizer-biontech-covid-19-vaccine-comirnaty-receives-full>

<sup>90</sup> European Medicines Agency (2022). Adapted vaccine targeting BA.4 and BA.5 Omicron variants and original SARS-CoV-2 recommended for approval. [online] ema.europa.eu. Available at: <https://www.ema.europa.eu/en/news/adapted-vaccine-targeting-ba4-ba5-omicron-variants-original-sars-cov-2-recommended-approval>

<sup>91</sup> CEPI (2022). What will it take? Global coalition outlines how to beat the next Disease X pandemic in 100 days. [online] cept.net. Available at: [https://cepi.net/news\\_cepi/what-will-it-take-global-coalition-outlines-how-to-beat-the-next-disease-x-pandemic-in-100-days/](https://cepi.net/news_cepi/what-will-it-take-global-coalition-outlines-how-to-beat-the-next-disease-x-pandemic-in-100-days/)

to be used where outbreaks arise.<sup>92</sup> Where DNDi conducts trials (e.g., in Latin America and Africa), they will continue to also support infrastructure improvements, laboratory renovations, and provision of essential equipment to ensure trials are carried out in accordance with Good Clinical Practice. The NIH ACTIV clinical trial working group and the Special Programme for Research and Training in Tropical Diseases (TDR) developed an inventory of clinical trial capacity that can be leveraged to support closing gaps in other geographies.<sup>93,94</sup> CEPI will progress developing clinical preparedness networks for vaccines and will synergise these with a focused entry into supporting coordinated evidence generation for therapeutics. Developing and maintaining clinical trial capacity globally is important to keep capacity ‘warm’ that can be diverted for the next pandemic. Further, industry and research organisations need to be willing to use diversified networks of clinical trial sites in all regions to ensure established capacity is maintained and increase representation of all population groups and globally-relevant disease burdens.

Regulatory stakeholders should collectively build lessons learnt from COVID-19. Country-led efforts need to maintain momentum in this space and develop implementation roadmaps to make use of risk-based regulatory processes. GCTC will convene a group of key global actors to explore effective implementation of the clinical trial guidance principles, particularly in role-specific contexts (e.g., working with regulatory agencies) to review and agree



streamlined and effective procedures from the GCTC principles. New regulatory processes can be codified through the ICH's standards for ‘Good Clinical Practice’ which are currently under revision. Related to post-licensure, ICMRA will work with the ICH, other partners, and regulators to harmonise and reduce duplication in post-approval Chemistry, Manufacturing, and Control (CMC) changes required to make DTVs globally available to patients. Finally, as indicated in the original 100 Days Mission report, regulatory processes would benefit from aligned mechanisms for mutual recognition of clinical trials and DTVs which should be explored in 2023 (starting with diagnostics to ensure they are available globally as a first line of defence).

## Regionalised Manufacturing of DTVs

### Context and aims



Once DTVs are developed and approved, sufficient manufacturing capacity that meets international quality standards is required to support demand across all regions in the event of an outbreak. During COVID-19, significant DTV manufacturing capacity was mobilised and industry scaled DTV supply by leveraging their expertise in end-to-end management of complex supply chains and collaboration with experienced contract manufacturers. However, the equity and access gap remained especially acute for vaccines in Africa and other LMICs. Building regionalised vaccine manufacturing capacity in a sustainable manner will be a long-term effort and therefore shouldn't be seen as a ‘silver bullet’ for equity and resilience. It needs to be progressed alongside other access improvements at all stages of the DTV value chain. In the long-term, to ensure equity and sustainability across all DTVs, regionalised manufacturing plans should ensure:

- 1** Sufficient capacity and capability (including workforce) to produce an initial regional DTV supply of approved products and associated adequate supply of raw materials
- 2** A sustainable collaborative ecosystem that supports regional capacity development, including technology transfer, financing models, and market shaping

Note that while major steps can be taken over the period to 2026, building sustainable regionalised manufacturing will require concerted focus over the coming decades.

<sup>92</sup> ISGlobal (2022). Presentation of the new PANdemic preparedness platform for Health and Emerging infections Response (PANTHER) [online] isglobal.org. Available at: <https://www.isglobal.org/-/presentation-of-the-new-pandemic-preparedness-platform-for-health-and-emerging-infections-response-panther>

<sup>93</sup> NIH ACTIV (2020). Clinical Trial Capacity Working Group overview. [online] nih.gov. Available at: <https://www.nih.gov/research-training/medical-research-initiatives/activ/clinical-trial-capacity-working-group>

<sup>94</sup> TDR (2021). Rapid Scoping Study on Global Clinical Trials Infrastructure. [online] tdr.who.int. Available at: <https://tdr.who.int/docs/librariesprovider10/essence/rapid-scoping-study-report.pdf>

## Progress

Building on the 2021 WHO resolution on ‘Strengthening local production of medicines and other health technologies to improve access’,<sup>95</sup> regionalised vaccine manufacturing has received significant political attention in 2022, including through the Indonesian presidency of the G20, the G7 Pact for Pandemic Readiness,<sup>96</sup> and numerous publications specifically focused on Africa, including from PAVM,<sup>97</sup> Gavi,<sup>98,99</sup> and the EU-Africa Business Forum (EABF) in coordination with African Manufacturers.<sup>100</sup>

Regional capacity proposals are designed to increase LMIC independence and aim to increase supply security, strengthen pandemic preparedness, and better tackle endemic diseases. To date, many regionalised manufacturing efforts have been focused on mRNA vaccines given their success during COVID-19 and ability to be rapidly reprogrammed to a new pathogen, which is reflected in the discussion of progress and future plans here. However, sustainable business models should plan beyond vaccine mRNA platforms (e.g., adenovirus, DNA, and others) and be based on both regional and global demand. Further, sustainable business models are likely to explore novel technologies such as modularised facilities and blow-fill-seal technology to achieve sustainable economics.

Industry efforts to build vaccine manufacturing capacity in Africa have been led by numerous players including Biovac,<sup>101</sup> Moderna,<sup>102</sup> BioNTech,<sup>103</sup> Afrigen,<sup>104</sup> Recipharm,<sup>105</sup> and Eva Pharma.<sup>106</sup> Biovac will develop manufacturing capabilities in South Africa to manufacture routine vaccinations administered in Africa as well as COVID-19 vaccines. Moderna will build an mRNA facility in Kenya that can manufacture up to 500 million vaccine doses per year. BioNTech began construction of their first “BioNTainer” site in Rwanda, which will formulate and manufacture mRNA vaccines and coordinate with local partners to fill-and-finish. Afrigen Biologics and Univercells entered into a

collaboration to develop the first African-owned COVID-19 mRNA vaccine in Cape Town. Recipharm, working with the Moroccan government and leading banks, is investing in a facility called Sensyo which aims to be the largest fill-and-finish platform in Africa, scaling up to manufacture more than 20 vaccines (using mRNA and other platforms). Eva Pharma announced a new vaccine manufacturing facility in Cairo for both egg-based and cell-culture vaccines.

International organisations, including Institut Pasteur de Dakar,<sup>107</sup> CEPI, and BMGF, among many others have also announced plans for expansion or creation of existing vaccine manufacturing capacity in Africa. The Institut Pasteur de Dakar, CEPI, and others have joined in a partnership<sup>108</sup> to build a vaccine manufacturing facility in Senegal that will produce COVID-19 mRNA vaccines as well as vaccines

*“Regional capacity proposals are designed to increase LMIC independence and aim to increase supply security to tackle endemic diseases”*

<sup>95</sup> WHO (2022). Strengthening local production of medicines and other health technologies to improve access. [online] who.int. Available at: [https://apps.who.int/gb/ebwha/pdf\\_files/WHA74/A74\\_ACONF1-en.pdf](https://apps.who.int/gb/ebwha/pdf_files/WHA74/A74_ACONF1-en.pdf)

<sup>96</sup> G7 Germany Presidency (2022). G7 Pact for Pandemic Readiness. [online] bundesgesundheitsministerium.de. Available at: [https://www.bundesgesundheitsministerium.de/fileadmin/Dateien/3\\_Downloads/G/G7/20220520\\_English\\_G7\\_Pact\\_for\\_Pandemic\\_Readiness.pdf](https://www.bundesgesundheitsministerium.de/fileadmin/Dateien/3_Downloads/G/G7/20220520_English_G7_Pact_for_Pandemic_Readiness.pdf)

<sup>97</sup> PAVM (2022). Partnership for African Vaccine Manufacturing (PAVM) Framework for Action. [online] africacdc.org. Available at: <https://africacdc.org/download/partnerships-for-african-vaccine-manufacturing-pavm-framework-for-action/>

<sup>98</sup> Gavi (2022). Expanding Sustainable Vaccine Manufacturing in Africa. [online] gavi.org. Available at <https://www.gavi.org/sites/default/files/document/2022/Gavi-Expanding-Sustainable-Vaccine-Manufacturing-in-Africa-2022.pdf>

<sup>99</sup> Gavi (2022). A New Era of Vaccine Manufacturing in Africa 2022. [online] gavi.org. Available at: <https://www.gavi.org/news/document-library/new-era-vaccine-manufacturing-in-africa>

<sup>100</sup> EU-Africa Business Forum (2022). Joint Declaration of the Business Organisations. [online]. Euafrica-businessforum.com Available at: [https://www.euafrica-businessforum.com/sites/default/files/joint\\_business\\_declaration\\_annexes\\_7th\\_eu-africa\\_business\\_forum.pdf](https://www.euafrica-businessforum.com/sites/default/files/joint_business_declaration_annexes_7th_eu-africa_business_forum.pdf)

<sup>101</sup> DFC (2022). Biovac and Development Partners Collaborate to Support South Africa's Vaccine Manufacturing Expansion and Advance Long-Term Health and Health Security Across Africa. [online] dfc.gov. Available at <https://www.dfc.gov/media/press-releases/biovac-and-development-partners-collaborate-support-south-africas-vaccine>

<sup>102</sup> <https://www.fiercepharma.com/manufacturing/moderna-taps-kenya-site-500m-mrna-manufacturing-facility>

<sup>103</sup> BioNTech (2022). BioNTech Starts Construction of First mRNA Vaccine Manufacturing Facility in Africa. [online] investors.biontech.de. Available at: <https://investors.biontech.de/news-releases/news-release-details/biontech-starts-construction-first-mrna-vaccine-manufacturing>

<sup>104</sup> Univercells (2022). New agreement paves way for development of first African-owned COVID-19 vaccine. [online] univercells.com. Available at: <https://www.univercells.com/news/new-agreement-paves-way-for-development-of-first-african-owned-covid-19-vaccine>

<sup>105</sup> ContractPharma (2022). Construction Works Launch at New Fill Finish Facility in Morocco. [online] contractpharma.com Available at: [https://www.contractpharma.com/contents/view\\_breaking-news/2022-01-28/construction-works-launch-at-new-fill-finish-facility-in-morocco/](https://www.contractpharma.com/contents/view_breaking-news/2022-01-28/construction-works-launch-at-new-fill-finish-facility-in-morocco/)

<sup>106</sup> Business Wire (2021). EVA Pharma's New Cairo Vaccine Manufacturing Facility Set for Production In 2022. [online] businesswire.com. Available at: <https://www.businesswire.com/news/home/20211108005660/en/EVA-Pharmas-New-Cairo-Vaccine-Manufacturing-Facility-Set-for-Production-In-2022>

<sup>107</sup> KeyPlants (2022). KeyPlants ships first-of-its-kind vaccine manufacturing facility to Africa. [online] keyplants.com Available at: <https://keyplants.com/keyplants-ships-first-of-its-kind-vaccine-manufacturing-facility-to-africa/>

<sup>108</sup> CEPI (2022). CEPI and Institut Pasteur de Dakar partner to advance COVID-19 vaccine manufacturing in Africa. [online] cepi.net. Available at: [https://cepi.net/news\\_cepi/cepi-and-institut-pasteur-de-dakar-partner-to-advance-covid-19-vaccine-manufacturing-in-africa/](https://cepi.net/news_cepi/cepi-and-institut-pasteur-de-dakar-partner-to-advance-covid-19-vaccine-manufacturing-in-africa/)

against other endemic diseases such as yellow fever. BMGF is also supporting the Institut Pasteur de Dakar to produce measles and rubella viral vector vaccine material, in collaboration with Batavia Biosciences and Univercells.<sup>109</sup> Further, CEPI and BMGF announced \$30 million in funding to Aspen Pharmacare to manufacture routine African vaccines.

Outside of Africa, Canada announced funding toward a Pan-American Health Organisation (PAHO) initiative to increase vaccine production in Latin America and the Caribbean.<sup>110</sup> Vaxthera began construction work to build a plant that will produce vaccines and biologics for Colombia and the region with capabilities for fill-and-finish, individual production blocks, and R&D centres.<sup>111</sup>

Note that many (but not all) of the efforts globally are focused on mRNA technology, and further progress is required to build and strengthen regional capacities across a diverse range of platform technologies. Further, as numerous initiatives detailed above, new manufacturing capacity should be flexible enough to produce both routine and pandemic vaccines. Strong routine vaccination strategies ensure that regional capacity is used and maintained, even during peacetime, to support the ability to scale up pandemic vaccine development when necessary.

Besides the direct support that routine vaccinations and consistent demand provides to manufacturing efforts, supportive economics, including multilateral purchasing commitments, can further ensure that physical manufacturing capacity is utilised efficiently. It is important to learn from past experiences in distributed manufacturing of influenza and COVID-19 vaccines. As an example, in March 2022, Aspen entered an agreement with Johnson & Johnson to fill-and-finish, as well as package and distribute their COVID-19 vaccine in South Africa (which was then converted into a full technology transfer agreement).<sup>112</sup> However, five months after the agreement, production was halted due to low demand and a consequent lack of long-term purchasing agreements.<sup>113</sup> Critically, regionalised manufacturing efforts should not be expected to be cost-competitive in the mid-term, but long-term economic viability for all stakeholders (manufacturers, private funders, etc.) can be managed, and the secondary bene-

fits to local economies and societies should be considered in any cost-benefit analysis.

Additionally, maintenance of the global supply-demand equilibrium needs to be considered to uphold successes to date in bringing affordable vaccines to LMICs. To this end, both Gavi and PAVM have led efforts to sustain overall market health and encourage new entrants to consider sustainability. Gavi has significant market influence as the largest single supplier of vaccines globally (including in Africa, ~50% by value in 2020<sup>114</sup>). Working with the G7, G20, and the African Union, Gavi has outlined and board-approved a ten-point plan for G7 Development Ministers, African countries, industry, and international partners to support the development of sustainable vaccine manufacturing in Africa,<sup>115</sup> and committed to its own four-pillar plan to support the agenda.<sup>116</sup> Gavi plans to provide portfolio planning support for antigens and products, adapt the Healthy Market Framework and Product Menu Criteria to facilitate listing and adoption of new regional products, and provide investors with more predictability around eventual demand. It will further develop plans for a financial instrument to support entry of African manufacturers. The PAVM framework includes a workstream on market design and demand intelligence as well as a programme to explore a potential procurement architecture that capitalises on current Africa-led pooled procurement mechanisms. Relatedly, the 7th EABF Joint Declaration outlined key success factors for an attractive health industry environment in Africa that applies to vaccine manufacturing, including sustainable financing, stable business practices that incentivise local innovation, predictable local demand, technology transfer, timely regulatory processes, and free trade. Further efforts to deliver on these success factors, as well as work to reduce the risks faced by new entrants in Africa is needed. Examples include improving confidence that long-term returns can be obtained and ensuring adequate collaboration among players in support of harmonisation of supply and demand.

