100 Days Mission

Implementation Report | 2024

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

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IPPS International Pandemic Preparedness Secretariat

100DM

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Mobilising the 100 Days Mission: The Clock is Ticking

Foreword from **Dr Mona Nemer**,
Chair of the International Pandemic Preparedness Secretariat and Chief Science Adviser of Canada

Three years ago, Chief Scientific Advisers from across the G7 came together to sound an alarm: despite the lessons learnt from the ravages of the COVID-19 pandemic, the world was still unprepared to effectively respond to emerging pandemic threats. The pandemic had caused profound health, social and economic damage, but the mobilisation of research and the rapid development of new knowledge and medical technologies offered optimism for pandemic preparedness and response (PPR). It was this optimistic view that resulted in the first 100 Days Mission (100DM) implementation report. The report outlined how the global community could work together to ensure timely global access to diagnostics, therapeutics, and vaccines within 100 days of a Public Health Emergency of International Concern (PHEIC). The report also provided the framework that the International Pandemic Preparedness Secretariat (IPPS) has used to track progress towards this mission over the past four years.

As Chief Science Adviser of Canada, I was involved in the development of these recommendations and strongly supported the Mission's goal of equipping the world with the tools to respond to future pandemic threats. This past year, in my capacity of Chair of the 100DM Steering Group, it has been an honour to collaborate with many partners towards the global implementation of our commitments. Amidst new and persisting outbreaks of infectious diseases with pandemic potential, the critical need for the 100DM has never been clearer.

Five years on from the declaration of the COVID-19 pandemic, the world continues to feel its social, economic and health impacts, and new variants of SARS-CoV-2 continue to spread. For the second time in two years, mpox has been declared a PHEIC, after being endemic in many countries for years. Other serious threats have emerged. They include the ongoing H5N1 outbreak across North America, and Marburg spread in Rwanda, among others. These demonstrate the range of risks we face, and the urgency of the 100DM. As a case in point, if concerted work to develop or advance tools for mpox had continued since the PHEIC was first declared in 2022 – particularly point-of-care diagnostics and therapeutics – our collective ability to respond to the resurgent mpox epidemic at day zero would have been markedly different. However, we also saw the benefit of having vaccines ready for scale-up at day zero, and accelerated regulatory approvals made possible due to vaccine development which had happened between outbreaks, enabling agile response. The Africa Centres for Disease Control and Prevention's (Africa CDC's) declaration of the first Public Health Emergency of Continental Security and Rwanda's swift activation of the 100DM in response to Marburg cases are shining examples of what can be achieved when best practices are embedded and institutionalised at regional and national levels.

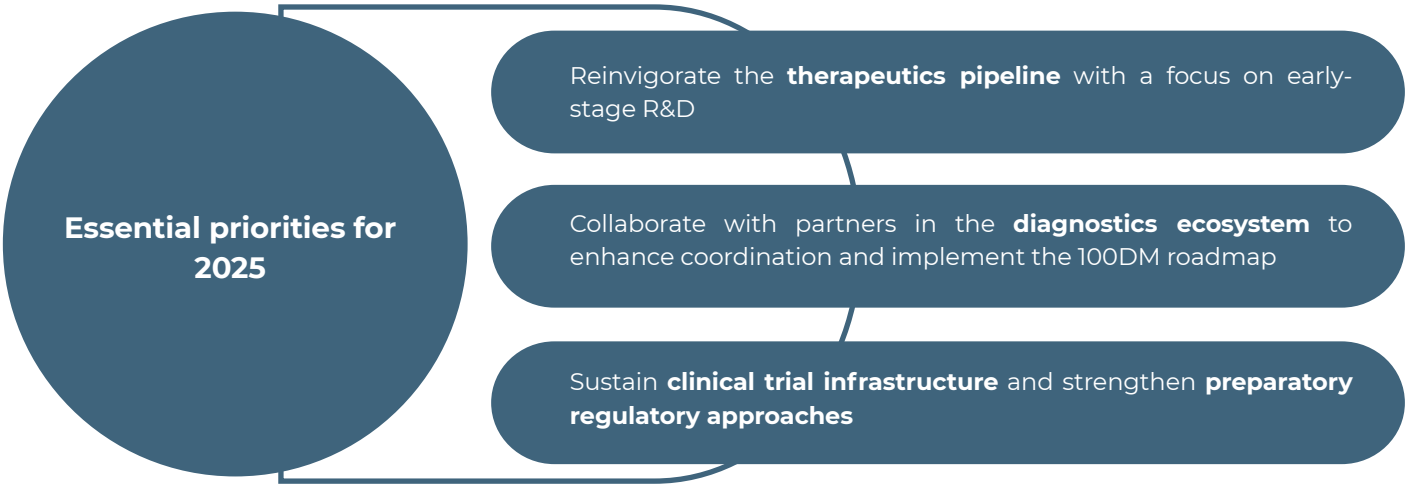
Globally, we all benefit from having adequate testing, vaccines and therapeutics that contain and manage infectious disease outbreaks where they start and before they become public health emergencies with huge economic and social costs. Pathogens of pandemic potential do not respect borders, which is why we must keep pandemic preparedness and response high on the political agenda, notwithstanding the many other ongoing global challenges and polycrisis. Prioritising resources to support implementation of the 100DM at a national, regional, and global level contributes to our collective health and economic security.

In 2024, IPPS identified the need for action in four priority areas to promote therapeutics and diagnostics R&D for priority viral families, support regulatory harmonisation and strengthen clinical trials infrastructure. I am encouraged by the progress that the 100DM partners have made but we still have a way to go to meet our ambitions.

Last year, our 100DM therapeutics roadmap recommended the establishment of a Therapeutics Development Coalition to reinvigorate the therapeutics pipeline for diseases with pandemic potential. Since then, we have been working with stakeholders from across industry, academia, government, and international organisations to implement this recommendation and chart the path forward.

Several collaborations have been established to strengthen clinical trial capacity, including the recently published WHO guidance on best practices for clinical trials, and efforts toward regulatory harmonisation — the regional initiatives across Africa, Latin America and Asia Pacific are noteworthy examples. Progress is also happening across the diagnostics ecosystem, where regulatory harmonisation would greatly accelerate timely availability of testing and monitoring.

However, significant work remains. For 2025, we have kept headline priority topics consistent with 2024 as the work is far from over, but have endeavoured to articulate more granular next steps.



Sustainable, coordinated funding for research and development in therapeutics and diagnostics is essential to fill crucial gaps – complacency will cost lives. We must implement guidance to strengthen global and regional clinical trial capacity, and harmonise regulatory approaches for diagnostics, vaccines, and therapeutics development and deployment.

The launch of the WHO pathogen prioritisation framework can help facilitate greater alignment across R&D of all three tools, leveraging global expertise and resources. For example, focusing efforts on developing diagnostics and therapeutics in tandem for an initial short list of pathogens will improve research and development efficiencies and enable test to treat programmes. These are interconnected – vaccines are not always available and we need to have fast, accurate tests to diagnose and treat illnesses.

As Canada and South Africa assume the G7 and G20 presidencies for 2025, there is a great opportunity to align efforts and sustain momentum across global, regional, and national levels. Both forums can play a key role in maintaining focus on the 100DM, fostering collective commitments and investments for global health and security.

I would like to thank everyone who contributed to advancing and tracking the implementation of the 100DM and who worked hard to produce this comprehensive report.

With unwavering determination, focused investment, and cross-sector partnerships, the ambition of the 100DM to ensure global health security is attainable. But the clock is ticking. Now is the time to act.

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EXECUTIVE SUMMARY

The 100 Days Mission (100DM) aims to ensure that safe, effective, and affordable diagnostics, therapeutics, and vaccines (DTVs) are ready for scaled production within 100 days of a declared Public Health Emergency of International Concern (PHEIC), maximising health impact and saving lives. The 100DM is paramount as the world grapples with an active mpox PHEIC, increasing rates of transmission of H5N1 influenza from animals to humans, and multiple regional outbreaks caused by viruses such as Marburg, Dengue, and Oropouche. Amidst these ongoing threats, the urgency of the 100DM has never been more evident. The distinction between endemic and epidemic diseases is blurring, and both can potentially lead to pandemics, influenced by environmental and behavioural changes. Global response systems must therefore evolve to overcome silos to enable seamless, timely sharing of data and expertise. While global health communities adapt and learn from their experiences, sustaining progress remains a significant challenge amidst polycrisis, limited resources, and competing political priorities in a rapidly changing global landscape, with further shifts anticipated in 2025.

Spotlights on embedding 100DM principles at national and regional levels:

Spotlights throughout the report highlight the 100 Days Mission in action, particularly implementation at the national and regional levels. Our belief is that every nation has the right to be able to equip themselves with tools and systems to be able to respond to disease outbreaks within 100 days, and we aim to celebrate where we see progress towards this goal.

2024 PROGRESS TOWARDS 100DM OBJECTIVES

In 2024, the International Pandemic Preparedness Secretariat (IPPS) diligently monitored global progress toward the 100DM through research, interviews, and feedback from partners. Despite substantial obstacles, progress was achieved in several key areas. Nevertheless, sustainable funding and coordinated R&D efforts are still essential to address critical gaps:

- **Coordination in the R&D ecosystem continues to improve:** Publication of the WHO pathogen prioritisation framework and development of Collaborative Open Research Consortium (CORCs) represent significant advances that could accelerate DTV R&D progress while fostering viral family-level collaboration. Additionally, the establishment of the G20 Coalition on Local and Regional Production, Innovation, and Equitable Access marks a significant step toward enabling equitable access to DTVs.

- **Progress in DTV R&D has been uneven with persistent access challenges:** While diagnostic development for priority pathogen families remained limited, with significant gaps in point-of-care tests, and the therapeutics pipeline remained alarmingly bare, more substantial advances were made in vaccines R&D. The Therapeutics Development Coalition gained momentum in 2024, catalysed by global consultations organised by IPPS and other key stakeholders. Partners effectively aligned on the Coalition's scope and objectives while defining essential components of its operational model to enable partnership-based approaches to early-stage therapeutic R&D. Notably, a strategic decision was made to initially concentrate efforts on two priority viral families. 2024 also saw meaningful advances in preclinical development of prototype vaccines and rapid response platforms, and ongoing efforts to build sustainable, geo-diversified manufacturing capabilities.

- **Expansion of geo-diversified trial networks and regional regulatory harmonisation efforts support rapid response capabilities:** In 2024, efforts focused on strengthening clinical trial and regulatory systems to support both routine and emergency needs - ensuring their long-term sustainability. Key developments include the publication of WHO's Guidance for Best Practices for Clinical Trials, initiatives from GloPID-R (a global research collaboration for infectious disease preparedness) and others to support coordination of funding and clinical trial networks during emergencies, and the expansion of regional trial networks. Notable progress was also made in regional reliance mechanisms and regulatory harmonisation efforts to support rapid response capabilities across Africa, Latin America, and Asia Pacific, including the operationalisation of the African Medicines Agency.

PRIORITY 100DM ACTION AREAS FOR 2025

While progress has been made, analysis from implementation partner feedback and the 100DM scorecard data (see Chapter 1) highlights key areas needing urgent attention in 2025. Rather than presenting an exhaustive list, these priorities highlight issues that have received insufficient attention to date and where tangible progress can be achieved in 2025. The headline priorities remain consistent with those of 2024 - as the work is far from over - though they are presented here with increased specificity on next steps:

Reinvigorate the therapeutics pipeline with a focus on early-stage R&D: In 2025, efforts will focus on operationalising the Therapeutics Development Coalition to strengthen the antiviral pipeline. This will include establishment of pre-clinical and clinical development teams and a virtual antiviral hub, ensuring alignment with the WHO pathogen prioritisation framework. The Coalition should focus on implementing proof-of-concept projects for two priority viral families, advancing candidates through preclinical and early clinical stages. Additionally, platform technologies should be advanced by demonstrating preclinical proof-of-concept for broad-spectrum antivirals, cross-reactive monoclonal antibodies (mAbs), and other innovative antiviral strategies.

Collaborate with partners in the diagnostics ecosystem to enhance coordination and implement the 100DM roadmap: In 2025, coordinated efforts from various diagnostic partners, including industry, research institutions, governments, regulatory bodies, and international organisations, are essential for advancing the 100DM. Stakeholders should collaborate on a comprehensive 100DM diagnostics roadmap that outlines roles, responsibilities, and collaboration principles. Governments and funders should allocate long-term funding for diagnostic research and development, prioritising point-of-care tests and enhancing multiplexing capabilities. Opportunities to align diagnostic development with therapeutic and vaccine R&D should be explored to enable integrated test-and-treat strategies and leverage shared resources. Strengthening global biobanking networks, simplifying regulatory pathways, and harmonising efforts through WHO's Global Benchmarking Tool will enable faster and more equitable development and deployment of diagnostics.

Sustain clinical trial infrastructure and strengthen preparatory regulatory approaches: In 2025, priority actions should focus on strengthening clinical trial infrastructure by improving coordination between regional and international trial networks and ensuring sustainability in inter-pandemic periods. Global guidance for emergency clinical trials should be developed and adopted, including specific procedures for rapidly transitioning from standard to emergency trial operations. Regulatory efforts should promote harmonisation and preparatory frameworks, including joint review processes to accelerate approval timelines. Regional reliance models should be adopted, supported by an appropriate number of globally recognised regulatory authorities in each region, to streamline emergency approvals and foster greater coordination in regulatory pathways. Flexible and responsive regulatory systems will be a key enabler for a 100DM response.

Lessons for future 100DM responses

This year's report includes a **case study in Chapter 5 on the 2024 mpox outbreak response through a 100DM lens.** In the 100 days following the August 14, 2024 mpox PHEIC declaration, IPPS tracked DTV availability and identified priority actions for accelerating the response. Through stakeholder interviews and an R&D funding review, this case study examines successes and areas for improvement in medical countermeasure (MCM) development and deployment. These insights can strengthen outbreak readiness, response, and preparedness across all 100DM areas nationally, regionally, and globally.

Key findings highlight issues from competing health priorities to evidence gaps in vaccine and therapeutic efficacy, especially for special populations. Proposed priority actions to strengthen current and future mpox responses from the interviews include:

Short-term

- Address liability issues for paediatric vaccine deployment.
- Strengthen ground-level implementation support.
- Enhance clade-specific/syndromic point-of-care diagnostic validation and deployment.

Medium - Long-term

- Develop clear frameworks for global-regional cooperation.
- Establish sustainable funding mechanisms for MCM development in an outbreak response.
- Strengthen regulatory harmonisation and emergency use pathways.
- Build sustainable and geo-diversified research and clinical trial infrastructure to advance R&D for DTVs.
- Enhance community engagement and accessibility in health systems.

100DM SCORECARD 2.0 HEADLINES:

The 100DM Scorecard, developed by Impact Global Health and IPPS, evaluates readiness to develop and deploy critical DTVs within 100 days of a PHEIC. It identifies gaps, tracks progress, and provides actionable insights based on public data. The first 100DM Scorecard was published in our 2023 implementation report, and Scorecard 2.0 now includes mpox and chikungunya, expanding on the original ten priority pathogens to align with the updated WHO pathogens with high pandemic potential. While the full scorecard can be found in Chapter 1, the indicator in Figure 1 shows the state of approved products, highlighting that there have been few new approved products since Scorecard 1.0.

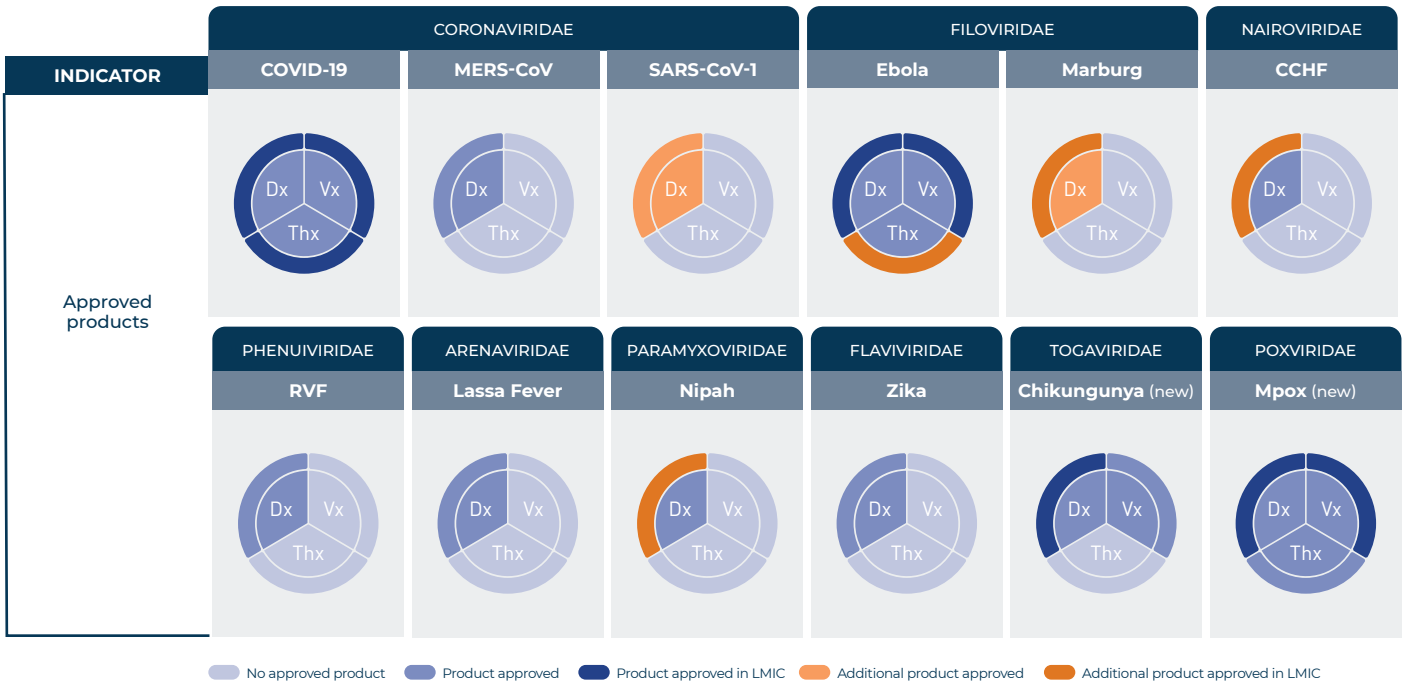


Figure 1. 100DM Scorecard product approvals (updated for period 30 August 2023 to 30 September 2024)

Key findings include:

- **DTV R&D funding for priority pathogens remains reactive:** Overall investment decreased across priority pathogens and DTVs, although there has been notable growth in funding for Disease X driven by **increased investments in disease-agnostic platform technologies.** Among DTV funding, diagnostic R&D saw strikingly limited investment, with only $13 million spent in 2023 (excluding COVID-19).