Technology transfer is also critically important for regionalised manufacturing efforts. From the outset of the pandemic, industry demonstrated how beneficial technology transfer can be: collaborations resulted in numerous voluntary partnerships for vaccine production, of which ~89%

<sup>109</sup> Fierce Pharma (2022). Univercells, Batavia Biosciences on tap to help bring affordable measles and rubella shots to Africa. [online] fiercepharma.net. Available at: <https://www.fiercepharma.com/manufacturing/univercells-teams-senegal-and-batavia-bring-affordable-measles-and-rubella-shots>

<sup>110</sup> PAHO (2022). Canada contributes over U\$ 11 million to PAHO's initiative to strengthen the regional manufacturing of vaccines. [online] paho.org. Available at: <https://www.paho.org/en/news/21-11-2022-canada-contributes-over-u-11-million-pahos-initiative-strengthen-regional>

<sup>111</sup> Vaxthera (2022). Construction work has begun to build the VaxThera plant, which will produce vaccines and biologics for Colombia and the region. [online] vaxthera.com. Available at: <https://www.vaxthera.com/en/novedades/inicia-construccion-de-la-planta-vaxthera-que-producira-vacunas-y-biologicos-para-colombia-y-la-region/>

<sup>112</sup> Aspen (2022). Aspen Concludes a Collaboration Agreement to Manufacture and Make Available Four Aspen-Branded Vaccines for Africa. [online] aspenpharma.com. Available at: <https://www.aspenpharma.com/2022/08/31/aspen-concludes-a-collaboration-agreement-to-manufacture-and-make-available-four-aspen-branded-vaccines-for-africa/>

<sup>113</sup> Reuters (2022). S.Africa's Aspen to Halt COVID Vaccine Output as J&J Orders Dry Up. [online] reuters.com. Available at: <https://www.reuters.com/article/safrica-aspen-pharmacare-idUSL4N2ZJ0ER>

<sup>114</sup> Gavi (2022). Expanding Sustainable Vaccine Manufacturing in Africa. [online] gavi.org. Available at: <https://www.gavi.org/sites/default/files/document/2022/Gavi-Expanding-Sustainable-Vaccine-Manufacturing-in-Africa-2022.pdf>

<sup>115</sup> Expanding sustainable vaccine manufacturing in Africa: Priorities for Support Delivered by Gavi and partners in response to a call from the African Union and G7 Development Ministers. <https://www.gavi.org/news/document-library/gavi-expanding-sustainable-vaccine-manufacturing-africa-2022>

<sup>116</sup> Gavi Board Decisions Outline "Year of Renewal" for Vaccine Alliance 8 December 2022 <https://www.gavi.org/news/media-room/gavi-board-decisions-outline-year-renewal-vaccine-alliance>

included technology transfer.<sup>117</sup> To date, there are several ongoing initiatives related to technology transfer, including the WHO's mRNA vaccine technology transfer hub, the COVID-19 Technology Access Pool (C-TAP) initiative, a 5-year waiver of Trade-Related Aspects of Intellectual Property rights (TRIPS) for COVID-19 vaccines,<sup>118</sup> as well as voluntary licensing partnerships entered into by individual companies. The WHO's mRNA vaccine technology transfer hub in South Africa produced its first batches of COVID-19 mRNA vaccines and trained eleven of the fifteen selected 'spokes' in 2022.<sup>119</sup> C-TAP provides a platform for developers of COVID-19 DTVs to share knowledge and data, and recently launched a request for public comment on local production and technology transfer.<sup>120</sup> The WHO, World Intellectual Property Organisation (WIPO) and World Trade Organisation (WTO) organised workshops focused on the future of intellectual transfer for COVID-19 and other technologies.<sup>121</sup> Still, the debate around intellectual property remains delicate. Every effort should be made to maintain the careful balance between enabling widespread access to products for those who need them most, and not disincentivising at-risk investment from R&D players that could produce future lifesaving tools in the future. Further, it is important for successful technology transfer efforts to ensure willing and capable partners on both the donor and recipient ends, including a healthy ecosystem of staff to actively receive, understand, and execute on the transferred technology.

Importantly, voluntary partnerships are ongoing for diagnostics and therapeutics, in addition to vaccines. Diagnostics players, including the US's DCN Dx<sup>122</sup> and UK's Global Access Diagnostics,<sup>123</sup> have brought new manufacturing processes to Brazil, Korea, and Senegal leading to large increases in testing capacity. Therapeutics players, including Pfizer, Gilead, Lilly, and MSD, signed voluntary royalty-free licensing agreements to expand access to therapeutics for COVID-19. Further, Shionogi and Pfizer, among others, entered a license with the Medicines Patent Pool to enable qualified generics manufacturers to develop and supply their therapeutics.<sup>124, 125</sup>

### Summary plans for 2023

With high political attention on regionalised manufacturing to address vaccine equity and access gaps witnessed during COVID-19, there is a clear need to reconcile propos-

als to ensure economic viability and adequate coverage across regions. Encouragingly, the new Regionalised Vaccine Manufacturing Collaborative (RVMC) sponsored by the World Economic Forum (WEF) in collaboration with the National Academy of Medicine and CEPI, launched in 2022 and will work to develop sustainable, long-term economic plans for regional vaccine manufacturing. RVMC will collaborate with existing thought-leaders in the space, including Gavi and PAVM to begin work in Africa. Gavi, in close collaboration with PAVM, the African Union, the G7 and other partners, will begin implementation of the recently published ten-point plan and will be working with partners to scope a new financial instrument, such as an Advance Market Commitment, to incentivise vaccine manufacturers and investors in Africa. Overall global capacity needs to be adequate across both platforms and geographies to be able to provide accessible DTVs in line with demand.

There is value in maintaining the breadth of initiatives working to develop regional capacity. For example, BioNTech will continue to grow its "BioNTainer" footprint by opening sites announced in Ghana, Senegal, and South Africa. Other players, including Biovac and Moderna should explore developing or expanding their regional capacity plans as well, in coordination with RVMC and PAVM. These efforts should also include plans to expand beyond mRNA to other platform technologies. CEPI is developing a preferred partnership network of vaccine development and manufacturing facilities to be able to rapidly respond to epidemics or pandemics.

Development of sustainable economic models for regional vaccine manufacturing would benefit from strong G7 and G20 leadership. The Indian G20 presidency plans to build on the gap analysis done by the Indonesian presidency to develop a network of R&D and manufacturing hubs. These would need to be active on a day-to-day basis to produce routine vaccinations if they are to maintain quality and usefulness. Further, these efforts should be underpinned by removal of trade restrictions for the movement of goods, personnel, and services to ensure a healthy supply chain. The WHO, WIPO, and WTO can work to define future technology transfer protocols beyond COVID-19 that the G7 can endorse to encourage continued industry engagement and future R&D [see Chapter 4

<sup>117</sup> IFPMA (2022). What it takes to enable tech transfer partnerships. [online] ifpma.org. Available at: <https://www.ifpma.org/global-health-matters/what-it-takes-to-enable-tech-transfer-partnerships/>

<sup>118</sup> WTO (2022). MC12 "Geneva package". [online] wto.org. Available at: [https://www.wto.org/english/thewto\\_e/minist\\_e/mc12\\_e/geneva\\_package\\_e.htm](https://www.wto.org/english/thewto_e/minist_e/mc12_e/geneva_package_e.htm)

<sup>119</sup> Devex (2022). South Africa's mRNA hub confronts old problems and new directions. [online] devex.com Available at: <https://www.devex.com/news/south-africa-s-mrna-hub-confronts-old-problems-and-new-directions-104398>

<sup>120</sup> WHO (2022). COVID-19 Technology Access Pool. [online] who.int. Available at: <https://www.who.int/initiatives/covid-19-technology-access-pool>

<sup>121</sup> WTO (2022). Twelfth WTO Ministerial Conference. [online] wto.org. Available at: [https://www.wto.org/english/thewto\\_e/minist\\_e/mc12\\_e/mc12\\_e.htm#outcomes](https://www.wto.org/english/thewto_e/minist_e/mc12_e/mc12_e.htm#outcomes)

<sup>122</sup> UNITAID (2021). FIND and Unitaaid invest to support technology transfer and boost local production of COVID-19 rapid tests in low- and middle-income countries. [online] unitaid.org. Available at: <https://unitaid.org/news-blog/find-unitaid-technology-transfer-covid-19/#en>

<sup>123</sup> GADx (2022). Global Access Diagnostics (GADx) Formed to Expand Affordable Access to Advanced Rapid Diagnostic Technologies. [online] global-accessdx.com. Available at: <https://www.globalaccessdx.com/global-access-diagnostics-gadx-formed-to-expand-affordable-access-to-advanced-rapid-diagnostic-technologies>

<sup>124</sup> IFPMA (2022). Impact of a Waiver of Intellectual Property Rights for COVID-19 Therapeutics. [online] ifpma.org. Available at: [https://www.ifpma.org/wp-content/uploads/2022/12/TRIPS-infographic\\_-\\_December-2022.pdf](https://www.ifpma.org/wp-content/uploads/2022/12/TRIPS-infographic_-_December-2022.pdf)

<sup>125</sup> FiercePharma (2022). Pfizer's Deal with Medicines Patent Pool Includes 35 Companies from 12 Countries to Produce Generic Paxlovid. [online] fiercepharma.com. Available at: <https://www.fiercepharma.com/pharma/pfizers-deal-medicines-patent-pool-includes-35-companies-12-countries-produce-generic>

– *Rigorous Global Health Governance*]. In the future, there is more work to be done to ensure adequate R&D funding is allocated to LMICs to support in-country innovation that can be used to spur development and manufacturing of DTVs in the long-term [see *Chapter 4 – Sustainable Pandemic Financing and Procurement for Equitable Access*].

*“Overall global capacity needs to be adequate across both platforms and geographies to be able to provide DTVs in line with demand”*

# Establishing 'Rules of the Road'

## Sustainable Pandemic Financing and Procurement for Equitable Access

### [Context and aims](#)



Equitable access to DTVs was a significant gap during the COVID-19 response. Though funding was mobilised for LMICs, there was a lag in the timing of funds available due to lack of dedicated fund(s) to support pandemic response and limited capacity for implementing agencies to provide funds at-risk. As a key example, COVAX was not sufficiently funded, at sufficient speed, to secure advance purchase agreements for vaccine doses on par with high-income country purchasers. COVAX has outlined key learnings from this experience and others in a September 2022 publication, calling for the use of contingent and innovative financing and the availability of at-risk, day 0 pandemic financing for all aspects of the DTV value chain from R&D to procurement to delivery.<sup>126</sup> Despite the lack of funding in the early COVID-19 response, COVAX raised \$12 million and delivered nearly 2 billion vaccines to LMICs. Further, the World Bank's IDA20 raised \$93 billion in December 2021 to support LMICs for COVID-19 recovery (allocated for July 2022 through June 2025).<sup>127</sup>

There is a strong economic and health case for continuing preparatory funding and further, establishing dedicated and sustainable response funding mechanisms to allow LMICs and upper-middle-income countries (UMICs) to purchase sufficient volumes of DTVs quickly and at-risk when a threat materialises. There are two core actions required to achieve this goal:

- 1** Establish financial mechanisms that enable immediate access to pandemic response funding to promote equitable access to DTVs in a PHEIC
- 2** Support LMICs in purchasing and distributing DTVs through equitable allocation and procurement of supplies, including eliminating trade barriers where applicable

Note that this section details efforts by independent organisations to strengthen financing and procurement mechanisms to enable pandemic readiness and emergency response but does not comment on country or regional fiscal efforts. Further, general funding provision for R&D is covered in the relevant DTV sections above.



<sup>126</sup> Gavi (2022). Covax: Key learnings for future pandemic preparedness and response. [online] gavi.org. Available at: [https://www.gavi.org/sites/default/files/covid/covax/COVAX\\_Key-Learnings-for-Future.pdf](https://www.gavi.org/sites/default/files/covid/covax/COVAX_Key-Learnings-for-Future.pdf)

<sup>127</sup> WHO (2021). Global Community Steps Up with \$93 Billion Support Package to Boost Resilient Recovery in World's Poorest Countries. [online] worldbank.org. Available at: <https://www.worldbank.org/en/news/press-release/2021/12/15/global-community-steps-up-with-93-billion-support-package-to-boost-resilient-recovery-in-world-s-poorest-countries>

## Progress

2022 was marked by significant efforts to develop dedicated pandemic funds. Notably, in September, the Pandemic Fund (formerly referred to as the Financial Intermediary Fund or FIF) was established by the G20 Joint Finance-Health Taskforce and under the trusteeship of the World Bank<sup>128</sup> with \$1.6 billion pledged (as of November 28, 2022).<sup>129</sup> This Fund is designed to provide a dedicated stream of additional, long-term financing to strengthen PPR in LMICs. Although the establishment of the Pandemic Fund was a step forward for emergency preparedness funding, it is not designed to support response funding or ensure mechanisms are in place to allow LMICs unfettered access to DTVs, marking an outstanding gap in the global PPR funding landscape.

There were numerous other funds created or replenished in 2022, including \$20 billion received by the IMF Resilience and Sustainability Trust (RST)<sup>130</sup> for longer-term financing for LMICs to develop pandemic preparedness, \$54 million granted to the WHO's Health Emergency Preparedness & Response (HEPR) programme<sup>131</sup> for both national preparedness and contingency funds for response, and \$6 billion sought for replenishment by the Global Fund<sup>132</sup> for preparation, prevention, detection, and response. Important to note here that all funds support pandemic preparation and only some support pandemic response. To put these funds into context, ACT-A estimates that it would require \$23.4 billion in response funding to deliver COVID-19 vaccines to populations living in underserved areas and countries.<sup>133</sup> This does not include preparation activities, including surveillance, therapeutics, clinical trials, or other funding requirements. It remains critical to ensure that response funds are available at the time that LMICs need them, for example through pre-agreed negotiation of automatic funding mechanisms.

The goal of PPR response funding is to ensure on-time access to DTVs for LMICs. A working paper published by the IMF in May 2022 found that 60-75% of the delay in vaccine deliveries to LMICs is attributable to the fact that LMICs signed purchase agreements later than HICs, which

placed them further behind the delivery line.<sup>134</sup> In response to this and as part of the IFPMA Berlin Declaration, key biopharmaceutical manufacturers will partially reserve real-time production of DTVs for priority populations,<sup>135</sup> including health care workers and high-risk individuals regardless of the country they live in.

By the end of 2022, COVAX had delivered nearly 2 billion vaccines<sup>136</sup> to LMICs, including the first “variant-containing vaccines” to LMICs roughly in parallel to first rollouts in HICs. This rollout was enabled by the 2022 Gavi COVAX Advance Market Commitment (AMC) Summit, which secured \$4.8 billion in commitments to help LMICs boost COVID-19 vaccinations and launched the Pandemic Vaccine Pool to ensure contingent financing is available in case of the need for new products or approaches.