- **The R&D landscape is heavily reliant on dominant funding sources,** particularly U.S. government agencies. While the U.S. itself benefits from their investments in terms of access to medical countermeasures and world-class scientific expertise, a more diverse funding ecosystem—drawing on contributions from governments, philanthropies, and industry partners—is essential to ensure global resilience. Such investment in MCM R&D not only mitigates the social and economic impacts of future outbreaks but also strengthens global R&D ecosystems and enhances biosecurity.

- The **therapeutics pipeline for non-COVID priority pathogens is limited,** with only 27 candidates in clinical development across 11 priority pathogens. This highlights the need to expand the pipeline's size and diversity, increase the pool of developers, advance candidates through all stages of development, and backfill the early-stage pipeline to mitigate high attrition rates.

- The vaccine pipeline saw the most candidates progress, however this was concentrated in translation from preclinical to phase 1 with **limited movement in later stage vaccine clinical development.**

- **There was minimal progress on key R&D enablers:** No new WHO Target Product Profiles were identified, and progress on the development and use of correlates of protection or the animal rule to accelerate product licensure was limited, highlighting the need for further efforts in this space to improve the efficiency and effectiveness of R&D.

ROLE OF MULTILATERAL FORA IN DELIVERING 100DM PRIORITIES IN 2025

The G7 and G20 have a crucial role to play in catalysing coordinated international action to prevent and prepare for future pandemics in partnership with other sectors. While not all challenges can be solved by G7 and G20 alone, there are certain policy commitments which could unlock action by other sectors to develop the pandemic tools we all need. IPPS recommends that the Canadian G7 and South African G20 Presidency work closely together to make policy commitments in the following areas, and stands ready to support:

- **Filling the gaps in R&D:** Sustain and coordinate preparedness investments in DTV R&D to prioritise the highest risk pathogens, including through cutting-edge AI technology. Ensure that public R&D funding prioritises compounds with accessible product profiles, such as oral administration, ease of manufacturing, and global distribution. Additionally, include equitable access plans at the appropriate stage of development. Both blocs should endorse the establishment and support of the Therapeutics Development Coalition to facilitate end-to-end therapeutics development for priority diseases. This will bolster the product pipeline and ensure alignment and coordination with ongoing initiatives like the WHO CORCs and G20 Coalition on Local and Regional Production.

- **Enabling technical response protocols:** Develop more resilient and diversified product development systems for MCMs by investing strategically in economically sustainable and geo-diversified manufacturing facilities with the capability for rapid response. Enhance integrated surveillance and early warning systems across human, animal, and environmental sectors to address the escalating challenges posed by climate change. Collaborate to establish a shared framework for regulatory preparedness to ensure the safe and expedited approval of DTVs during health emergencies.

- **Enhancing Collective Health Security:** Partner globally to expand biosafety, biosecurity, and pre-clinical capabilities. Promote innovations for effective bio-risk management, intensify capacity building with Global South partners, and agree on a common risk assessment framework for AI. Support the establishment of a new international standard on AI safety and security for biological design tools.

FUTURE DIRECTION FOR IPPS

The IPPS has two years left of its mandate, which expires at the end of 2026. During this remaining time, we plan to continue supporting and elevating our existing implementation partners. We aim to build sustainable coalitions in previously neglected areas and ultimately ensure the sustainable delivery of the 100DM. The IPPS will continue to leverage its three key areas of action: catalysing scientific exchange through the 100DM STEG, providing comprehensive updates on the state of DTV readiness through the 100DM Scorecard and outbreak response trackers, and advocating for the systemic commitments required through the G7 and G20.

1 Introduction

REMINDER OF THE GOALS OF THE 100 DAYS MISSION IN 2025

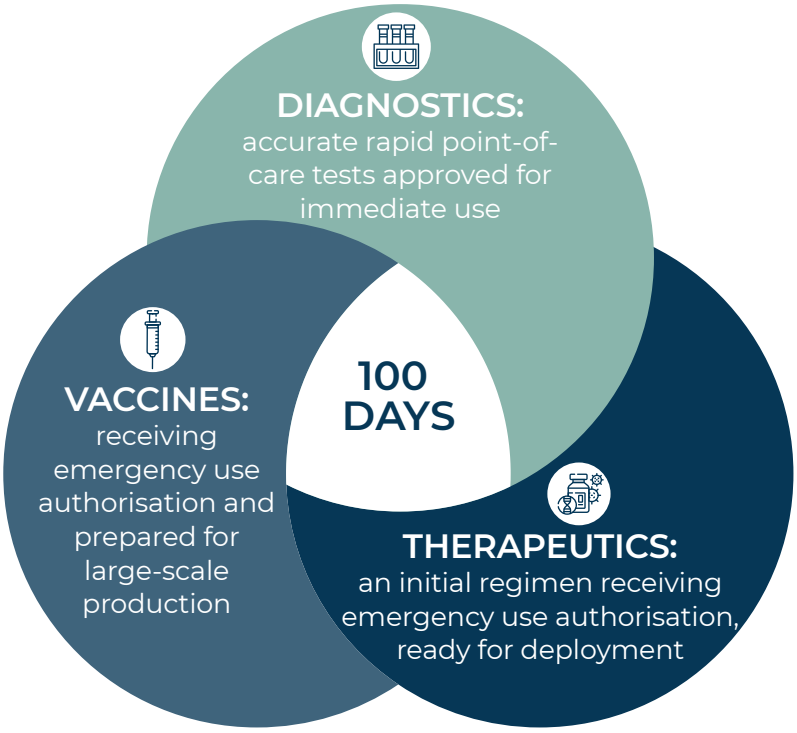
The 100 Days Mission (100DM) was originally conceptualised in 2021 at the height of the COVID-19 pandemic out of a desire to not waste the lessons learned, to capture the best of the innovation and collaboration seen, and to learn from the mistakes and challenges that saw inequitable access to critical tools around the world. Ultimately it was recognised that if we had diagnostics, therapeutics, and vaccines (DTVs) available faster, the course of the pandemic could have been dramatically different.

A modelling study from Imperial College London's MRC Centre for Global Infectious Disease Analysis estimates that over eight million lives could have been saved during the COVID-19 pandemic if safe and effective vaccines had been developed in 100 days, with the greatest impact in lower middle-income countries.[1] This underscores the importance of investing in preparedness and aligns with the overarching goals of the 100DM.

While vaccines are a critical tool for preparedness, the equitable delivery of diagnostics and therapeutics is also vital in saving lives. During COVID-19, several life-saving therapeutics were deployed; however, delays in regulatory processes hindered the timely availability of some treatments.[2,3,4]

This highlights not only the benefit of accelerating DTV development, but also the need for efficient regulatory frameworks and robust infrastructure to ensure countermeasures reach those in need. Access and equity in DTV development and delivery are central principles of the 100DM. The COVID-19 pandemic reinforced the principle that global safety is contingent on universal protection. The 100DM's goal is to ensure preparedness efforts are in place in advance of a pandemic to lay the foundations for DTVs to be delivered anywhere in the world without compromising safety, efficacy, or accessibility.