Beyond funds received, WHO Member States have begun drafting a Pandemic Instrument that currently includes measures to strengthen the coordination and implementation of supportive financing mechanisms, including pooled purchasing mechanisms,<sup>137</sup> set to be negotiated by 2024. However, no material progress has been made on existing proposals for pre-negotiated financing and procurement mechanisms as of December 2022.

*“As part of the IFPMA Berlin Declaration, biopharmaceutical manufacturers will partially reserve real-time production of DTVs for priority populations”*

<sup>128</sup> WHO (2022). New Fund for Pandemic Prevention, Preparedness and Response Formally Established. [online] who.int. Available at: <https://www.who.int/news/item/09-09-2022-new-fund-for-pandemic-prevention--preparedness-and-response-formally-established>

<sup>129</sup> Commitments to date have been made by Australia, Canada, China, the European Commission, France, Germany, India, Indonesia, Italy, Japan, Republic of Korea, New Zealand, Norway, Singapore, South Africa, Spain, the United Arab Emirates, the United Kingdom, the United States, the Bill & Melinda Gates Foundation, the Rockefeller Foundation, and Wellcome Trust. World Bank (2022). Available at: [https://www.worldbank.org/en/topic/pandemics/brief/factsheet-financial-intermediary-fund-for-pandemic-prevention-preparedness-and-response#:~:text=As%20of%20September%209%2C%202022,2019\)%20to%20establish%20a%20FIF.](https://www.worldbank.org/en/topic/pandemics/brief/factsheet-financial-intermediary-fund-for-pandemic-prevention-preparedness-and-response#:~:text=As%20of%20September%209%2C%202022,2019)%20to%20establish%20a%20FIF.)

<sup>130</sup> IMF (2022). IMF Press Release. [online] IMF. Available at: <https://www.imf.org/en/News/Articles/2022/10/12/pr22348-md-announces-operationalization-of-rst>

<sup>131</sup> Health Emergency Preparedness & Response (2022). [online] healthemergencies.org. Available at: <https://www.healthemergencies.org/>

<sup>132</sup> The Global Fund (2022). Pandemic Preparedness and Response Thematic Report. [online] theglobalfund.org. Available at: [https://www.theglobalfund.org/media/11986/thematic\\_pandemic-preparedness-response\\_report\\_en.pdf](https://www.theglobalfund.org/media/11986/thematic_pandemic-preparedness-response_report_en.pdf)

<sup>133</sup> WHO (2021). New ACT-Accelerator Strategy Calls for US\$ 23.4 Billion in International Investment to Solve Inequities in Global Access to COVID-19 Vaccines, Tests and Treatments. [online] who.int. Available at: <https://www.who.int/news/item/28-10-2021-new-act-accelerator-strategy-calls-investment>

<sup>134</sup> IMF (2022). IMF Working Paper on Finance Vaccine Equity: Funding for Day-Zero of the Next Pandemic. [online] imf.org. Available at: <https://www.imf.org/en/Publications/WP/Issues/2022/05/25/Finance-Vaccine-Equity-Funding-for-Day-Zero-of-the-Next-Pandemic-518280>

<sup>135</sup> IFPMA (2022). Berlin Declaration. [online] ifpma.org. Available at: <https://www.ifpma.org/resource-centre/berlin-declaration-biopharmaceutical-industry-vision-for-equitable-access-in-pandemics/>

<sup>136</sup> Gavi (2022). COVAX Data Brief. [online] Available at: [https://www.gavi.org/sites/default/files/covid/covax/COVAX-data-brief\\_17.pdf](https://www.gavi.org/sites/default/files/covid/covax/COVAX-data-brief_17.pdf)

<sup>137</sup> WHO (2021). World Health Assembly Agrees to Launch Process to Develop Historic Global Accord on Pandemic Prevention, Preparedness and Response. [online] who.int. Available at: <https://www.who.int/news/item/01-12-2021-world-health-assembly-agrees-to-launch-process-to-develop-his-toric-global-accord-on-pandemic-prevention-preparedness-and-response>

**When mpox spread to 110 countries across the globe in 2022, there already was an approved mpox vaccine...**



RT-PCR diagnostics tests were available from previous outbreaks



A vaccine by Bavarian Nordic was licensed in the EU, US, and Canada for use against mpox and smallpox in adults

*Typically, therapeutics for mpox are not needed for patients with healthy immune systems*

**...however, a lack of preparation led to delays in an equitable rollout of DTVs in both HICs and LMICs**



Reliance on government-affiliated labs to conduct testing limited diagnostics availability, which was further exacerbated by minimal standardisation or validation of tests



Late inspections of key manufacturing facilities caused delays in vaccine shipments



Countries with existing licensure did not have enough vaccines in national stockpiles, and there were inadequate mechanisms for rapid licensure in other geographies including Africa

Figure 9. The mpox outbreak in 2022 is an example of a recent outbreak. For mpox, the international community was not prepared to respond to the next pandemic despite the recent learnings from COVID-19<sup>138</sup>, which delayed vaccine access in HICs and LMICs.

### Summary plans for 2023

Funds committed or received to date have demonstrated global support for pandemic preparedness in advance of a pandemic but leave an outstanding gap in response funding for LMICs in the case of a pandemic. G7 and G20 governments have an opportunity to produce tangible results in pandemic response financing in 2023.

The G20 Joint Finance-Health Taskforce, working with multilateral development banks (MDBs) and global health institutions, should collaborate to set up automatic loan or grant mechanisms and pooled purchasing mechanisms (e.g., by following the ACT-A model) for LMICs. Under this objective, Gavi has been developing a toolkit of financial instruments which would allow flexibility and accelerated access to at-risk liquidity by frontloading pledges made to Gavi and the COVAX AMC. This includes facilities developed with the International Development Finance Corporation (DFC) and the European Investment Bank (EIB) and allows donors to frontload pledges for immediate impact. COVAX will continue efforts to deliver COVID-19 vaccines in 2023. Plans approved “in principle” by the Gavi Board will continue to support 91 AMC-supported countries in 2024-2025. Gavi is planning and costing for multiple scenarios, from incorporation of COVID-19 vaccines into routine vaccination programmes to a worst-case scenario pandemic. Gavi is also exploring the development of instruments to

support future pandemic response, including a contingent financing capability for the International Finance Facility for Immunisation (IFFIm) and extension of innovative and contingent financing facilities developed for COVAX. Further, it would be beneficial for the G20 to make the case for non-ODA financing for PPR in support of global economic security and benefits.

G7 governments and funders should specify that DTVs developed with public funds must reserve a fixed percentage of subsequent supply for LMICs (in line with the Berlin Declaration) and report on progress no later than the 2023 Implementation Report. Additionally, work by the G7 can influence DTV access by other mechanisms, including technology transfer and voluntary licensing agreements.

The INB will deliver a progress report on negotiations of the WHO Pandemic Instrument at the 76th WHA which will provide more detailed measures on financing and procurement [see Chapter 4 – *Rigorous Global Health Governance*] by the review in 2023. This could include governments, industry, and other stakeholders working together to map surge financing capacities and develop or realign mechanisms to address gaps and improve equitable and timely access of DTVs for LMICs.

<sup>138</sup> NBC News (2022). What Went Wrong with the Rollout of the Monkeypox Vaccine. [online] nbcnews.com. Available at: <https://www.nbcnews.com/health/health-news/went-wrong-rollout-monkeypox-vaccine-rcna38017>

## Rigorous Global Health Governance

### [Context and aims](#)



Governance and international coordination are key aspects of an agile and effective pandemic response, particularly in declaring a PHEIC, directing R&D, running clinical trials, and ensuring common approaches to access and equity. The COVID-19 pandemic was an unprecedented time of need for international governance and coordinated decision-making for which there were minimal existing models to leverage. There is broad agreement from the international community that strengthened coordination with representation of diverse constituencies is essential to improve dialogue, global cooperation, and oversight of pandemic readiness to accelerate progress against the 100 Days Mission and in support of developing safe and effective DTVs.

While strengthening global health architecture is an important enabler of the 100 Days Mission, it is acknowledged that this goes beyond application to DTV development and therefore will not be a feature of future 100 Days Mission Implementation reports. Still, efforts to strengthen the global health architecture (including through Recommendation 14 of the 100 Days Mission which purports establishment of a Global Health Board) are critically important and will continue to be a part of G7 and G20 processes, in collaboration with the WHO.

### [Progress](#)

The most impactful step toward global PPR governance was the establishment of the INB following a special session of the WHA in December 2021.<sup>139</sup> The INB is in the process of defining a legally-binding WHO Pandemic Instrument that will set guidance for the response to future pandemics and define “rules of the road” for member states and some international organisations focused on ensuring fair, equitable and timely access to DTVs. This includes logistical mechanisms necessary for an effective global supply chain, pooled purchasing mechanisms, pre-agreed trade restrictions, and equitable distribution protocols for strategic stockpiles. A draft of the Pandemic Instrument will be reviewed by the WHA in 2023 and finalised mid-2024.<sup>140</sup> Wider stakeholders, including other international organisations, academic institutions, and industry should also agree on how they will work together in support of R&D, manufacturing, procurement, and in-country delivery and can test these operational arrangements during disease outbreaks.



### [Summary plans for 2023](#)

To support establishing strong PPR governance, the INB will submit a draft of the Pandemic Instrument for review at the WHA in 2023 and take forward feedback to finalise the draft in 2024.

The G20 Joint Finance-Health Taskforce should continue developing coordinated arrangements between Finance and Health Ministers, focusing on addressing economic risks and vulnerabilities, such as with resource mobilisation.<sup>141</sup> The Taskforce should report to the Finance and Health Ministers in 2023 on progress made against the G20 Rome Declaration which focused on enhancing dialogue and global participation while adopting a ‘One Health’ approach,<sup>142</sup> as well as sharing good practices from past finance-health coordination and analysis of economic risks and vulnerabilities from pandemics.<sup>143</sup>

<sup>139</sup> WHO (2022). Intergovernmental Negotiating Body. [online] who.int. Available at: <https://inb.who.int/>

<sup>140</sup> WHO (2021). World Health Assembly Agrees to Launch Process to Develop Historic Global Accord on Pandemic Prevention, Preparedness and Response. [online] who.int. Available at: <https://www.who.int/news/item/01-12-2021-world-health-assembly-agrees-to-launch-process-to-develop-his-toric-global-accord-on-pandemic-prevention-preparedness-and-response>

<sup>141</sup> G20 (2022). G20 Bali Leaders' Declaration. [online] consilium.europa.eu. Available at: <https://www.consilium.europa.eu/media/60201/2022-11-16-g20-declaration-data.pdf>

<sup>142</sup> G20 (2020): G20- Rome Leaders' Declaration. [online] governo.it. Available at: <https://www.governo.it/sites/governo.it/files/G20ROMELEADERSDECLARATION.pdf>

<sup>143</sup> Information disclosed in proforma document or interviews with Japanese government

## Strengthening and Upskilling a Dedicated Workforce



The 100 Days Mission is focused specifically on development of medical countermeasures and the enablers required to support the process, including clinical trials, manufacturing, and finance. However, in discussion of pandemic preparedness, it would be remiss not to mention workforce in both preparing and responding to a pandemic: a strong workforce is key to the overall pandemic preparedness ecosystem. In 2022, Germany's G7 Presidency underscored this point in the G7 Pandemic Readiness Pact, which includes a focus on workforce strengthening in support of PPR.

The WHO, supported by the BMGF, is working with a broad set of stakeholders from around the world to support the establishment of a Global Health Emergency Corps, which is envisioned as a trained and connected network of national, regional and global leaders to coordinate outbreak prevention and response.<sup>144</sup> The WHO also launched a Rapid Response Teams (RRT) Training and Implementation Package to enable member states to plan, implement, and evaluate training for RRT managers and members at national and sub-national levels.<sup>145</sup> Additionally, the WHO Academy in Lyon is expected to be finished in 2024 and will offer online and in-person courses to health workers and others around the world.<sup>146</sup> The EC recently published strategy emphasises the need to improve primary healthcare systems, including through built-in surge capacity, and focuses on numerous partner countries such as Egypt, Kenya, and Cuba.<sup>147</sup> Workforce strengthening, including strengthening universities to feed R&D, is likely to remain a central part of the pandemic conversation in future years but will not be discussed directly as part of the 100 Days Mission progress.

*“A strong workforce is key  
to the overall pandemic  
preparedness ecosystem”*



<sup>144</sup> WHO (2022). New WHO Strategy Aims to Strengthen Rapid Response to Health Emergencies. [online] who.int. Available at: <https://news.un.org/en/story/2022/10/1129272>

<sup>145</sup> WHO (2022). RRT Training and Implementation Package. [online] extranet.who.int. Available at: <https://extranet.who.int/hslp/package/rapid-response-teams-training-implementation-package-member-states>

<sup>146</sup> WHO (2022). WHO Academy. [online] who.int. Available at: <https://www.who.int/about/who-academy#:~:text=The%20WHO%20Academy%20hub%20is,distance%20and%20hybrid%20learning%20classrooms>

<sup>147</sup> EC (2022). EU Global Health Strategy to Improve Global Health Security and Deliver Better Health for All. [online] ec.europa.eu. Available at: [https://ec.europa.eu/commission/presscorner/detail/en/ip\\_22\\_7153](https://ec.europa.eu/commission/presscorner/detail/en/ip_22_7153)

# The Year Ahead

## The 100 Days Mission Context and Timeline

The 100 Days Mission was set forth in the context of a global crisis. With high COVID-19 infection rates, there was demonstrable medical need and significant political attention due to equitable access concerns and connections to the global economy. Further, there was a strong funding climate for research and a desire to build on momentum from the early pandemic response.

Although today attention to pandemic preparedness has waned both politically and financially in many settings, there remains continued support for the 100 Days Mission from global partners, industry, academia, and beyond. Pandemic preparedness efforts are supported by overall health system strengthening which is a key focus of nu-

merous governments. Further, there is momentum building from the health agendas of Japan's G7 Presidency and India's G20 Presidency with dedicated efforts to improve PPR and build on the efforts of past presidencies. There are key pandemic response tools that have been developed or are in development, including the WHO's HEPR framework, a new access to countermeasures platform to replace ACT-A, and the ongoing Pandemic Instrument negotiations. The International Pandemic Preparedness Secretariat can support and focus these tools by convening relevant stakeholders, monitoring, and supporting progress, and ensuring continuity of efforts. In light of the current PPR context, there are significant efforts underway and hope for continued preparatory efforts to support a strong response to another pandemic.

## A 100 days Mission Reporting Timeline: The Year Ahead

STEG dates to be confirmed

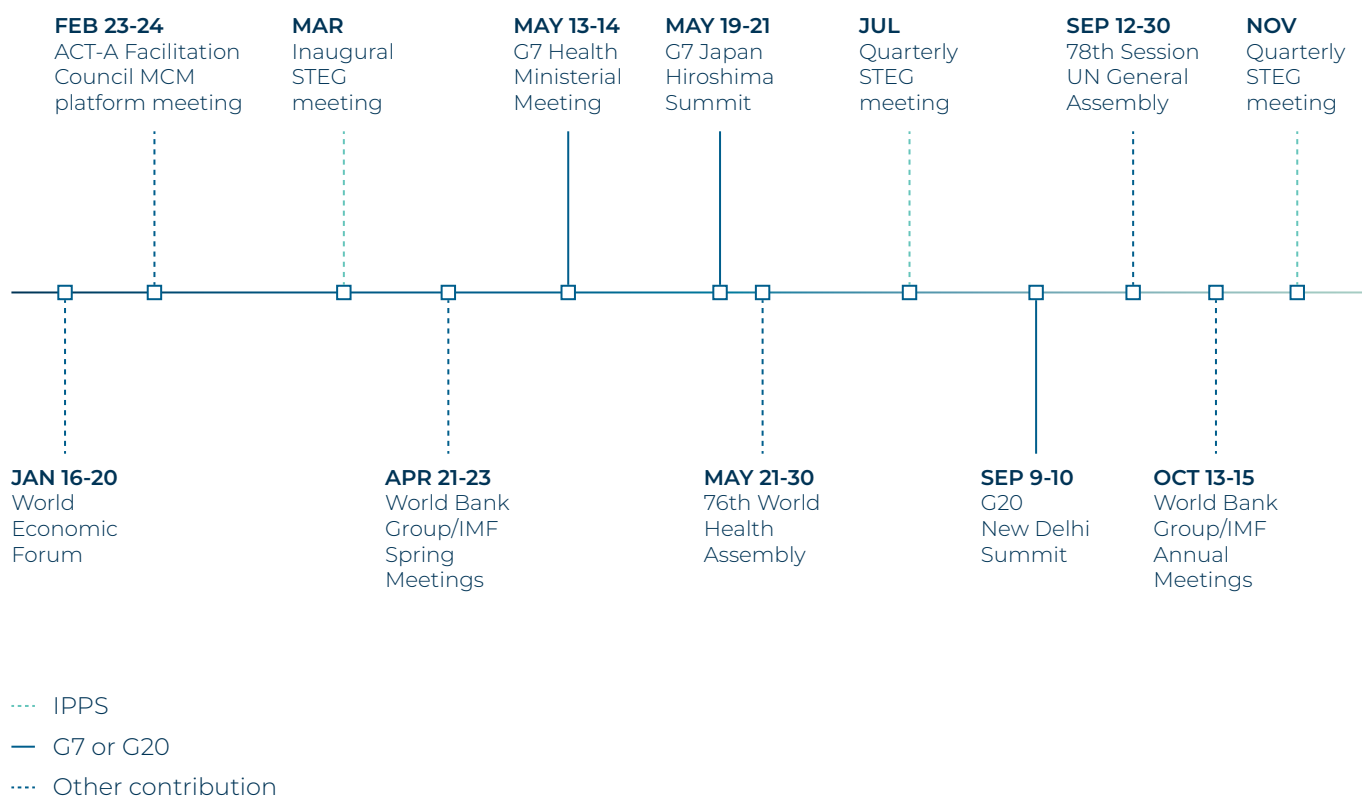


Figure 10. There are various global health meetings related to PPR scheduled in 2023. Stakeholders at each of these meetings will discuss key aspects that support the 100 Days Mission.

*“There is momentum building from the health agendas of Japan’s G7 Presidency and India’s G20 Presidency with dedicated efforts to improve PPR and build on the efforts of past presidencies”*

# Afterword

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Dr. Yasumasa Fukushima

Title: Dr. Yasumasa Fukushima, Chief Medical and Global Health Officer, Ministry of Health, Labour and Welfare, and Acting Director-General, Office of Healthcare Policy, Cabinet Secretariat of the Japanese Government  
Source: Japan Ministry of Health, Labour and Welfare

## Afterword from Japanese Presidency of the G7

The 100 Days Mission is an ambitious, yet worthwhile goal to better prepare the world for future pandemics. The COVID-19 pandemic revealed vulnerabilities in our present system, resulting in huge discrepancies in the availability of the DTVs, especially among vulnerable populations. The 100 Days Mission should continue to hold equitable access of the DTVs as one of its focused areas and propose a way forward towards a stronger and more protected world against the threat of pandemics, drawing upon the lessons that we have learned through our past experiences.

More importantly, the 100 Days Mission requires collective efforts of wide-ranging stakeholders. Public-private collaboration, with a shared understanding of the principles and the values, is critical for achieving its goal. I believe it is important for both the public and private sectors to recognize what is required towards the goal of the 100 Days Mission, reflect on the gaps that exist at present, and address the emerging issues in each work plan. Monitoring progress across the relevant entities is an essential process, in which the newly established International Pandemic Preparedness Secretariat is expected to play a catalytic role. Collaboration can be promoted through discussions among multilateral stakeholders on how to overcome obstacles, promote supportive enablers, and support the private sector in delivery of the 100 Days Mission.

Japan will host the G7 Summit in Hiroshima in May, in which global health will certainly be highlighted as a key piece of the agenda. We are of the view that global health is critical not only from the viewpoint of health, but also from a broader perspective including the global

economy and security. With this basic understanding, we attach great importance to three provisional themes: strengthening the global health architecture for improved PPR for public health emergencies, promoting more resilient, equitable and sustainable universal health coverage (UHC), and promoting health innovation which will support achievement of aforementioned objectives. These themes are in line with the main policy goals of Japan's Global Health Strategy, which was launched in May 2022. The 100 Days Mission spans broad areas essential to pandemic PPR through the 6 priorities proposed for 2023: surveillance, cross-DTV R&D coordination, therapeutics coordination, manufacturing, clinical trials and regulatory processes, and financing and procurement. Each of these requires a multi-sectoral and comprehensive approach, supported through effective health systems and UHC.

The 100 Days mission will enter into the third year since its inception in 2021 under the UK presidency and we need to see tangible progress towards 2026. We are ready to receive the baton and collaborate with the other G7 countries, relevant stakeholders, and the Secretariat in our capacity to keep up the momentum for the achievement of the 100 Days Mission.

### **Dr Yasumasa Fukushima**

*Chief Medical and Global Health Officer, Ministry of Health, Labour and Welfare*

*Acting Director-General, Office of Healthcare Policy, Cabinet Secretariat of the Japanese Government*

# Afterword

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Mr. Lav Agarwal

# Afterword from Indian Presidency of the G20

Over the course of past presidencies, the G20 has strengthened and advocated for a more resilient, responsive, and inclusive global health architecture. Amongst the proposed health priorities for India's 2023 G20 presidency, India will build upon ongoing efforts of both the WHO and previous G20 presidencies to strengthen cooperation in the pharmaceutical sector, focusing particularly on addressing gaps in access to and availability of safe, effective, and affordable quality Vaccines, Therapeutics, and Diagnostics (VTDs). These efforts will span three key sections of the value chain: R&D, manufacturing, and mobilisation.

Pending consultation with G20 members and international organisations, India proposes the establishment of regional R&D and manufacturing hubs, as well as a global, end-to-end Medical Countermeasures Coordinating platform (MCC Platform). These platforms aim to ensure the development of and equitable access to safe and effective VTDs, in line with 100 Days Mission. This could be done by transforming the former ACT-A to be used as a Global MCC Platform. This effort will put global VTDs manufacturing on a sustainable footing to ensure the technology and the workforce is prepared to respond to a future pandemic.

As we learnt from the COVID-19 crisis, our levels of pandemic preparedness have a global impact. It is therefore imperative that the 100DM is sustained globally and implemented inclusively. The 100DM represents a significant

global scientific endeavour, and core to the mission of reducing the time it took to develop a vaccine for COVID-19 to just 100 days is strengthening global scientific expertise and capacity. Therefore, G20 countries must collaborate towards cost-effective and quality R&D and support establishment of an Institutional platform for global end-to-end medical countermeasure development in collaboration with diverse stakeholders.

Despite numerous successes in the global COVID-19 response, there were also key challenges that led to lack of timely access to the VTDs needed by all populations. The 100 Days Mission aims to ensure the world is better prepared to respond to future pandemic threats through availability of safe, effective, and affordable VTDs within the first 100 days of a pandemic threat and the objectives of the 2023 G20 presidency aim to make this mission ever more achievable.

India stands ready to collaborate with all partners under its G20 presidency to strengthen sustainable mechanisms and effective partnerships to ensure rapid access to safe, effective, and affordable medical countermeasures for endemic and pandemic diseases and maintain the momentum towards the achievement of the 100 Day mission.





## **Mr. Lav Agarwal**

*Additional Secretary, Ministry of Health & Family Welfare, Government of India*

## **Acknowledgements**

This report represents independent views of the International Pandemic Preparedness Secretariat. However, we would like to acknowledge the numerous individuals that have contributed to the report and provided their time and insights, including implementation partners through interviews and proformas. This report has been written in collaboration with a team from the Boston Consulting Group.

# Annex A: Summary of Recommendations

 Topic	 Recommendation	 2022 Summary Progress Update	 Proposed 2023 and Future Year Reporting & Key Milestones
<b>Diagnostics R&amp;D</b>	<p>2. Build prototype [vaccines and] diagnostic libraries applicable to representative pathogens of pandemic potential.</p>	<ul style="list-style-type: none"> <li>The WHO, with partners including CEPI, convened a Prioritisation Advisory Committee to define priority pathogens of pandemic potential (including viruses and bacteria). This work will select priority viral families, prototype pathogens within each family, and 'Disease X' threats.</li> <li>Industry re-committed to Diagnostics R&amp;D through the March 2022 Berlin Declaration.</li> <li>Multiple players released multi-pathogen antigen tests that can simultaneously diagnose SARS-CoV-2 and influenza A/B from a single nose swab</li> <li>In August 2022, the WHO stressed the importance of diagnostics in preparing for 'Disease X' and, in coordination with FIND, began developing TPPs intended for readers of RDTs to promote consistency and accuracy in test performance and reporting.</li> </ul>	<p><b>2023</b></p> <ul style="list-style-type: none"> <li>The WHO Prioritization Advisory Committee will publish its updated selection of priority pathogens of pandemic potential in early 2023. Following this, the WHO R&amp;D Blueprint will develop R&amp;D roadmaps and diagnostics TPPs for each priority pathogen, including 'Disease X'.</li> <li>Key diagnostics players, in coordination with FIND, will explore mechanisms to ensure adequate funding to initiate work on prototype diagnostic libraries, including garnering investment against FIND's \$50-80 million proposed plan.</li> <li>A global diagnostics coordinator should be identified to coordinate diagnostics R&amp;D efforts across the international community, in accordance with the WHO's pandemic virus prioritization, including knowledge exchange and collaboration.</li> </ul> <p><b>Future Years</b></p> <ul style="list-style-type: none"> <li>A global diagnostics coordinator will work with partners, including the WHO, industry, and academia, to support the 2026 goal of developing of prototype diagnostics libraries that have broad coverage of eight to ten virus families.</li> <li>A global diagnostics coordinator will work toward the 2026 goal to establish an on-going, adequate, and sustainable R&amp;D ecosystem.</li> </ul>
	<p>6. Strengthen the role of the international system in R&amp;D capability and coordination for [therapeutics and] diagnostics.</p> <p><i>Note that progress against this recommendation has been broadened to diagnostics R&amp;D coordination more broadly, beyond a potential CEPI role.</i></p>	<ul style="list-style-type: none"> <li>CEPI re-iterated that Diagnostics are not in scope of their current efforts. However, CEPI will collaborate with FIND and other groups to develop diagnostic libraries by sharing of materials resulting from CEPI's virus family vaccine library development.</li> </ul>	
<b>Therapeutics R&amp;D</b>	<p>3. Develop prototype antiviral therapeutics, including antibody therapies, for pathogens of pandemic potential.</p> <p><i>Note that progress against this recommendation has been broadened from respiratory to all pandemic pathogens regardless of transmission (e.g., skin-to-skin, blood-borne, vector-borne)</i></p>	<ul style="list-style-type: none"> <li>The WHO, with partners including CEPI, convened a Prioritisation Advisory Committee to define priority pathogens of pandemic potential (including viruses and bacteria). This work will select priority viral families, prototype pathogens within each family, and 'Disease X' threats.</li> <li>Several new therapeutics for COVID-19 came to market, including mAbs (e.g., bebtelovimab, sotrovimab) and small molecule antivirals (e.g., molnupiravir, combination nirmatrelvir/ritonavir).</li> <li>Industry re-committed to Therapeutics R&amp;D through the March 2022 Berlin Declaration.</li> <li>NIAID awarded ~\$577 million to establish nine AViDD centres for pathogens of pandemic concern. Centres will conduct research to develop candidate direct-acting antivirals (mostly small molecules, some biologics, no host-directed therapies) against coronaviridae (including SARS-CoV-2), flaviviridae, paramyxoviridae, togaviridae, picornaviridae, filoviridae, arenaviridae, and bunyaviridae.</li> <li>Novo Nordisk Fonden, Open Philanthropy, and the Bill &amp; Melinda</li> </ul>	<p><b>2023</b></p> <ul style="list-style-type: none"> <li>The WHO Prioritization Advisory Committee will publish its updated selection of priority pathogens of pandemic potential in early 2023. Following this, the WHO R&amp;D Blueprint will develop R&amp;D roadmaps and therapeutics TPPs for each priority pathogen, including 'Disease X'.</li> <li>Key therapeutics players across industry, funders, and academia (including BARDA, HERA, the Cumming Centre, AViDD centres, READDI Inc, PAD centres, DNDi, etc.), should jointly identify a body, or bodies, to act as a global therapeutics coordinator for information sharing and technical collaboration across therapeutics efforts. The International Pandemic Preparedness Secretariat can support these efforts as requested.</li> <li>To meet the 2026 goal of ~25 Phase-2 ready antiviral therapeutics assets, R&amp;D centres across industry and academia need to advance discovery efforts, conduct candidate selections on 60-100 programmes and prepare to progress 40-60 programmes through</li> </ul>