A reminder of the end goals of the mission are outlined below. This initiative focuses on delivering three key medical countermeasures (MCMs) within 100 days of a pandemic threat being declared by the World Health Organisation (WHO) as a Public Health Emergency of International Concern (PHEIC):



1 Gregory Barnsley et al., "Impact of the 100 days mission for vaccines on COVID-19: a mathematical modelling study," The Lancet Global Health 12, no. 11 (2024), https://doi.org/10.1016/S2214-109X(24)00286-9.
2 NHS England, COVID treatment developed in the NHS saves a million lives (2021), https://www.england.nhs.uk/2021/03/covid-treatment-developed-in-the-nhs-saves-a-million-lives/.
3 Allen S et al., Game Changer: Paxlovid Reduces Hospitalizations and Saves Lives (Epic Research, 2022), https://www.epicresearch.org/articles/game-changer-paxlovid-reduces-hospitalizations-and-saves-lives.
4 A. C. Kalil, "Remdesivir saves lives. Were 3 years needed to learn that?," Lancet Respir Med 11, no. 5 (May 2023), https://doi.org/10.1016/s2213-2600(23)00036-x.

The focus must be on extensive research and innovation before a pandemic emerges. Using a 100DM perspective to improve the "marathons" of DTV development through to deployment will automatically enable the "sprint" to provide safe and effective MCMs to emerging threats. It involves streamlining response processes, developing programmable platforms for vaccines and therapeutics, and promoting regular use of accurate diagnostics. For the purposes of this report 'programmable platform technologies' references disease-agnostic, reproducible technologies that support streamlined regulatory processes and plug-and-play manufacturing.

For the purposes of the 100DM, Day Zero is provisionally defined as the WHO's declaration of a PHEIC. However, it is widely recognised that this is too late to initiate effective outbreak responses. Preparedness must begin well in advance of a PHEIC, and response activities should be triggered by earlier signals. While a PHEIC offers a global reference point, reliance on it as the starting trigger may limit the potential for truly rapid containment of an outbreak. That is not to say that regions and nations cannot trigger their own 100-day response with the declaration of an emergency. We saw Africa Centres for Disease Control and Prevention (Africa CDC) do so in August 2024 with its own declaration of a Public Health Emergency of Continental Security (PHECS) for mpox before the global PHEIC was declared. We also saw Rwanda trigger their own 100-day mission to respond to the Marburg outbreak as soon as it was detected at the end of September 2024. **The most important element is that any triggers are connected to clear pre-agreed actions for financing and accelerating product development and distribution, and off-ramps identified that will enable leverage of the response for future outbreaks.**

HOW TO USE THIS REPORT: KEEPING OUR EYES ON THE PRIZE

This year's report retains the customary focus on the end goals we are all seeking to achieve, while highlighting the most globally relevant areas of progress and challenge.

Within each section, we have reiterated the overarching goals, critical bottlenecks to achieving these goals and the proposed inputs needed in 2025 to maintain satisfactory progress. The chapters provide high-level analysis, and a summary of 2025 milestones for the whole global health community to work towards. Assessment of progress against the original recommendations, and more granular planned partner commitments and recommended priority actions are summarised in Annex A based on input from over 40 implementation partners from governments, industry, academia, Civil Society Organisations (CSOs) and international organisations (see Annex C for full list of contributors), in the form of survey responses, interviews and desk research.

Written input was requested from implementation partners through standardised pro formas covering; progress in 2024, barriers, risks, and enablers to achieving 100DM goals and planned future activities which was then combined with desk research. To keep the report concise, not all updates were included, focusing on key advances with broader impact and potential for wider adoption in the field. The draft report was then reviewed by key implementation partners who provided input and was finalised with input from the International Pandemic Preparedness Secretariat (IPPS) Steering Group and Science and Technology Expert Group (STEG), and Impact Global Health.

100DM Framework Outputs, Outcomes, and Impact

VISION: **within 100 days of a recognised international trigger (e.g. WHO PHEIC), diagnostics, therapeutics and vaccines are approved* and ready to be produced at scale for global deployment**

SPHERE OF CONTROL	SPHERE OF INFLUENCE		SPHERE OF INTEREST
IPPS activities	100DM 2025 outputs	100DM long term outcomes	Impact
Facilitating and convening multisectoral collaborations	**DIAGNOSTICS R&D** ○ Publish 100DM diagnostics roadmap ○ Develop rapid point-of-care tests for at least two priority viral families ○ Reduce complexity of diagnostic regulatory pathways	• Diagnostics R&D is coordinated in a sustainable ecosystem • Development of diagnostics libraries provides broad coverage for priority viral families • Diagnostics routinely linked to testing and treatment	✓ DTVs are rapidly developed, and equitably distributed based on greatest impact and need, in the event of a pandemic threat
	THERAPEUTICS R&D ○ Therapeutics Development Coalition launched and operationalised ○ Coalition is supported to take de-risked candidates through preclinical and early clinical development, bringing assets to phase 2 for at least two viral families	• Prototype therapeutics libraries developed, supported by pre-agreed procedures in place for therapeutic repurposing and equitable access • At least two therapeutics products for the WHO viral families with high pathogen potential, ideally with different mechanisms of action	
	VACCINES R&D ○ Progress vaccine candidates for priority viral families to clinical stages ○ Establish economic risk-sharing models to enable development of diverse platform technologies	• Continued work on vaccine libraries covering WHO priority pathogen families • Rapidly programmable platform technologies available • Vaccine platforms optimised for large-scale production	
Providing technical expertise (STEG, implementation reports)	**CLINICAL TRIALS AND REGULATORY PROCESSES** ○ Global emergency use clinical trial guidance finalised and adopted, utilising regional networks ○ Regulators coordinate to adopt preparatory regulatory approaches ○ Regional reliance models adopted, enabled by an appropriate number of globally recognised regulatory authorities in each region	• Clinical trial sites are sustained between pandemics • Best practices on clinical trial design and innovative and adaptive trial designs utilised • Master trial protocols pre-agreed for use in emergencies, emphasising real-world evidence for product licensure • Preparatory and harmonised regulatory frameworks adopted by regulators for pathogens where traditional randomised controlled trials are unfeasible • Strengthened and aligned regulatory capacity in all regions with pharmacovigilance enabled from the outset	✓ Products authorised for use in humans (e.g. EUA) within 100 days due to pre-emptive data generation and high-quality clinical trials mobilised rapidly utilising existing infrastructure
	SURVEILLANCE ○ Collaborative surveillance enhanced through international networks ○ National capacities for data collection and early warning systems strengthened ○ Digitally connected diagnostics feed into the surveillance system	• International network(s) of global/regional/local surveillance systems identifies outbreaks and enables trusted data sharing • Reliable, fair, safe, and fit-for-purpose mechanisms for rapid exchange of pathogen samples enable equitable R&D efforts for DTVs	✓ Pathogens are characterised using genomic sequencing and other integrated approaches, with surveillance data shared to prevent outbreaks from escalating into pandemics
Influencing global political agendas	**SUSTAINABLE AND GEO-DIVERSIFIED MANUFACTURING** ○ Regional authorities supported to implement sustainable manufacturing capacities ○ Continued strengthening of public-private partnerships within regional manufacturing strategies for drug substances, drug products and intermediaries ○ Preparatory voluntary licensing systems expanded on a case-by-case basis and as appropriate	• There is capacity and capability to produce DTVs in each region • The ecosystem supports voluntary licensing, technology transfer, supply-side incentives for investment and demand-side procurement mechanisms • Developers and manufacturers align on platforms that can be adapted to produce both routine and pandemic products	✓ Each region produces technologies, pivoting its manufacturing sites along the value chain in response to threats, ensuring equitable and timely access to critical inputs
	SUSTAINED PANDEMIC FINANCING AND EQUITABLE PROCUREMENT ○ Global recommendations set on surge financing, stockpiling strategy, and advanced market commitments ○ Procurement agreements prioritise equitable access	• Mechanisms enable the automatic release of funding (e.g., for procurement) tied to globally agreed trigger points • LMICs can purchase and distribute DTVs through equitable allocation and procurement of supplies	✓ Countries have access to and mobilise funding to reduce pandemic threat escalation

*Approved, available under Emergency Use Authorisation (EUA). 100DM long term outcomes and impact remain unchanged from 3rd implementation report.

100 DAYS MISSION SCORECARD & ANALYSIS

The 100DM Scorecard was designed to objectively evaluate our readiness to develop and deploy critical DTVs for epidemic response within 100 days of a pandemic threat. Developed by Impact Global Health in partnership with the International Pandemic Preparedness Secretariat, this Scorecard highlights gaps, identifies progress, and offers actionable insights based on publicly available data. By providing a structured assessment of key R&D indicators across the WHO R&D blueprint priority pathogens, the Scorecard enables stakeholders to make informed decisions to advance preparedness, build resilience, and ultimately strengthen our collective response to future pandemics. Currently, the Scorecard is focused on the biomedical R&D that supports the 100DM due to data availability and funding limitations. For further information on the future vision of an expanded Scorecard and the definitions and sources for the indicators, see Future of the Scorecard (Version 3.0) and Annex E respectively.

The WHO R&D blueprint underwent significant transformation in 2024, now providing a scientific framework for epidemic and pandemic research preparedness and incorporating additional pathogen families. To reflect these changes, the Scorecard this year includes mpox and chikungunya in addition to the ten priority pathogens from last year. The table below compares the current and previous WHO pathogens and viral families with those now included in Scorecard 2.0.