Topic	Recommendation	2022 Summary Progress Update	Proposed 2023 and Future Year Reporting & Key Milestones
		<p>Gates Foundation announced a \$90 million PAD fund to bring small molecule antivirals to Phase 2 readiness for coronaviridae, paramyxoviridae, and orthomyxoviridae.</p> <ul style="list-style-type: none"> <li>READDI, Inc. was awarded \$130 million from NIAID (AViDD) and other funders to build a pipeline of preclinical broad-spectrum small molecule antiviral leads. READDI is actively implementing plans to translate these and other leads to Phase 2-readiness. READDI's work is initially focused on five priority viral families, and includes direct-acting antivirals and host-directed therapies (HDTs). Candidate HDTs target both host factors for virus replication and host symptoms.</li> <li>AHEAD100 garnered funding to begin efforts to develop mAbs for Rift Valley Fever. AHEAD100 is seeking further funding for the remainder of their targets.</li> </ul>	<p>Investigational New Drug (IND)-enabling studies in 2024/25. In 2023 this should also involve identifying partners for Phase 1 studies.</p> <ul style="list-style-type: none"> <li>CEPI will launch a call for proposal for Nipah mAb development for pre-/post-exposure prophylaxis.</li> <li>Key therapeutics players with an expressed interest in biologic therapies (such as AHEAD100, CEPI, Wellcome Leap, the Cumming Centre for Pandemic Therapeutics, and select AViDD centres) should work with proposed therapeutics coordination body/bodies, to target investment and progress efforts to address gaps to mAbs meeting WHO TPPs and develop alignment to begin de-risking programmable antiviral platform technology to complement mAbs.</li> </ul> <p><b>Future Years</b></p> <ul style="list-style-type: none"> <li>R&amp;D centres across industry and academia will work to achieve the 2026 goal of progressing 25 therapeutics assets against priority virus families to Phase 2 readiness.</li> <li>Key therapeutics players, with an expressed interest in Biologic therapies will work to achieve the 2026 goal of having rapidly programmable antiviral platforms (including mAbs and others) evolved towards WHO TPPs for delivery in a health emergency, and able to be rapidly re-purposed to 'Disease X'.</li> <li>A global therapeutics coordination body, or bodies, will work toward the 2026 goal to establish an on-going, adequate, and sustainable R&amp;D ecosystem for therapeutics. This includes work to develop a partnership model to enable industry to take forward de-risked candidates, and progress them through clinical development.</li> </ul>
	5. Invest in simplified cheaper routes for producing monoclonal antibodies and other new therapeutic modalities.	<ul style="list-style-type: none"> <li>CEPI and Wellcome Leap began work with 17 selected organisations under their \$60 million RNA Readiness and Response (R3) programme. The programme is focused on reducing costs and increasing access to RNA-based biologic products (e.g., mAbs, vaccines).</li> <li>The Cumming Global Centre for Pandemic Therapeutics was launched at the Doherty Institute in Melbourne based on a \$226 million (AUD 250 million + AUD 75 million over 10 years) donation. The Centre will enable rapid design and development of treatments for PPR pathogens, through a twenty-year research program focused on novel therapeutics platform technologies and 'plug and play' approaches.</li> </ul>	
	<p>6. Strengthen the role of the international system in R&amp;D capability and coordination for therapeutics [and diagnostics]</p> <p><i>Note that progress against this recommendation has been broadened to therapeutics R&amp;D coordination more broadly, beyond a potential CEPI role.</i></p>	<ul style="list-style-type: none"> <li>Over 2022, CEPI committed to begin work in therapeutics where adjacent to their core vaccines mission but are not currently planning to take on additional efforts including a coordinating role for therapeutics (with sufficient funding, CEPI plans to establish evidence-generation platforms for therapeutics beginning in 2023). This work in therapeutics is part of an entry strategy that may evolve in the future.</li> <li>NIH held an inaugural annual meeting between the nine funded AViDD centres.</li> </ul>	
<b>Vaccines R&amp;D</b>	2. Build prototype vaccines [and diagnostic] libraries applicable to representative pathogens of pandemic potential.	<ul style="list-style-type: none"> <li>The WHO, with partners including CEPI, convened a Prioritisation Advisory Committee to define priority pathogens of pandemic potential (including viruses and bacteria). This work will select priority viral families, prototype pathogens within each family, and 'Disease X' threats. CEPI also began a partnership with UC Davis in November 2022 to develop a ranking system to assess the likelihood of a 'Disease X' emergence from a family of viruses.</li> <li>Industry re-committed to Vaccine R&amp;D through the March 2022 Berlin Declaration.</li> </ul>	<p><b>2023</b></p> <ul style="list-style-type: none"> <li>The WHO Prioritisation Advisory Committee will publish its updated selection of priority pathogens of pandemic potential in early 2023. Following this, the WHO R&amp;D Blueprint will develop R&amp;D roadmaps and vaccine TPPs for each priority pathogen, including 'Disease X'.</li> <li>CEPI should share their ranking of virus families by 'Disease X' emergence potential.</li> <li>Following prioritisation, CEPI and the WHO should work with R&amp;D centres across academia and industry to align on a research</li> </ul>

Topic	Recommendation	2022 Summary Progress Update	Proposed 2023 and Future Year Reporting & Key Milestones
		<ul style="list-style-type: none"> <li>Additional public and philanthropic funding was pledged to support Vaccine R&amp;D. Japan launched SCARDA with \$1.2 billion (JPY 150.4 billion) for Vaccine R&amp;D and clinical trial infrastructure. BARDA made announcements of intent to invest in at least five different vaccine platforms across an array of virus families with pandemic potential and to develop at least one vaccine candidate for each virus family. CEPI achieved a \$2 billion replenishment (out of a \$3.5bn goal) to support the 5-year CEPI 2.0 strategy focused on building vaccine libraries.</li> <li>After replenishment, CEPI launched multiple calls for proposal, including on development of state-of-the-art immunogen design for vaccine libraries against emerging and select endemic infectious diseases. CEPI launched specific calls for the development of vaccines against Rift Valley fever and broadly protective SARS-CoV-2 and betacoronavirus vaccines. CEPI published their latest thinking on the 100 Days Missions 'Delivering Pandemic Vaccines in 100 Days: What will it take?'.</li> <li>The WHO announced that the first doses of one of the three candidate vaccines against the Sudan ebolavirus arrived in Uganda for a clinical safety trial, 79 days after the outbreak was declared.</li> <li>CEPI and HERA have agreed to strengthen their cooperation in the development of medical countermeasures, including information exchange on end-to-end vaccine R&amp;D.</li> </ul>	<p>roadmap for vaccine libraries covering priority pathogen families and ensuring a share of R&amp;D outside of HICs is funded.</p> <ul style="list-style-type: none"> <li>CEPI will begin pilot projects to create vaccine libraries for paramyxoviridae and arenaviridae.</li> <li>CEPI, working with funding and delivery partners (including BARDA, SCARDA, HERA), will continue to fund research to prepare for a rapid pivot towards 'Disease X' by demonstrating efficacy of vaccine platforms in humans, development of vaccine libraries, and customisability against pathogens through application to endemic diseases (e.g., RVF, pan-corona).</li> <li>Industry, academia, and public-private partnerships, will invest in R&amp;D to accelerate development of innovations to meet WHO TPPs (e.g., needle-free formulations, improved thermostability), including through Gavi's continued collaboration with Vaccine Innovation Prioritisation Strategy (VIPS) alliance partners (the WHO, BMGF, United Nations Children's Fund (UNICEF) and the Programme for Appropriate Technology in Health (PATH)) to drive vaccine product innovations forward.</li> </ul> <p><b>Future Years</b></p> <ul style="list-style-type: none"> <li>Key vaccine players including CEPI will work towards achieving the 2026 goal to have vaccine libraries developed for the ten high priority virus families (four through clinical PoC, six through pre-clinical PoC, using learnings from CEPI's initial pilot vaccine libraries (paramyxoviridae and arenaviridae) and conducting preclinical and clinical trials of selected subset of its vaccine library.</li> <li>CEPI will work with partners, to achieve the 2026 goal to have safe and effective rapidly programmable vaccine platform technology (including mRNA vaccine technologies) able to be rapidly re-purposed and deployed globally at scale to an emerging 'Disease X' threat, and accessible for use by all populations in all regions.</li> <li>Industry, academia, and public-private partnerships will work to achieve the 2026 goal to optimise vaccine platforms for large scale production and simplified routes of administration and storage (i.e., to comply with the WHO TPPs).</li> </ul>
	4. Invest in modernising vaccine technology by targeting vaccine preventable diseases.	<ul style="list-style-type: none"> <li>CEPI launched multiple calls for proposal, including for innovation in RNA vaccine platform technologies; several are undergoing due diligence for support. Once selected, CEPI will pair developers of mRNA technologies with vaccine library immunogens. As part of this work, CEPI began landscaping analyses of mRNA developers and technological advances.</li> <li>In October 2022, CEPI signed a partnering agreement with SK bioscience to develop mRNA vaccines for Japanese encephalitis and Lassa Fever. The Japanese Encephalitis vaccine will be supported to licensure and the Lassa Fever vaccine will be an exemplar vaccine for the vaccine library of its virus family.</li> <li>Additional advances were made by the vaccines R&amp;D industry. Moderna announced a commitment to advance vaccines targeting 15 pathogens identified as the biggest public health risks by the WHO and CEPI into clinical studies by 2025 and began a Phase 1 trial for an mRNA Nipah virus vaccine, in collaboration with NIAID. Pfizer began dosing patients in a Phase 3 trial for its quadrivalent mRNA influenza vaccine candidate. GSK and Pfizer presented positive top-line results from their respective respiratory syncytial virus (RSV) vaccine Phase 3 trials.</li> </ul>	

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	12. Stimulate a move towards innovative technologies to reduce the complexity of vaccine manufacturing processes and make technology transfer and scalable manufacturing easier in a pandemic by investing in R&D.	<ul style="list-style-type: none"> <li>CEPI launched multiple calls for proposal, including on innovative technologies to improve vaccine thermostability.</li> <li>CEPI and Wellcome Leap began work with 17 selected organisations under their \$60 million RNA Readiness and Response (R3) programme. The programme is focused on reducing costs and increasing access to RNA-based biologic products (e.g., mAbs, vaccines) [see Rec 5].</li> <li>Through the March 2022 Berlin Declaration, Industry players (incl. IFPMA and DCVMN) committed to working towards reducing manufacturing complexities.</li> </ul>	See previous page
<b>Strengthening Global Surveillance</b>	7. Governments should normalise the use of accurate diagnostics for coronavirus and influenza in point-of-care and nonclinical settings.	<ul style="list-style-type: none"> <li>In September 2022, a policy brief from the WHO urged nations to sustain COVID-19 testing programmes, including asymptomatic diagnosis and contact tracing.</li> <li>In September 2022, FIND &amp; Unitaid launched a 4-year, \$15.9M initiative to increase TB diagnostics usage in primary care across 9 countries (Cameroon, Bangladesh, Brazil, India, Kenya, Malawi, Nigeria, South Africa, and Vietnam).</li> </ul>	<p><b>2023</b></p> <ul style="list-style-type: none"> <li>Though many G7 governments stopped obligatory routine COVID-19 testing in 2022, G7 Health Ministries will promote routine clinical and non-clinical use of diagnostics for a range of pathogens endemic in their countries.</li> <li>The WHO will explore opportunities to increase role for diagnostics and integrated surveillance as part of primary health care system strengthening and universal health coverage planning and advocacy.</li> <li>The Pandemic Hub, in collaboration with diagnostics players such as FIND, should explore approaches for sustainable integration of routine diagnostics in primary care settings (including defining mechanisms for affordable uptake in LMICs).</li> <li>IPSN (to be operationalised in December 2022) will publish an investment case for pathogen genomic surveillance in early 2023.</li> <li>The WHO will support governments to establish environmental surveillance, especially in areas with high zoonotic risk.</li> <li>The Pandemic Hub and CEPI will host additional tabletop exercise(s) with international partners to simulate the early warning phase of a pandemic.</li> <li>The WHO BioHub will share learnings from the Switzerland sample sharing pilot to inform benefits sharing protocol.</li> <li>Epiverse will begin deploying Epiverse-TRACE tools with country partners to test epidemiological modelling capabilities, with particular focus on LMICs. Epiverse also plans to publish a global maturity assessment of data capabilities.</li> <li>GPDA will publish a case study and blueprint for obtaining and using non-traditional, commercially held data (e.g., social media) for epidemic preparedness and response..</li> </ul> <p><b>Future years</b></p> <ul style="list-style-type: none"> <li>Routine use of diagnostics should be embedded into clinical and non-clinical settings for regionally relevant pathogens, with mechanisms to support diagnostics accessibility and affordability in LMICs.</li> </ul>
	8. WHO should support an enhanced role for diagnostics in the surveillance of pandemic threats.	<ul style="list-style-type: none"> <li>In March 2022, the WHO's Strategic Preparedness, Readiness and Response plan to end COVID-19 was published which stated the importance of integrating diagnostics into multi-disease surveillance through decentralised and multiplex testing.</li> <li>In April 2022, the WHO published a 10-year strategy to strengthen global surveillance for PPR pathogens. As part of this strategy, the Pandemic Hub co-facilitated an outbreak simulation at the G7 Health Ministers Conference, established the Pandemic &amp; Epidemic Intelligence Innovation Forum, and hosted three sessions with global experts on surveillance.</li> <li>CEPI conducted a 'live fire' exercise to stress-test governments on overall pandemic preparedness and response.</li> <li>The UK Health Security Agency (UKHSA)'s New Variant Assessment Platform (NVAP) provided training, reagents and sequencing capacity to Brazil, Nepal, Ethiopia, Kenya, Nigeria and Pakistan as well as regional stakeholders (including the WHO Regional Offices, Africa Centre for Disease Control (CDC) and the Caribbean Public Health Agency (CARPHA)).</li> </ul>	
	21. Explore the scope for a system that enables biological samples to be collected and shared immediately and unhindered in a pandemic.	<ul style="list-style-type: none"> <li>In March 2022, the WHO BioHub hosted a technical consultation to explore access &amp; benefits sharing of clinical samples (including mechanisms used by the WHO Pandemic and Influenza Preparedness (PIP) Framework and the ACT-A COVAX Pillar).</li> <li>The WHO BioHub piloted a sample sharing facility in Switzerland using SARS-CoV-2 samples. Eleven countries participated by signing a Standard Material Transfer Agreement for access and benefits sharing within the pilot and four countries shipped samples.</li> </ul>	

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		<ul style="list-style-type: none"> <li>In October 2022, the WHO BioHub released a detailed set of requirements for laboratories to participate in biological sample sharing.</li> <li>The WHO announced plans to expand the respiratory pathogens covered by the Global Influenza Surveillance and Response System (GISRS). The new 'GISRS+' system will leverage an existing network of 153 global laboratories.</li> </ul>	<ul style="list-style-type: none"> <li>The Pandemic Hub and IPSN, with key implementation partners, should establish an international network of local surveillance systems to rapidly identify and characterise local outbreaks, including through supporting increased equity of surveillance capacity in LMICs.</li> <li>Based on outcomes of the Switzerland pilot, the WHO BioHub will consider an international network of trusted facilities that can rapidly exchange pathogen samples across borders, with suitable access, benefits sharing mechanisms and reciprocity agreements in place to ensure rapid / immediate pathogen accessibility.</li> <li>Epiverse, with key implementation partners, will support development of strengthened local data capabilities and a global ecosystem of interoperable data analytics platforms.</li> </ul>
	22. Support the recommendations of the Science Academies of the G7 and endorse the development of a roadmap towards a more systematic approach to data capture, standards, sharing and analysis for health emergencies.	<ul style="list-style-type: none"> <li>Epiverse, established by data.org, a member of GPDA, published the first visual map of interoperability across existing global health analytics software (Epiverse-CONNECT) and launched an open-source software package for epidemiological data modelling and analysis (Epiverse-TRACE).</li> <li>The Pandemic Hub took ownership of the EIOS system which uses artificial intelligence to identify signals from publicly available health data.</li> <li>HERA established a laboratory network called <i>DURABLE</i>, funded with \$26.5 million (€25 million) under the EU4Health program to provide real-time data and early signals of the potential emergence or spread of biological health threats, promote data exchange, and inform global decision-making.</li> <li>HERA and the WHO launched a new partnership that will fund four global initiatives: (1) epidemic and pandemic intelligence through the WHO Hub for Pandemic and Epidemic Intelligence, (2) development of new medical countermeasures for tackling antimicrobial resistance, (3) the scaling of national capacities for COVID-19 and Emerging Pathogens in Africa, (4) C-TAP to ensure a fast, coordinated, and successful effort to facilitate access to relevant technologies.</li> </ul>	
<b>Improvements to Clinical Trial and Regulatory Processes</b>	9. Scope out how an international network of clinical trial platforms could be implemented to enable a coordinated and efficient approach to testing of DTVs.	<p><i>Note: The update for recommendations 9 and 18 have been combined to reflect the integrated delivery mechanism.</i></p> <ul style="list-style-type: none"> <li>The 75th WHA adopted a resolution to support development of a more equitable global clinical trials ecosystem, including improving trial prioritisation, strengthening capacity and regulatory frameworks, and increasing transparency [see Rec 11].</li> <li>Several efforts have been undertaken to support clinical trial capacity strengthening. GloPID-R's Asia Pacific Hub launched a 3-year grant to coordinate regional PPR funding. TDR mapped global clinical trials infrastructure and identified opportunities to strengthen capacity. PANTHER was launched to develop a flexible clinical research platform in Africa. CEPI recruited laboratories into a centralised network for vaccines testing, focusing on laboratories in South America, Africa, and Oceania. BMGF invested in site capacity readiness for large-scale COVID-19 vaccine trials in Latin America, Africa, and Asia, primarily in infrastructure improvements. The WHO has continued to expand and build LMIC clinical trial</li> </ul>	<p><b>2023</b></p> <ul style="list-style-type: none"> <li>At the 76th WHA, the WHO will report progress related to the strengthening clinical trials resolution, with key relevance to the 100 Days Mission.</li> <li>GloPID-R will operationalise the African Regional Hub.</li> <li>GloPID-R will launch the Pandemic PACT tool to improve global research coordination.</li> <li>Regulatory authorities from G7 and G20 countries should lead on collaboratively identifying pathways for mutual recognition in DTVs. As an example, following approval of the IVD roadmap, there is an opportunity for the MHRA to work with regulatory authorities to help define international assessment protocols and establish more effective quality assurance processes in diagnostics.</li> <li>GCTC will convene a group of key global actors to explore effective implementation of the clinical trial guidance principles, particularly in role-specific contexts (e.g., working with regulatory agencies) to</li> </ul>

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	18. Explore the creation of regional mechanisms to coordinate and prioritise clinical trials of DTVs.	<p>capabilities within its network of trial sites used for the Solidarity Trial for Vaccines (10+ countries) and Therapeutics (54+ countries).</p> <ul style="list-style-type: none"><li>• In January 2022, ECRAID was launched as the first pan-European trial network that provides a single point of access to 2000+ trial sites across 40+ countries.</li><li>• In February 2022, the UK DHSC and GloPID-R convened a ‘Funders Roundtable’ with funding agencies, the WHO and G7 stakeholders to improve coordination and efficiency in funding trials; insights will be consolidated into guidelines for funders.</li></ul>	<p>review and agree streamlined and effective procedures building on the GCTC principles.</p> <ul style="list-style-type: none"><li>• ICMRA should operationalise cross-SRA collaboration to embed best practice between pandemics.</li><li>• The WHO International Clinical Trials Registry Platform (ICTRP) working group will provide minimum data requirements for clinical trial reporting.</li><li>• Results of public consultations for risk-proportionate regulatory frameworks should be shared and implementation plans developed based on the outcomes.</li></ul>	
	10. Develop a common regulatory framework that better defines criteria and standards for effectiveness, quality and use cases for diagnostics.	<ul style="list-style-type: none"><li>• The MHRA updated criteria and standards for effectiveness, quality, and use-cases of diagnostics into the In-Vitro Diagnostics (IVD) Roadmap for pandemic preparedness.</li></ul>	<p><b>Future years</b></p> <ul style="list-style-type: none"><li>• International leaders should agree to a prioritisation process for clinical trials submitted to an international clinical trial network.</li><li>• The WHO, GCTC, GloPID-R and other key implementation partners will continue to support countries to strengthen their trial infrastructure, first in locations where outbreaks have historically emerged and ensure that capacity is used to test routine and outbreak products to ensure its maintenance.</li><li>• Implementation plans related to risk-proportionate frameworks proposed should be developed and aligned.</li><li>• Funders, regulatory authorities, and other actors along the clinical trial lifecycle, supported by the WHO, GCTC, GloPID-R and other relevant stakeholders, streamlined clinical trial processes and have achieved increased efficiency in trial delivery and more timely reporting of trial results.</li><li>• Regulatory authorities will define a pre-agreed framework for accelerated emergency procedures in a PHEIC.</li></ul>	
	11. Transform the approach to clinical trial regulation, shortening the time to authorise trials and streamlining the requirements and guidelines relating to trial conduct.	<ul style="list-style-type: none"><li>• In March, the GCTC published draft guidance for well-planned, well-run, and clinically relevant randomized controlled trials.</li><li>• In August, the Accelerating Clinical Trials in the EU (ACT-EU) initiative published a workplan to transform clinical trial initiation, design, and execution.</li><li>• There has also been country-specific progress in transforming clinical trials including by G7 countries. The US began developing a pathway to achieving clinical trial readiness for a PHEIC, including governance models for international coordination. The UK’s MHRA and Health Canada proposed risk-proportionate legislative frameworks, but outcomes from public consultations have not yet been shared. Japan continued addressing challenges in conducting decentralised clinical trials.</li><li>• The WHO announced that the medical products regulatory agencies of China, Egypt, Nigeria, and South Africa reached maturity level 3 and Korea and Singapore reached maturity level 4.</li></ul>		
	19. Stringent Regulatory Authorities and the WHO should form an international alliance in a pandemic to support timely exchange of knowledge and information relating to standards and guidelines for DTVs.	<p><i>Note: The update for recommendations 19 and 20 have been combined to reflect the integrated delivery mechanism.</i></p> <ul style="list-style-type: none"><li>• In October 2022, the UK’s MHRA and Brazil’s Anvisa, on behalf of the ICMRA, published an updated framework for regulatory authorities to use in a global health crisis, leveraging lessons learnt from the December 2021 joint WHO-SRA reflections on flexible regulatory processes used during COVID-19. The Framework recommended accelerated procedures such as coordinating clinical evaluation and expediting manufacturing through supporting technology transfer mechanisms.</li></ul>		
	20. Stringent Regulatory Authorities and the WHO exchange experience and best-practice on regulatory evaluation of other types of studies (e.g., human challenge trials, immunogenicity studies) during pandemics to support the development of appropriate protocols and guidelines.			

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<b>Regionalised Manufacturing</b>	<p>16. Governments and industry should share risk to maintain vaccine manufacturing capacity.</p> <p><i>Note: Recommendation 16 extended to cover manufacturing capacity across DTVs.</i></p>	<ul style="list-style-type: none"> <li>In the March 2022 Berlin Declaration, industry made a joint commitment to support a diverse and sustainable manufacturing footprint for DTVs. Tech transfer for COVID vaccines continued to be a major topic for WHO, WIPO and WTO.</li> </ul> <p><u>Vaccines:</u></p> <ul style="list-style-type: none"> <li>Several multi-lateral frameworks were launched to support Vaccine manufacturing including the PAVM Framework for Action at Africa CDC, the WEF-supported RVMC (both in coordination with CEPI), the G7 Pact for Pandemic Readiness, and Gavi's ten-point plan on 'Expanding sustainable vaccine manufacturing in Africa'.</li> <li>In December 2022, the Gavi Board approved the first three pillars of a strategy to 1) facilitate regional vaccine manufacturing, including support for antigen and product portfolio planning, 2) adapt the Healthy Market Framework and Product Menu Criteria to facilitate listing and adoption of new regional products and 3) provide investors in new manufacturing capacity with more predictability around eventual demand. Gavi's board further requested the Gavi Secretariat to work on detailed proposals for pillar 4: design and operationalisation of an Advance Market Commitment over the next year to support pillars 1-3.</li> <li>mRNA manufacturing commenced in Africa with the first batches from the WHO mRNA hub in South Africa. Additional spokes were selected for technology transfer.</li> <li>BioNTech prepared a site in Rwanda for the first "BioNTainer" modular manufacturing unit. Moderna identified Kenya for manufacturing of mRNA vaccines and Pfizer partnered with Biovac to manufacture the Pfizer-BioNTech COVID-19 vaccine in South Africa. Afrigen Biologics and Univercells began a collaboration to develop the first Africa--owned vaccine. Recipharm is developing Sensyo Pharmatech which will integrate research, clinical development, manufacturing, and marketing. Eva Pharma is constructing a vaccine manufacturing site in Cairo to produce both egg-based and cell-culture based vaccines.</li> <li>CEPI and BMGF announced \$30 million to support a 10-year agreement with Aspen Pharmacare and the Serum Institute to expand the supply and sourcing of Pneumococcal, Rotavirus, Polyvalent Meningococcal, and Hexavalent vaccines in Africa. Project MADIBA, a partnership led by Insitut Pasteur de Dakar, began installation of a vaccine manufacturing facility in Senegal that will produce COVID-19 mRNA vaccines as well as vaccines against other endemic diseases such as yellow fever. BMGF is also supporting Insitut Pasteur de Dakar to produce measles and rubella vaccine material.</li> <li>Multiple national governments in Africa launched plans aimed at bolstering their local manufacturing capacity. Most plans are yet to identify relevant funding streams. Canada announced funding support to increase vaccine production Latin America and the</li> </ul>	<p><b>2023</b></p> <ul style="list-style-type: none"> <li>PAVM will continue to garner support and investment against their Framework for Action, from African governments and regulatory authorities, industry, donors, and research institutions towards the longer-term goal to meet 60% of African vaccine demand through local production by 2040. PAVM will support all vaccine manufacturers on the continent across a vaccine portfolio of 22 diseases.</li> <li>Gavi will drive and coordinate execution against their ten-point plan with G7 Development Ministers, African countries, international partners including development financial institutions, the WHO, CEPI, the Global Fund, and the private sector. Gavi will work up detailed proposals for the design and operationalisation of Pillar 4, an Advance Market Commitment to accelerate the expansion of end-to-end African vaccine manufacturing.</li> <li>Following launch of its global framework at Davos in January 2023, RVMC will consolidate donors and nations towards a sustainable long-term economic model for regionalised DTV manufacturing. To achieve this, governments (including G7 and G20 nations), global health funders, and industry should work on building sustainable ecosystems and market shaping to support increases in regional DTV capacity. This should complement the G20's plans to promote a network of R&amp;D and manufacturing hubs building on the gap analysis done by Indonesia.</li> <li>The G20 has an opportunity to commit to coordinated support for emerging regional manufacturing hubs, including investment in enabling regulatory, trade and policy environments.</li> <li>Industry and donor-led programmes should continue to build regional manufacturing capacity across DTVs in the spirit of optimising regional coverage.</li> <li>The WHO mRNA hub in South Africa will begin clinical trials of their COVID-19 mRNA vaccine and train further spokes.</li> <li>Further BioNTech "BioNTainer" sites will be developed in Ghana, Senegal, and South Africa.</li> </ul> <p><b>Future Years</b></p> <ul style="list-style-type: none"> <li>By 2026, governments (including G7 and G20 nations), global health funders, and industry, should have collaborated to build expanded capacity for DTV manufacturing available to contribute to meeting regional demand in the event of an outbreak, adhering to international standards. This should include expanded capabilities of existing manufacturers in LMICs, enhancing capacity in all currently low-capacity regions. Regional manufacturing should be developed as part of an ecosystem spanning the entire value chain (including R&amp;D and workforce). This effort is likely to need continued focus beyond 2026.</li> </ul>

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<b>Regionalised Manufacturing</b>		<p>Caribbean via PAHO. Vaxthra began construction of a plant to produce vaccines and biologics in Columbia.</p> <ul style="list-style-type: none"> <li>CEPI launched a call for proposals to establish a network of vaccine manufacturing facilities.</li> </ul> <p><u>Diagnostics:</u></p> <ul style="list-style-type: none"> <li>Over 2022, FIND and UNITAID supported increasing regional manufacturing capacity for diagnostics through technology transfer programmes for modular rapid Antigen test manufacturing. This included new commercial production of COVID-19 Ag rapid diagnostic tests by DCN Dx, WAMA Diagnostica in Brazil, and DiaTROPiX in Senegal.</li> </ul> <p><u>Therapeutics:</u></p> <ul style="list-style-type: none"> <li>Pfizer, Gilead, Lilly, and MSD signed voluntary royalty-free licensing agreements to expand access to therapeutics for COVID-19.</li> <li>Pfizer and 38 generic manufacturers signed agreements with the MPP to produce generic versions of the oral COVID-19 treatment nirmatrelvir co-packaged with ritonavir, for 95 low and middle income low- and middle-income countries. Shinogi entered a similar license with the MPP for ensitrelvir.</li> </ul>	<p><i>See previous page</i></p>
<b>Sustainable Pandemic Financing &amp; Procurement for Equitable Access</b>	<p>13. The IMF to explore expanding their Article IV consultation with member countries to include a pandemic preparedness assessment, and draw on the analysis and expertise of others. Concurrently, multilateral development banks continue to support investment to strengthen and prepare health systems as part of their core day-to-day business..</p>	<p><i>[The recommendation on Article IV amendments will not be taken forward following assessments by the IMF in 2021.]</i></p> <ul style="list-style-type: none"> <li>The G20 Joint Finance-Health Taskforce established the Pandemic Fund in September 2022, under the trusteeship of the World Bank and technical guidance of the WHO, to provide a dedicated stream of additional, long-term financing to strengthen PPR capabilities in low- and middle-income countries and address critical gaps through investments and technical support. It received over \$1.6 billion in financial commitments to date.</li> <li>The IMF Resilience and Sustainability Trust was established in October 2022 to focus on tackling longer-term structural challenges in LMICs, including PPR. It received \$20 billion to date.</li> <li>The Global Fund proposes allocating \$6 billion over three years to strengthen health systems and pandemic preparedness from its November 2022 replenishment.</li> <li>The World Bank's HEPR programme was established in 2020 to support LMICs and countries with low health emergency preparedness and response capabilities to improve their PPR capacities. Since then, it has allocated \$54 million to 32 countries for health emergency preparedness.</li> </ul>	<p><b>2023</b></p> <ul style="list-style-type: none"> <li>The G20 Joint Finance-Health Taskforce working with multilateral development banks (MDBs) and global health institutions should agree upon the design of a contingent financing mechanism in the event of a PHEIC, to include set up automated loan mechanisms and pooled purchasing mechanisms (e.g., using ACT-A as a model).</li> <li>Gavi will explore the development of instruments to support future pandemic response, including a contingent financing capability for the IFFIm and extensions financing facilities developed for COVAX.</li> <li>G7 governments and funders should specify that DTVs developed with public funds must reserve a fixed percentage of subsequent supply for LMICs (in line with the Berlin Declaration) and explore additional benefit sharing (data, access plans, licensing, etc.). Progress should be shared no later than the 2023 Implementation Report.</li> <li>The next iteration of the WHO Pandemic Instrument for PPR will provide more detailed measures on financing and procurement by the review in 2023. This includes ensuring governments, industry and other stakeholders are working together to agree on distribution protocols that support rapid access for LMICs [see Rec 17].</li> <li>The ACT-A Facilitation Council working with the WHO, G20 and affected countries to continue exploring how to create a new standalone medical countermeasures platform in consultation with ACT-A Facilitation Council participants.</li> </ul>