Table 1. Prioritisation of viral families of high pandemic potential

WHO 2018 Prioritisation (Scorecard 1.0)	WHO 2024 Prioritisation – viral families of high pandemic potential	Scorecard 2.0
Arenaviridae Priority pathogen: Lassa Fever virus	**Arenaviridae** Priority pathogen: Mammarenavirus lassaense (Lassa Fever virus)	**Arenaviridae** Indicator: Lassa Fever virus
Coronaviridae Priority pathogen: MERS-CoV SARS-CoV-1	**Coronaviridae** Priority pathogen: *Subgenus* Merbecovirus (MERS-CoV) *Subgenus* Sarbecovirus (SARS-CoV-1, COVID-19)	**Coronaviridae** Indicators: MERS-CoV SARS-CoV-1 COVID-19
Filoviridae Priority Pathogens: Ebola virus Marburg virus	**Filoviridae** Priority pathogens: Orthoebolavirus zairense (Zaire Ebola virus) Orthoebolavirus sudanense (Sudan Ebola virus) Orthomarburgvirus marburgense (Marburg virus)	**Filoviridae** Indicators: Ebola virus Marburg virus
Flaviviridae Priority Pathogen: Zika virus	**Flaviviridae** Priority pathogen: Orthoflavivirus zikaense (Zika virus) Orthoflavivirus denguei Orthoflavivirus flavi	**Flaviviridae** Indicators: Zika virus
	Hantaviridae Priority pathogens: Orthohantavirus sinnombreense Orthohantavirus hantanense	
Nairoviridae Priority Pathogen: Crimean-Congo Haemorrhagic Fever (CCHF)	**Nairoviridae** Priority Pathogen: Orthonairovirus haemorrhagiae (CCHF)	**Nairoviridae** Indicators: Crimean-Congo Haemorrhagic Fever (CCHF)
	Orthomyxoviridae Priority Pathogens: Alphainfluenzavirus Influenzae H1, H2, H3, H5, H6, H7, H10	
Paramyxoviridae Priority Pathogens: Nipah and henipaviral diseases	**Paramyxoviridae** Priority pathogen: Henipavirus nipahense (Nipah virus)	**Paramyxoviridae** Indicator: Nipah virus
Phenuiviridae Priority pathogen: Rift Valley Fever (RVF)	**Phenuiviridae** Priority pathogen: Bandavirus dabieense	**Phenuiviridae** Indicator: Rift Valley Fever (RVF)
	Poxviridae Priority pathogens: Orthopoxvirus variola Orthopoxvirus monkeypox (mpox)	**Poxviridae** Indicator: mpox
	Togaviridae Priority pathogens: Alphavirus chikungunya (Chikungunya) Alphavirus venezuelan	**Togaviridae** Indicator: Chikungunya

100DM SCORECARD

		CORONAVIRIDAE			FILOVIRIDAE		NAIROVIRIDAE	PHENUIVIRIDAE	ARENAVIRIDAE	PARAMYXOVIRIDAE	FLAVIVIRIDAE	TOGAVIRIDAE	POXVIRIDAE
	INDICATOR	COVID-19	MERS-CoV	SARS-CoV-1	Ebola	Marburg	CCHF	RVF	Lassa Fever	Nipah	Zika	Chikungunya (new)	Mpox (new)
NOW	R&D funding for diagnostics, therapeutics and vaccines (2020-2023)	Δ from 2022: ▼ $17.1b	Δ from 2022: ▼ $43m	Δ from 2022: ▼ $53m	Δ from 2022: ▼ $654m	Δ from 2022: ▼ $252m	Δ from 2022: ▼ $35m	Δ from 2022: ▼ $36m	Δ from 2022: ▼ $87m	Δ from 2022: ▲ $97m	Δ from 2022: ▼ $196m	Δ from 2022: ▲ $116m	* only 2022-2023 funding data available Δ from 2022: $82m
		45% 28% 8% 20%	91% 6% 1% 2%	42% 41% 16% 1%	73% 19% 5% 3%	98% 1% 0.3%	76% 10% 9% 4%	74% 23% 3% 1%	96% 3% 1% 0.5%	90% 5% 4% 1%	87% 3% 3% 7%	51% 28% 14% 7%	86% 7% 6% 1%
		U.S. government, Aggregate industry, German government, Other	U.S. government, Samsung Foundation, Aggregate industry, Other	U.S. government, Aggregate industry, Japanese government, Other	U.S. government, Aggregate industry, European Commission, Other	U.S. government, Advanced Technology, International (ATI), UK government	U.S. government, European Commission, UK government, Other	European Commiss, U.S. governm, UK governm, Ot	U.S. government, Wellcome, European Commission, Other	U.S. government, Aggregate industry, Gates Foundation, Other	U.S. government, UK government, Aggregate industry, Other	U.S. government, European Commission, Aggregate industry, Other	U.S. government, Aggregate industry, UK government, Other
	Approved products	Dx Vx Thx	Dx Vx Thx	Dx Vx Thx	Dx Vx Thx	Dx Vx Thx	Dx Vx Thx	Dx Vx Thx	Dx Vx Thx	Dx Vx Thx	Dx Vx Thx	Dx Vx Thx	Dx Vx Thx
		No approved product; Product approved; Product approved in LMIC						Additional product approved; Additional product approved in LMIC					
FUTURE READINESS	Candidates tested in humans	Phase III: 64 Vx, 17 Thx; II: 52, 25; I: 57, 17; Late stage: 87 Dx	Phase III: 0, 0; II: 0, 2; I: 2, 1; Late stage: 7 Dx	Phase III: 0, 0; II: 0, 0; I: 0, 0; Late stage: 0 Dx	Phase III: 1, 1; II: 1, 1; I: 6, 4; Late stage: 16 Dx	Phase III: 0, 0; II: 1, 0; I: 3, 1; Late stage: 1 Dx	Phase III: 0, 0; II: 0, 1; I: 2, 1; Late stage: 11 Dx	Phase III: 0, 0; II: 1, 0; I: 3, 0; Late stage: 5 Dx	Phase III: 0, 0; II: 1, 3; I: 2, 1; Late stage: 13 Dx	Phase III: 0, 0; II: 0, 0; I: 5, 2; Late stage: 1 Dx	Phase III: 0, 0; II: 3, 0; I: 11, 1; Late stage: 0 Dx	Phase III: 2, 1; II: 1, 0; I: 3, 1; Late stage: 2 Dx	Phase III: 0, 1; II: 2, 2; I: 2, 3; Late stage: 20 Dx
		Candidate has progressed; Candidate has become inactive											
	Platform technologies used in clinical candidates	Dx Vx Thx	Dx Vx Thx	Dx Vx Thx	Dx Vx Thx	Dx Vx Thx	Dx Vx Thx	Dx Vx Thx	Dx Vx Thx	Dx Vx Thx	Dx Vx Thx	Dx Vx Thx	Dx Vx Thx
		No platform technology used; Less than three platform technologies used; Three or more platform technologies used						New platform technologies used, less than three; New platform technologies used, three or more					
	Disease X R&D funding (2020-2023)	DIAGNOSTIC PLATFORMS Δ from 2022: ▲ $336m				THERAPEUTIC PLATFORMS Δ from 2022: ▲ $756m				VACCINE PLATFORMS Δ from 2022: ▲ $666m			
		74% 12% 5% 9% — U.S. government, Gates Foundation, European Commission, Other						86% 8% 3% 4% — U.S. government, Gates Foundation, European Commission, Other		43% 43% 5% 9% — Gates Foundation, U.S. government, Aggregate industry, Other			
R&D ENABLERS	Use of animal rule to support licensure	✖	✖	✖	✔	✖	✖	✖	✖	✖	✖	✖	✖
	Correlates of protection	✔	✖	✖	✖	✖	✖	✖	✖	✖	✖	✖	✖
	WHO Target Product Profiles — Vx	✔	✔	✖	✔	✔	✖	✖	✔	✖	✖	✖	✖
	WHO Target Product Profiles — Thx	✔	✖	✖	✖	✖	✖	✖	✖	✖	✖	✖	✖
	WHO Target Product Profiles — Dx	✔	✖	✖	✖	✖	✖	✖	✖	✖	✖	✖	✖

No change in enablers in 2023 vs 2022 | R&D enabler has become inactive | ▲ Increase in funding in 2023 vs 2022 | ▼ Decrease in funding in 2023 vs 2022 | Highlights U.S. government's leading role in this space | $ = US dollars | Vx - Vaccines; Thx - Therapeutics; Dx - Diagnostics | Due to rounding percentage totals may appear to exceed 100%

The 100 Days Mission Scorecard draws from Impact Global Health's G-FINDER R&D funding data and Infectious Disease R&D Tracker. More details on sources used in Annex E

DETAILED SCORECARD ANALYSIS

Key Progress Updates in 2024

The past year[5] has revealed few systemic changes in the R&D ecosystem that could sustain and accelerate regulatory approvals and clinical development for priority pathogens. The loops between reaction and preparedness are not yet closed. Thus, opportunities are abundant for policymakers, funders, and developers to support an ecosystem that can achieve the 100DM.