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	15. Governments should build in conditions into DTV funding contracts for LMIC access to access DTVs at not for profit and scale, which is to be enacted if a PHEIC is declared.	<ul style="list-style-type: none"> <li>As part of the IFPMA Berlin Declaration in 2022, associated biopharmaceutical industry players have stated support to partially reserve real-time productions of DTVs for priority populations, including health care workers and high-risk individuals regardless of the country they live in, and will take measures to increase affordability and availability, calling on both stakeholders and industry to work together on delivery of this plan.</li> <li>In April, the German government signed pandemic preparedness contracts with five German-based manufacturers to ensure manufacturers will maintain manufacturing and supply capacity of mRNA vaccines for future emergency situations.</li> </ul>	<ul style="list-style-type: none"> <li>MDBs will deliver an update on their progress in implementing the recommendations of the G20 Independent Review of MDBs' Capital Adequacy Frameworks within their own governance frameworks in Spring 2023.</li> </ul> <p><b>Future Years</b></p> <ul style="list-style-type: none"> <li>MDBs and global health institutions including Gavi should have clear financial mechanisms established that enable immediate access to funding for LMICs for their pandemic response to ensure equitable access to DTVs in a PHEIC.</li> <li>Governments in HICs should have established clear mechanisms that support LMICs in purchasing and distributing DTVs in an affordable and timely manner through equitable allocation and procurement of supplies, including the elimination of trade barriers.</li> </ul>
	23. A PHEIC should trigger the activation of an automatic mechanism to procure and distribute DTVs. Further work is needed to determine how such a facility could operate and we recommend considering basing this on advance commitments that are pre-negotiated well before a pandemic.	<ul style="list-style-type: none"> <li>Gavi is in ongoing discussions with IFFIm donors to explore the potential to develop a contingent financing mechanism to provide rapid, day-zero financing to support equitable access to vaccines for a future pandemic.</li> <li>No material progress has been made on the proposal for global automatic funding mechanisms.</li> </ul>	
	24. As part of countries' bilateral DTV procurement, any advance purchase agreements with manufacturers should include a requirement for products provided to LMICs to be provided at not for profit. This must also be done within a similar timeframe to when HICs are supplied.	<ul style="list-style-type: none"> <li>No material progress has been made on the proposal for LMIC access mechanisms in advance purchase agreements.</li> </ul>	
	25. Multilateral development bank loans should be made available so LMICs can purchase DTVs above the 30% provided through the DTV financing facility in line with recommendation 23. Normal access limits or policies applied by multilateral development banks should not prevent countries receiving urgent finance during a pandemic.	<ul style="list-style-type: none"> <li>The G20 Indonesian Presidency released an independent review on MDB's Capital Adequacy Frameworks (CAF), recommending loosening capital adequacy policies to meet the growing needs of developing countries, a roadmap to deliver is in development.</li> <li>In April, Japan International Cooperation Agency (JICA) signed a loan agreement of \$200 million with African Export-Import Bank to support the development of pharmaceutical production in Africa, including vaccine production lines and health-related facilities.</li> </ul>	
<b>Rigorous Global Health Governance</b>	1. A regular review of the implementation of the recommendations in this report, beginning with an initial stocktake before the end of 2021.	<ul style="list-style-type: none"> <li>A dedicated International Pandemic Preparedness Secretariat has been established that will support the implementation of the 100DM and produce annual implementation reports. This 2nd implementation report has been prepared by the Secretariat.</li> </ul>	<p><b>2023</b></p> <ul style="list-style-type: none"> <li>The Secretariat will track progress across implementation of the 100 Days Mission and write the 2023 Implementation Report under the advisement of a Steering Group and Science and Technology Expert Group.</li> </ul>

Topic	Recommendation	2022 Summary Progress Update	Proposed 2023 and Future Year Reporting & Key Milestones
	14. Establishing a Global Health Board reporting to the G20 to provide oversight of pandemic readiness on an annual basis.	<ul style="list-style-type: none"> <li>No material progress has been made on the proposal for a Global Health Board but discussions on the future of the global health architecture are ongoing with the WHO and G7 and G20. Given the broad nature of such a forum, the Secretariat will not provide progress updates on this recommendation in future Implementation reports.</li> </ul>	<ul style="list-style-type: none"> <li>The INB will submit a draft of the Pandemic Instrument for review at the WHA in 2023 and take forward feedback to finalise the draft in 2024.</li> <li>The G20 Joint Finance-Health Taskforce will continue developing coordinated arrangements between Finance and Health Ministers, focusing on addressing economic risks and pandemic vulnerabilities such as with resource mobilisation. The Taskforce should report to the Finance and Health Ministers in 2023 on progress made.</li> <li>G7 and G20 governments should agree on a proposal for future strengthening of global health decision making structures – whether this be the Global Health Board or an alternative Global Health Board, to be taken forward and reported separately from the 100 Days Mission given broader scope.</li> </ul> <p><b>Future Years</b></p> <ul style="list-style-type: none"> <li>The Secretariat will continue to perform annual reviews and draft implementation reports, including a mid-way review of the 100 Days Mission and its recommendations in 2024. The Secretariat should be stood down by the end of 2026.</li> <li>The INB will present a finalised Pandemic Instrument at the 77th WHA in 2024.</li> <li>The WGIHR will present proposed amendments to the IHR (2005) at the 77th WHA in 2024.</li> </ul>
	17. As part of the proposed WHO Treaty on Pandemic Preparedness setting guidance for pandemics, the WHO should define ‘rules of the road’ and set out guidance on good practice for all relevant stakeholders in a pandemic, pre-negotiated with governments, industry and international organisations.	<ul style="list-style-type: none"> <li>In July 2022, the INB released a working draft of a Pandemic Instrument, which will be used for discussion amongst WHO Member states ahead of formal negotiations on the Instrument in Feb 2023. The final version of the pandemic instrument will be a legally binding document that provides detailed guidance for all relevant stakeholders in a pandemic.</li> <li>The WHO Member States established the Working Group on IHR amendments (WGIHR) to explore amendments to the IHR (2005), to be agreed at the 77th WHA in 2024.</li> <li>The WHO and others published key learnings from the ACT-A programme for future pandemics.</li> </ul>	

# Annex B: Glossary of Terms

- **Aids Healthcare Foundation (AHF)** – Global Public Health Institute at the University of Miami
- **Access to COVID-19 Tools Accelerator (ACT-A)** – A global collaboration launched in April 2020 to accelerate the development, production, and equitable access to COVID-19 tests, treatments, and vaccines
- **Accelerating Clinical Trials in the EU (ACT-EU)** – an initiative to transform how clinical trials are initiated, designed and run, strengthening the EU's position in the global clinical trial ecosystem
- **Anti-viral therapeutics** – Therapeutics to treat or prevent viral infections
- **Antiviral Drug Discovery Centers for Pathogens of Pandemic Concern (AViDD)** – A set of research centres funded by the U.S. NIAID as part of the Antiviral Program for Pandemics
- **Anvisa** – The Brazilian Health Regulatory Agency
- **Artificial Intelligence (AI)** – Intelligence demonstrated by machines
- **Biomedical Advanced Research and Development Authority (BARDA)** – An authority within the U.S. Department of Health and Human Services, for the development of medical countermeasures for public health medical emergencies
- **Bill and Melinda Gates Foundation (BMGF)** – A global foundation focused on helping all people lead healthy, productive lives
- **Coalition for Epidemic Preparedness Innovations (CEPI)** – An organisation that provides R&D funding for vaccines to stop future epidemics
- **Clinical trial** – A prospective research study on human participants designed to answer specific questions about biomedical or behavioral interventions, including DTVs. Clinical trials generate data on dosage, safety, and efficacy
- **Platform trials** – A clinical trial with a single master protocol in which multiple treatments are evaluated simultaneously, with mechanisms to add and remove new treatments throughout the trial
- **CMC (Chemistry, Manufacturing, and Control)** – refers to product-specific information, typically submitted in Investigational New Drug (IND) applications
- **COVID-19 Technology Access Pool (C-TAP)** – WHO initiative launched in 2020 to facilitate faster equitable and affordable access to COVID-19 health products for people in all countries through development of a single platform for developers to share intellectual property, knowledge, and data
- **COVID-19 Vaccines Global Access (COVAX)** – The vaccine pillar of ACT-A, co-led by Gavi, CEPI, the WHO and key delivery partner UNICEF. Houses the COVAX Facility, a COVID-19 vaccine procurement pool led by Gavi and CEPI
- **COVID-19** – The disease caused by the virus SARS-CoV-2
- **DCVMN** – Developing Countries Vaccine Manufacturer Network, an international public health driven industry association of vaccine manufacturers from developing countries
- **Diagnostics** – Products which diagnose diseases, commonly known as tests
- **Disease** – A deviation from normal healthy functioning, in this report typically refers to infectious diseases that affect humans
- **Disease X** – Term that represents the knowledge that a serious international epidemic could be caused by a pathogen currently unknown to cause human disease
- **Drugs for Neglected Diseases initiative (DNDi)** – A not-for-profit research organisation developing new treatments for neglected patients
- **DTV** – Diagnostics, Therapeutics and Vaccines
- **Emergency Use Listing (EUL)** – A WHO procedure for assessing and listing vaccines with the aim of making them more readily available to people affected by a public health emergency
- **European Clinical Research Alliance on Infectious Diseases (ECARID)** – initiative that aims to advance clinical research in the field of infectious diseases by establishing a long-term, financially self-sustainable, clinical research network in Europe
- **Endemic disease** – A disease that is regularly found in a population or area
- **Epidemic disease** – A disease that affects a large number of people within a region, population or community
- **Equitable access** – The notion that those with equal needs have equal access. In this report usually referring to DTVs such that DTVs are distributed globally based on clinical need
- **EU-Africa Business Forum (EABF)** – meeting held every three years, co-organised by the European Commission, the African Union commission, EU and African business organisations
- **European Clinical Trial Network for Infectious Disease (ECRAID)** – A legal entity providing access to a pan-European clinical trial network

- [European Commission \(EC\)](#) – The executive body of the European Union
- [Foundation for Innovative New Diagnostics \(FIND\)](#) – An organisation aiming to ensure equitable access to reliable diagnostics around the world
- [G7](#) – The Group of 7 nations, an intergovernmental organisation consisting of Canada, France, Germany, Italy, the United Kingdom, the United States, Japan and the European Union
- [G20](#) – The Group of 20, a forum for international economic cooperation between 19 countries and the European Union
- [Gavi](#) – The Vaccine Alliance, an organisation aiming to increase access to immunisation in developing countries. Formerly the Global Alliance for Vaccines and Immunisation.
- [Genomic sequencing](#) – A scientific methodology to identify the genetic material found in an organism or virus
- [Genomic surveillance](#) – The collection of statistically significant genomic sequence data to represent populations. Genomic sequence data is then compared to help track the spread of a virus, detect new variants, and monitor trends in circulating variants
- [Global Initiative on Sharing Avian Influenza Data \(GISAIS\)](#) – open access platform to share genomic data for viruses; initially for influenza but has been expanded to include COVID-19
- [Global Fund](#) – An international financing and partnership organisation fighting AIDS, Tuberculosis and Malaria epidemics
- [Global Health Security Agenda \(GHSA\)](#) – global effort of more than 70 countries, international and non-governmental organisation, and private sector companies to enhance detection and response of infectious diseases
- [Global Research Collaboration for Infectious Disease Preparedness \(GloPID-R\)](#) – A global coalition of research funders, which invests in research to improve pandemic, epidemic, and outbreak preparedness and response
- [Global Pandemic Data Alliance \(GPDA\)](#) – An alliance formed in September 2021 to drive forward implementation of the G7 recommendations to improve safe data access and use for health emergencies
- [Good Clinical Trials Collaborative \(GCTC\)](#) – A partnership launched in June 2020 to develop guidance to enable and promote informative, ethical and efficient randomised controlled clinical trials
- [HDT \(Host-directed therapy\)](#) – type of therapeutic intervention that targets the host-mediated response to a pathogen (rather than acting directly on the pathogen itself)
- [Health Emergency Preparedness and Response Authority \(HERA\)](#) – An EU department launched in 2020 to improve Europe's capacity and readiness to respond to health emergencies
- [HICs](#) – High-Income Countries
- [International Coalition of Medicines Regulatory Authorities \(ICMRA\)](#) – A voluntary coordinating and advocacy group of regulatory authorities
- [International Clinical Trials Registry Platform \(ICTRP\)](#) – WHO-led effort ensure that a complete view of research is accessible to all those involved
- [International Council for Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use \(ICH\)](#) – An initiative bringing together regulatory authorities and pharmaceutical industry to increase harmonisation through development of technical guidelines and requirements across the pharmaceutical product lifecycle.
- [International Federation of Pharmaceutical Manufacturers & Associations \(IFPMA\)](#) – An international industry association representing research-based pharmaceutical companies and associations
- [International Health Regulations \(IHR\)](#) – A binding instrument of international law last revised in 2005 to prevent, protect against, control and provide a public health response to the international spread of disease
- [International Monetary Fund \(IMF\)](#) – An international financing agency of the United Nations that promotes global growth through financial stability and monetary cooperation
- [Infectious diseases](#) – Diseases caused by pathogens that can be spread between organisms
- [Institut Pasteur](#) – A private, non-profit foundation aiming to prevent and treat infectious disease through supporting research, teaching and public health initiatives through partnerships with international scientific authorities.
- [INTREPID Alliance](#) – A research-based pharmaceutical industry initiative to discover and develop antivirals for future pandemics
- [International Pathogen Surveillance Network \(IPSN\)](#) – A network for pathogen genomic surveillance to advocate for and strengthen global surveillance coverage and capacity
- [LMICs](#) – Low and Middle-Income Countries
- [mAbs](#) – Monoclonal antibodies
- [Machine Learning \(ML\)](#) – Methods that leverage data to improve performance on a set of tasks
- [Multilateral Development Bank \(MDB\)](#) – An international financial institution chartered by two or more countries, with a purpose to encourage economic development in developing countries
- [Medicines and Healthcare products Regulatory Agency \(MHRA\)](#) – The UK's regulatory authority. The MHRA is also a WHO designated 'Stringent Regulatory Authority'.
- [Modular manufacturing processes](#) – Using an assembly line type process for manufacturing, in this report referring particularly to vaccine manufacturing