Funding Landscape Analysis

Funding streams are not yet fully balancing the need to invest in preparedness as well as response. The R&D spend in 2023 remained reactive. Non-COVID DTV funding fell by 31% from 2022 to 2023 - for all but two pathogens, Chikungunya and Nipah - while COVID-19 R&D experienced a steeper 50% decline. Declining funding in the aftermath of a pandemic or epidemic is to be expected – particularly when there have been successful product launches as seen with COVID-19 and Ebola. However, while it is not clear where this funding goes outside of an outbreak, it is not currently being redirected to preparedness for these priority pathogens. We are still seeing significant decreases in funding for other pathogens which have not had active outbreaks (Figure 2); for example, Rift Valley Fever experienced a striking 92% reduction, while Crimean-Congo Haemorrhagic Fever (CCHF), Middle East respiratory syndrome (MERS), and severe acute respiratory syndrome (SARS) saw substantial decreases of 66%, 84%, and 77% respectively. Some positive movements emerged, with Chikungunya benefiting from significant European Commission (EC) funding, and Nipah receiving increased support from the U.S. Department of Defence (DOD).

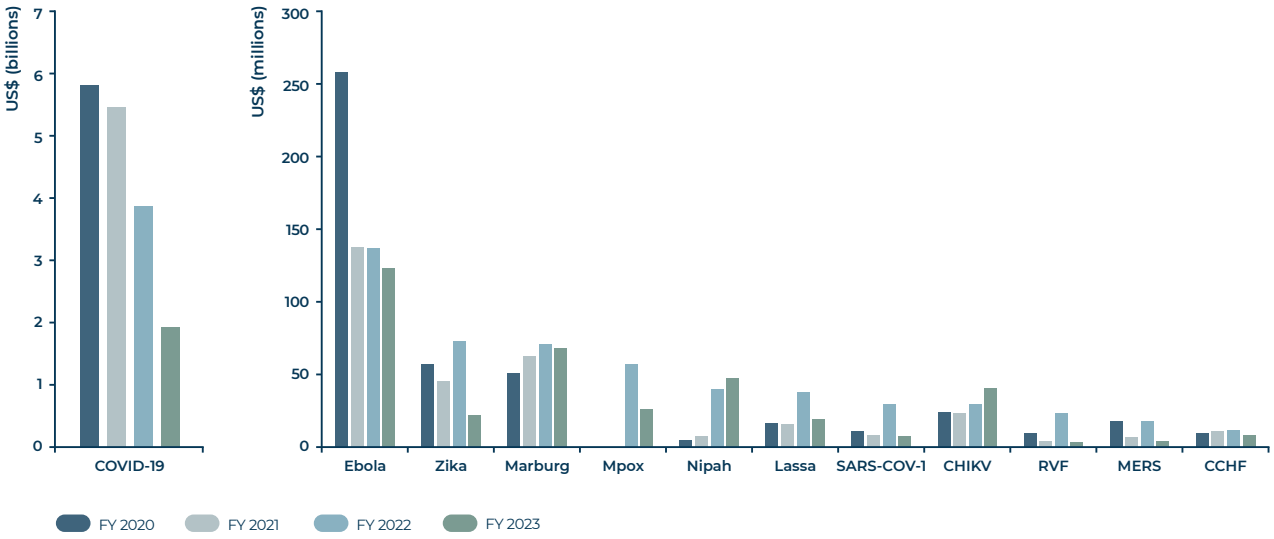


Figure 2. DTV R&D funding by pathogen, 2020-2023.[6]

The decline in mpox R&D funding between 2022 and 2023 underscores the reaction speed of the funding landscape to invest at the declaration of a PHEIC (July 2022), but also drawback once the PHEIC is removed (May 2023). The decline in funding was driven by the top funder, the U.S. National Institutes of Health (NIH), which in 2022 made up over three-quarters of mpox R&D funding, highlighting the vulnerability of reliance on one dominant funder. This was partially offset by first-time industry funding for the clinical development of mpox vaccines, an indication of the potential commercial market, and small but stable funding from the French and Canadian governments. To meet the 100DM and move away from reacting to outbreaks, we need appropriate funding benchmarks for priority pathogens during preparedness periods as well as funding gap estimates for response.

Major funding changes in 2023 primarily originated from key U.S. institutions, with the U.S. NIH reducing funding by $641 million (44%) and Biomedical Advanced Research and Development Authority (BARDA) cutting $650 million (60%), although the bulk of the decrease was linked to COVID-19. The U.S. DOD provided a contrasting trend by tripling its investment in Disease X platform technologies, with a particular focus on biologic technologies.

5 Based on G-FINDER data for Financial Year (FY 2023) and updated indicator data as of September 30 2024.
6 Impact Global Health, G-FINDER data portal: tracking funding for global health R&D, https://gfinderdata.impactglobalhealth.org/.

Platform technologies comprised almost 90% of U.S. DOD's investment in 2023, as investment in diseases they had previously focused on (COVID-19 and Ebola, both of which have a complement of approved products) each decreased by at least 70%. This approach from the U.S. DOD is forward thinking and shows their shifting investment remains aligned with pandemic preparedness R&D that can benefit multiple viral families. Overall, between 2014-2023, the U.S. government accounted for 60% of all R&D funding, and 68% when excluding COVID-19 investments.

These funding patterns underscore the volatile nature of the current R&D landscape and the heavy reliance on the U.S government. This highlights opportunities for other governments, foundations, and private companies to get involved and even the field. Support for a healthy and diverse clinical pipeline requires more than reactionary funding peaks at risk of political shifts. This highlights the need for a more diverse and sustainable funding ecosystem to ensure consistent progress in developing countermeasures against priority pathogens and the opportunity for governments, philanthropic organisations, and industry to have impact in this space.

Approved products

Diagnostics saw six new tests gain regulatory approval, evenly distributed between Chikungunya and Ebola – both of which already had existing tests available. These tests were predominantly laboratory tests, but both Ebola and Chikungunya also have a near point-of-care test.[7] It is important to note that the change in Marburg virus diagnostics from Scorecard 1.0 is the result of an internal methodological review which reclassified a pan-filoviral test. This is now reflected as an approved test for Marburg but does not represent a new product being approved in the last year.

In the therapeutics space, the only change in product approvals was the WHO prequalification of atoltivimab, maftivimab, and odesivimab-ebgn, a combination monoclonal antibody (mAb) treatment for Zaire ebolavirus infections, in November 2023. Prequalification is designed to support low- and middle-income countries (LMIC) procurement, although in practice further action is needed to ensure access. Overall, Ebola now benefits from a complete regimen of DTVs with LMIC approvals. Additionally, tecovirimat, initially approved for smallpox utilising the U.S. Food and Drug Administration (FDA)'s Animal Rule regulations, received market authorisation by the European Medicines Agency (EMA) for mpox in June 2022. Tecovirimat, however, has not been found to be active against the recent clade Ib.[8]

No new vaccines were approved or prequalified by WHO for pathogens included in Scorecard 1.0; however, for new pathogens added to Scorecard 2.0, vaccines have been approved for mpox, including WHO prequalification for modified vaccinia Ankara–Bavarian Nordic (MVA-BN) and Emergency Use Listing of LC16m8 (see Chapter 5: Mpox case study).[9,10]

Clinical candidates

Within the clinical pipeline, early-stage development saw most activity, predominantly in the transition of candidates from preclinical to phase 1 trials. Therapeutics saw only two pipeline progressions: ribavirin, a repurposed small molecule therapeutic advanced to phase 1 clinical trials for CCHF, and the biologic, interferon-B1b, progressed to phase 2 for the treatment of MERS – marking incremental steps for these two diseases which currently have no approved therapeutics. Seven vaccine candidates entered phase 1 clinical development. Lassa Fever, which lacks an approved vaccine, saw one vaccine candidate progress from phase 1 to phase 2. Only one candidate – a pan-filoviral vaccine – progressed to phase 3 trials; though Ebola vaccines are already approved, these target Zaire ebolavirus, and Marburg remains without an approved vaccine. In diagnostics, two candidates reached late-stage development: an enzyme-linked immunosorbent assay (ELISA) test for Rift Valley Fever and a point-of-care Loop-Mediated Isothermal Amplification (RT-LAMP) assay for MERS.

While it is encouraging to see preclinical candidates advancing to human testing – crucial for expanding our preparedness capabilities – it is concerning that there are so few late-stage advancements and product approvals. Running phase 2/3 trials outside of outbreaks is challenging, which may be the reason for this pattern; however, more attention should be dedicated to consolidating new approaches and alternatives to late-stage clinical development and how R&D enablers can support this.

R&D Enablers

No developments were seen for R&D enablers such as the use of the animal rule for licensure or correlates of protection (CoP). A WHO Target Product profile (TPP) for Nipah was archived, which highlights the 'shelf-life' of these documents. The WHO's updated pathogen prioritisation framework may present an opportunity for new TPPs to be published and existing ones to be reviewed. Few CoPs are widely accepted by product developers and regulatory authorities, and there is a need for coordination in this space. Similarly, the lack of standardised animal models for epidemic diseases is an obstacle to leveraging the animal rule pathway outside of outbreaks. Further work is needed to support regulatory harmonisation and de-risk R&D.

7 FIND, Pathogen Diagnostics Readiness Index (PDxRI) (2024), https://www.finddx.org/data-and-impact/dashboards/diagnostic-readiness-index/.
8 WHO, WHO-PQTm SCIENTIFIC DISCUSSION Atoltivimab, maftivimab, and odesivimab 100 mg/mL solution for infusion (Regeneron Pharmaceuticals, Inc.) BT-EB002 (2023), https://extranet.who.int/prequal/sites/default/files/whopar_files/BT-EB002%20part6bv1.03_Dec2023%20%281%29.pdf.; EMA, Tecovirimat SIGA (2022), https://www.ema.europa.eu/en/medicines/human/EPAR/tecovirimat-siga.; National Institute of Allergy and Infectious Diseases, The antiviral tecovirimat is safe but did not improve clade I mpox resolution in Democratic Republic of the Congo (2024), https://www.nih.gov/news-events/news-releases/antiviral-tecovirimat-safe-did-not-improve-clade-i-mpox-resolution-democratic-republic-congo.
National Institute of Allergy and Infectious Diseases, The antiviral tecovirimat is safe but did not improve clade I mpox resolution in Democratic Republic of the Congo (2024), https://www.nih.gov/news-events/news-releases/antiviral-tecovirimat-safe-did-not-improve-clade-i-mpox-resolution-democratic-republic-congo.
9 WHO, WHO prequalifies the first vaccine against mpox (2024), https://www.who.int/news/item/13-09-2024-who-prequalifies-the-first-vaccine-against-mpox.
10 WHO, WHO adds LC16m8 mpox vaccine to Emergency Use Listing (2024), https://www.who.int/news/item/19-11-2024-who-adds-lc16m8-mpox-vaccine-to-emergency-use-listing

Platform Technologies Deep Dive

Platform technologies, defined as disease-agnostic, reproducible technologies that support streamlined regulatory processes and plug-and-play manufacturing, show varying levels of development across product types.

Therapeutics shows the least platform diversity, with a clear binary between small molecule drugs and mAbs. However, regulatory attention to this area is increasing, as evidenced by the FDA's draft guidance on platform technology designation released in May 2024, which could signal a shift in the landscape.

Diagnostic platforms remain concentrated in conventional technologies, with quantitative Real-Time Reverse Transcription Polymerase Chain Reaction (qRT-PCR, 24 candidates) and ELISA/EIA (18 candidates) platforms comprising nearly 80% of the field (Figure 3). While this shows a lack of diversity and innovation that could support preparations for Disease X, any new innovations must prioritise affordability and accessibility, particularly in resource-limited regions. The dominance of these traditional methods likely stems from developers' preference for building upon existing, widely available platforms.

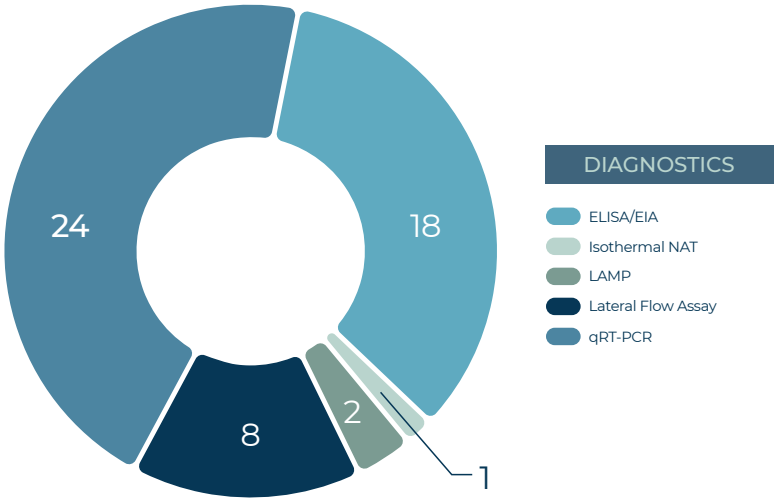


FIGURE 3. DIAGNOSTIC PLATFORM TECHNOLOGIES USED IN NON-COVID CLINICAL CANDIDATES.[11]

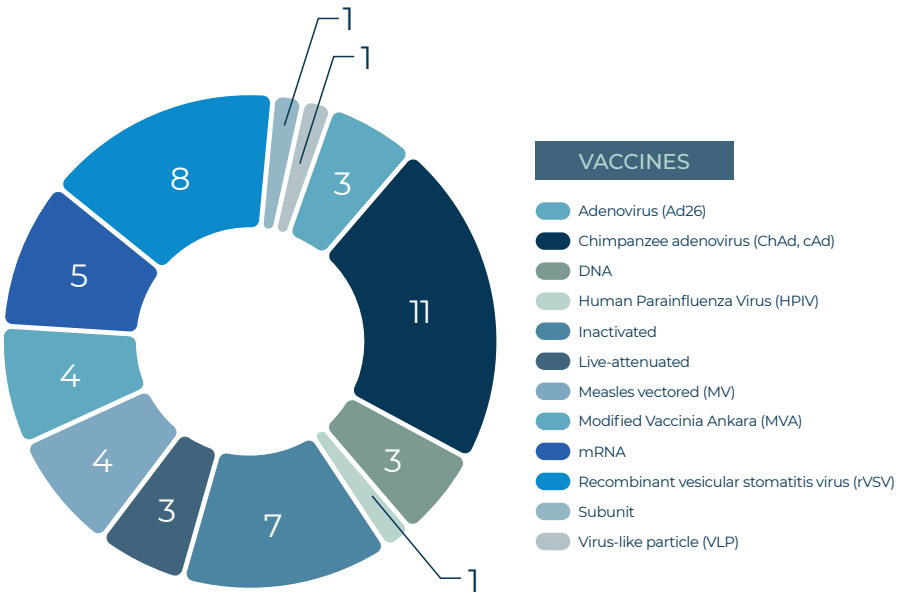


FIGURE 4. VACCINE PLATFORM TECHNOLOGIES USED IN NON-COVID CLINICAL CANDIDATES.[12]

The vaccine landscape demonstrates the greatest platform diversity, utilising seven different platforms for non-COVID pathogens (Figure 4). Viral vectors dominate, representing 60% of candidates (31 total), with particular emphasis on chimpanzee adenovirus (11 candidates) and recombinant vesicular stomatitis virus (rVSV) (eight candidates).

The varying maturity of platform technologies across product and MCM types reflects both progress and remaining gaps in the R&D landscape. While vaccines show encouraging diversity, and diagnostics build on established foundations, the limited range in therapeutics suggests opportunities for focused development to strengthen overall preparedness capabilities.

11 Impact Global Health, Infectious Disease R&D Tracker, https://www.impactglobalhealth.org/data/infectious-disease.
12 Impact Global Health, Infectious Disease R&D Tracker.

Future of the Scorecard (Version 3.0)

The initial vision for Scorecard 2.0 included a broader set of indicators that would address different facets of the pandemic preparedness and response (PPR) ecosystem and be more focused on LMIC needs. The current Scorecard remains R&D-focused given the available data, but further funding would enable future scorecards to cover broader facets of the PPR ecosystem, for example, clinical trials, controlled human infection models, and manufacturing capacity, as well as additional Scorecard deep-dives for specific regions through partnerships with key stakeholders. For Scorecard 3.0, we have agreed to integrate the Coalition for Epidemic Preparedness Innovations (CEPI) and UC Davis spillover tool, which explores and directly compares hundreds of viruses, host, and environmental risk factors to identify viruses with the highest risk of zoonotic spillover from wildlife to humans.[13] This addition will enhance our ability to predict and rank potential pandemic threats. However, the successful implementation of these improvements will require sustained funding support and enhanced data collection capabilities.