- **mRNA** – Messenger ribonucleic acid: in vaccines it stimulates/teaches cells to make a specific protein which generates an immune response
- **US National Institute of Allergy and Infectious Diseases (NIAID)** – One of the 27 institutes and centres that make up the US National Institutes of Health, focused on conducting and supporting research to better understand, treat, and ultimately prevent infectious, immunologic, and allergic diseases
- **US National Institutes of Health (NIH)** – A medical research centre in the US Department of Health
- **New Variant Assessment Platform (NVAP)** – A platform set up by the UK government that deploys the UK's sequencing and virus assessment capabilities to help other countries respond to coronavirus (COVID-19) and strengthen global health security
- **One Health Approach** – A collaborative, multisectoral, and transdisciplinary approach, working at the local, regional, national, and global levels, with the goal of achieving optimal health outcomes recognising the interconnection between people, animals, plants, and their shared environment
- **PAD** – Pandemic Antiviral Discovery, a research funding initiative created by BMGF, the Novo Nordisk Foundation, and Open Philanthropy
- **PAHO (Pan-American Health Organisation)** – specialised health agency of the Inter-American System and Regional Office for the Americas of the World Health Organization (WHO) that engages in technical cooperation with member countries to fight communicable and noncommunicable diseases
- **Pandemic** – An epidemic occurring worldwide, or over a very wide area, crossing international boundaries and usually affecting a large number of people
- **Pandemic Hub** – WHO Hub for Pandemic & Epidemic Intelligence
- **PANORAMIC (Platform Adaptive trial of NOvel antiVIRals for eArly treatMent of COVID-19 In the Community)** – UK-wide clinical study sponsored by the University of Oxford and funded by the National Institute for Health and Care research identify new treatments for those suffering from COVID-19 to get better quicker and without needing to be treated in hospital
- **PATH** – global team of innovators working to accelerate health equity by sharing the expertise, resources, and innovations of private industry
- **Pathogen** – an organism causing disease to its host
- **Partnership for African Vaccine Manufacturing (PAVM)** – initiative launched by the African Union to boost vaccine manufacturing in Africa
- **Phase 2** – The second phase of clinical trials, following phase 1 safety studies. Phase 2 trials test safety and efficacy in ideal conditions. It precedes (and is sometimes combined with) large-scale phase 3 trials which test effectiveness in real-world conditions
- **PHEIC** – Public Health Emergency of International Concern, declared by WHO
- **PPR** – Pandemic Preparedness and Response
- **Priority pathogens** – A list of diseases and pathogens prioritized for R&D in public health emergency contexts by the WHO R&D Blueprint team, due to be updated in early 2023
- **'Programmable' technologies** – denotes the transformative impact of new technology platforms and approaches, like mRNA, which allow scientists to rapidly amend medical tools to respond to a specific pathogen
- **Proof of Concept (PoC)** – evidence based on an experiment or pilot programme that demonstrates feasibility
- **Prototype diagnostic/therapeutic/ vaccine** – Broad-spectrum or generic DTVs developed in response to a class of pathogen e.g., coronavirus, that could be rapidly adapted to respond to a specific type of pathogen e.g., COVID-19
- **Prototype pathogen** – one of a single type from a pathogen group or family with similar characteristics, against which it is possible to produce prototype DTVs
- **R0** – a figure that expresses the average number of cases of an infectious disease that arise by transmission from a single infected individual
- **Rapidly Emerging Antiviral Drug Development Initiative (READDI)** – A global nonprofit initiative aiming to develop new broad-spectrum antiviral drug solutions against viral families of pandemic potential
- **Randomised Evaluation of COVID-19 Therapy (RECOVERY Trial)** – A randomised evaluation of COVID-19 therapy, large-enrolment clinical trial of possible treatments for severe COVID-19 infection
- **Randomised Controlled Trial (RCT)** – A trial in which subjects are randomly assigned to one of two groups: one (the experimental group) receiving the intervention that is being tested, and the other (the comparison group or control) receiving an alternative (conventional) treatment
- **Rapid Diagnostic Test (RDT)** – A medical diagnostic test that is easy to use and provides quick results, typically in 20 minutes or less
- **Regulatory Authority (RA)** – government authority responsible for governing regulatory and licensing activity related to human trials
- **R&D** – Research and Development
- **REMAP-CAP (Randomised, Embedded, Multi-factorial, Adaptive Platform trial for Community-Acquired Pneumonia)** – International collaboration with 250 participating networks to evaluate treatment for CAP, which was leveraged during the pandemic for patients with known or suspected COVID-19
- **Regionalised Vaccine Manufacturing Collaborative (RVMC)** – A WEF-supported Collaborative launched in 2022 to close the Global Vaccine Equity Gap by promoting a new model of Regionalized Vaccine Manufacturing

- **Rules of the road** – Denotes expected protocols of behaviour and collaboration for use in a pandemic context. These protocols should form part of a wider suite of guidance WHO sets out (for instance, covering travel and PPE) which must be agreed in advance and demonstrate a step-change from business as usual when a PHEIC is declared
- **Solidarity Therapeutics trial** – A global RCT set up by the WHO to provide robust results on life-saving treatments (remdesivir, lopinavir, hydroxychloroquine, and interferon) for those hospitalized with severe or critical COVID-19, started in March 2020 (the first of the Solidarity trials)
- **Small molecule antivirals** – Chemical compounds typically comprising only 20-100 atoms. These therapeutics can enter cells easily due to low molecular weight
- **Strategic Center of Biomedical Advanced Vaccine Research and Development for Preparedness and Response (SCARDA)** – A vaccine-research initiative funded by the Japanese government
- **Stringent Regulatory Authorities (SRA)** – National drug regulatory authorities which are members or observers or associates of the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use, as defined by WHO
- **Science and Technology Expert Group (STEG)** – Advisory group to the International Pandemic Preparedness Secretariat
- **Target Product Profile (TPP)** – The desired R&D outcome of a product that is aimed at addressing a particular disease or diseases
- **Technology transfer** – The process of transferring the knowledge, physical objects, skills and technology management required to manufacture DTVs with a particular emphasis on the challenges and complexity of vaccine manufacturing technology transfer
- **Therapeutics** – The branch of medicine concerned with the treatment of disease and the action of remedial agents. Commonly referred to as medicines or treatments
- **Tropical Disease Research (TDR)** – a Special Programme for Research and Training in Tropical Diseases co-sponsored by UNICEF, the United Nations Development Programme, the World Bank and the WHO
- **UMICs** – Upper-Middle-Income Countries
- **UNICEF** – United Nations Children's Fund, is an agency of the United Nations responsible for providing humanitarian and developmental aid to children worldwide
- **Unitaid** – An international financing and partnership organisation hosted by the WHO funding initiatives to address diseases such as AIDS, Tuberculosis and Malaria
- **UK Department of Health and Social Care (UK DHSC)** – A department in UK Government responsible for government policy on health and adult social care.
- **UK Health Security Agency (UKHSA)** – An executive agency, sponsored by the UK Department of Health and Social Care
- **Vaccine** – A product that stimulates a person's immune system to produce immunity to a specific disease, protecting the person from that disease
- **Vaccine Innovation Prioritisation Strategy (VIPS) Alliance** – three-year collaboration between the Gavi Secretariat, the WHO, BMGF, UNICEF and PATH to develop a single integrated framework to evaluate and prioritise vaccine product innovations and to drive these innovations forward
- **Virus** – A sub-microscopic infectious agent that replicates only inside the living cells of an organism
- **Virus families** – Classification of viruses according to characteristics (e.g., single or double stranded); viruses in the same family have similar characteristics
- **Wellcome** – A global charitable foundation supporting science to solve urgent health issues
- **Working Group on Amendments to the International Health Regulations (2005) (WGIHR)** – group launched in 2022 to develop a package of reforms ready for the 77th WHA in 2024
- **World Health Assembly (WHA)** – The decision-making body of the World Health Organization
- **World Health Organization (WHO)** – An agency of the United Nations that sets standards for disease control, healthcare, and medicines; conducts education and research programs; and publishes scientific papers and reports
- **World Economic Forum (WEF)** – An international organisation that brings together its membership of political and business leaders on a yearly basis to discuss major issues concerning the world political economy
- **World Intellectual Property Organisation (WIPO)** – Global database that provides free of charge access to legal information on intellectual property
- **World Trade Organisation (WTO)** – An intergovernmental organisation that deals with the global rules of trade between nations to facilitate and regulate international trade

# Annex C:

## Methodology

This report provides detailed coverage of progress against the 100 Days Mission and each of the 25 recommendations (from January to December 2022), based on three data sources, collected in Q4:

- Desk research for relevant documents and datasets
- Structured interviews with key global health and PPR stakeholders
- Pro-forma surveys from key stakeholders

### Desk research for relevant documents and datasets

Sources for desk research includes (but is not limited to):

- Implementation and strategy reports of key initiatives related to PPR
- Updated guidelines, protocols, and frameworks from regulatory authorities
- Press releases and publications from international organisations
- Resolutions and agreements from international governance forums
- Annual reports and press releases from relevant private sector organisations
- Peer reviewed research literature from academic institutions
- External evaluations of international progress towards PPR

### Structured interviews with key global health and PPR stakeholders

31 interviews were conducted with representatives from implementation partners. The interview guide covered the following topics for discussion:

- Progress in 2022 compared to the original ambition
- Key players and coordination mechanisms
- Potential overlap or duplication across other recommendations
- Recent advancements in science & technology that support delivery
- Challenges that could provide a risk to delivery
- Future path, confidence in achieving ambition and any potential scope amendments

### Collection of pro-forma surveys from key stakeholders

Written input was requested from implementation partners through standardised pro-formas across the following topics:

- Progress in 2022
- Plans to take forward 100DM and proposed milestones
- Alignment of 100DM with ongoing priorities and approach to implementation
- Organizations identified as collaborators and engagement framework
- Barriers, risks, and enablers to achieving 100DM by 2026
- Future path, progress indicators and what constitutes a successful outcome

The draft report was reviewed by key implementation partners who provided input and was finalised with input from the Secretariat Steering Group.

# Annex D:

## Secretariat detail

### Steering Group organisations

The Secretariat Steering Group comprises representatives from the following organisations:

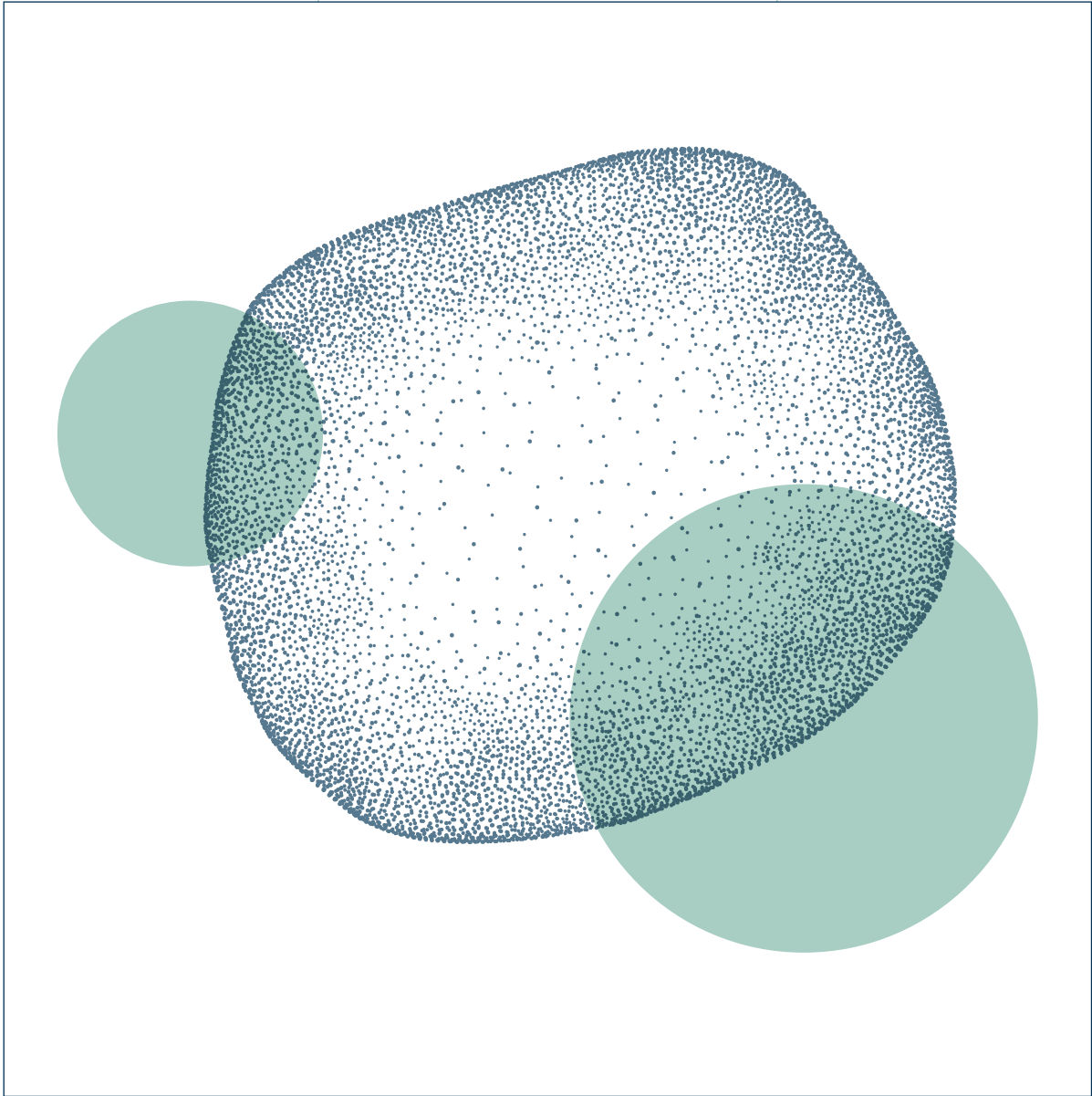
- Representatives from the current, past year, and incoming G7 presidencies
- Current G20 presidency
- World Health Organisation (WHO)
- Wellcome Trust
- Bill and Melinda Gates Foundation (BMGF)
- International Federation of Pharmaceutical Manufacturers & Associations (IFPMA)
- STEG Co-Chairs
- Sir Patrick Vallance, UK Chief Scientific Advisor (Independent Chair)
- Insight into innovative and accessible formulations for diagnostics, therapeutics and vaccines (for example, to optimise rollout and community engagement)
- Management and oversight of large-scale international clinical trials
- Knowledge of global regulatory processes

### Process for STEG nominations

Achieving the 100 Days Mission will require the successful creation of a variety of ambitious science and technology capabilities in a very short timeframe. To help achieve this, a Science and Technology Expert Group (STEG) is being set up to provide technical advice, expertise, and an assurance on progress to the Secretariat and its Steering Group. The STEG's mission will be to galvanise support from the global scientific community on pandemic preparedness through meetings, periodic scientific working groups, assessments, and other related activities.

At the time of writing, the STEG is openly inviting nominations for membership via the following website: [wellcome.org/100DaysMission](https://wellcome.org/100DaysMission). This will run until 5th February 2023 and will then go to selection by an independent selection panel. Members will be selected to show geographical diversity and gender balance, as well as ensuring adequate representation across the following criteria:

- Technical expertise in disciplines such as biology, biotechnology, immunology, pharmacology, vaccinology, epidemiology, virology, molecular biology, social science, and/or data science
- Expertise in one of the following priority areas of the mission: surveillance, research and development coordination, clinical trials and regulation, regionalised manufacturing or financing
- Leadership roles in academia, philanthropies, industry or international organisations



**Second  
Implementation Report**  
31st January 2023