13 UC Davis, Spillover Viral Risk Ranking, https://spillover.global/.

Spotlight 1: Pandemic Preparedness in India

In August 2024, NITI Aayog, a public policy think tank of the Government of the Republic of India, published a report on future pandemic preparedness and emergency response in India. An expert group was convened to assess what learnings could be taken from the COVID-19 pandemic and applied to any future public health crisis. The framework sets out a roadmap for responding to a pandemic within the first 100 days of an outbreak and sets out recommendations across four pillars:

- Governance, Legislation, Finance and Management
- Data Management, Surveillance and Early Predictive Warning, Forecasting and Modelling
- Research and Innovation, Manufacturing, Infrastructure, Capacity building/Skilling
- Partnership, Community engagement including risk communication, Private sector partnerships, and International collaborations

NITI Aayog used the 100DM scorecard to develop a similar set of indicators that can be used to monitor progress towards this framework. The report also emphasised that this framework can be tested using viruses already circulating in the country.[14]

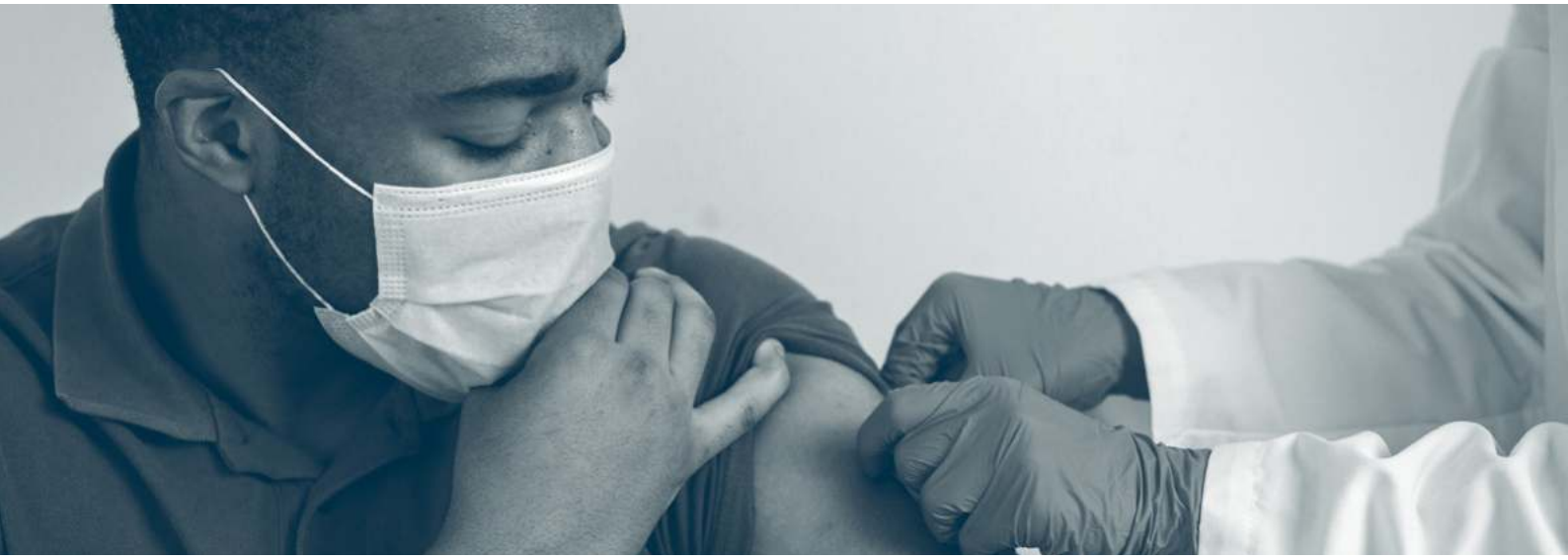
The Indian Government have also developed a more focused National Pandemic Preparedness Plan for Respiratory Viruses. This builds on the WHO Preparedness and Resilience for Emerging Threats (PRET) initiative that the same systems, capacities, knowledge, and tools can be leveraged and applied for groups of pathogens based on their mode of transmission. It is hoped that this will proactively address and mitigate the impact of future respiratory pandemics. The framework behind this plan was established by convening leaders and experts from academia alongside national and state level officials for a workshop that was then presented to an expert panel. [15,16]

This approach of convening multisectoral officials and experts to pull together ideas and review learnings from COVID-19 to establish a pandemic preparedness plan could be adopted by other countries to ensure countries can leverage instruments in a coordinated, timely and equitable way to tackle pandemics. Furthermore, countries should develop a Scorecard or similar approach tailored to their national or regional context to monitor progress to ensure they can deliver the 100DM.

14 NITI Aayog, Future Pandemic Preparedness and Emergency Response: A Framework for Action (2024), https://www.niti.gov.in/sites/default/files/2024-09/Report-of-the-Exper-Group--Future-Pandemic-preparedness-and-emergency-response_0.pdf.
15 WHO, Preparedness and Resilience for Emerging Threats (PRET), https://www.who.int/initiatives/preparedness-and-resilience-for-emerging-threats.
16 WHO, India gets "PRET" for future pandemics: a national consultation on developing the content framework for the National Pandemic Preparedness Plan for Respiratory Viruses (2024), https://www.who.int/news/item/12-02-2024-india-gets-pret--for-future-pandemics-a-national-consultation-on-developing-the-content-framework-for-the-national-pandemic-preparedness-plan-for-respiratory-viruses.

2

Research & Development



SYNERGIES ACROSS DEVELOPMENT OF DIAGNOSTICS, THERAPEUTICS AND VACCINES

There have been several cross-cutting developments in 2024 that enhance coordination and R&D progression across DTVs for infectious disease management. This progress aligns with 100DM champions' consistent advocacy for an integrated approach to break down silos between these countermeasures. The WHO pathogen prioritisation framework offers important opportunities to guide R&D across all three areas, supporting development of globally accessible TPPs to guide product development, and leveraging both traditional methods and innovative technologies like artificial intelligence (AI) for advancements in disease tracking, drug discovery, and innovative clinical trial design. Among the WHO priority pathogens, a full complement of TPPs have only been established for COVID-19, highlighting that a significant expansion of TPPs will be required to realise this vision. This chapter highlights opportunities to harness synergies across these MCMs; their unique challenges are detailed in subsequent chapters.

CROSS-FUNCTIONAL RESOURCE SHARING IN R&D DESIGN

Greater alignment in R&D across DTVs (for example, around priority viral families) could accelerate development across all countermeasures by enabling targeted R&D efforts and more efficient use of shared resources. Accessible biobanks, building on the Foundation for Innovative New Diagnostics (FIND)'s biobank services in the diagnostics arena, may help facilitate this approach to cross-functional R&D.[17]

While there is currently a lack of coordinated or established mechanisms for sharing material and knowledge across diagnostic, therapeutic and vaccine tools, there are many deliverables and resources across the product development pathway that may be shared across modalities, for example:

- **Cross-functional use of biomarkers:** Genetic sequences arising from vaccine antigen design can be used to inform molecular diagnostics development. Conserved antigen sequences can be used to raise broadly neutralising antibodies. Structural biomarker data can be used in small molecule drug design, providing insights into active sites or binding pockets.
- **Antibody-antigen insights:** mAb identification and epitope mapping can help inform vaccine antigen design, and support selection of high affinity ligands for development of antigen-based rapid diagnostic tests.
- **Protein production platforms:** Stable cell lines for production of antigens or therapeutic proteins are also used to produce recombinant proteins for assays or diagnostic tests.
- **Study-derived materials:** Material from vaccine pre-clinical studies, clinical studies and epidemiology studies could be used during development, evaluation, or validation of diagnostic assays.
- **Mechanism of action:** Insights into immune responses from vaccine studies may reveal potential pathways that can be targeted by therapeutics.

17 FIND, Biobank services, https://www.finddx.org/what-we-do/cross-cutting-workstreams/biobank-services/.

While intellectual property (IP) is a key enabler for incentivising product development, certain IP and access terms can create barriers to sharing assay methods, reagents, and sequence data, potentially limiting collaboration in critical areas. Moreover, the knowledge of what is being developed under one pillar may not be visible to the other pillars. Enhanced coordination between pillars and between public and private entities remains crucial for ensuring rapid access to resources during both the preparedness and emergency response phases.

ADVANCING PREPARATORY REGULATORY APPROACHES & LEVERAGING LEARNINGS ACROSS MODALITIES TO ACCELERATE DTV APPROVAL

Reducing regulatory approval timelines without compromising safety is critical for delivering the 100DM. Engagement with regulators from early stages of R&D is therefore crucial to map the most efficient pathways for product approval. Pre-aligned yet flexible regulatory pathways to streamline approval processes may be enabled by:

- **Supporting approvals of platform technologies:** Continued development of diverse platform technologies builds regulator confidence and experience, potentially enabling more efficient approval processes. This could be facilitated through platform technology master files (PTMF) that capture and standardise information and data on innovative platforms for re-use in regulatory reviews of other products using the same platform. In May 2024, U.S. FDA released its draft guidance for receiving a platform technology designation, which would provide an expedited pathway for the development of drugs or biologics utilising approved platforms.[18]

- **Adoption of regulatory acceptance of correlates of protection:** While academic literature supports various correlates of protection (CoP) for priority pathogens, few are widely accepted by product developers and regulators as highlighted in the 100DM scorecard. Pathogen or viral family-specific CoP could enable immunobridging strategies as a complementary source of evidence for regulatory and public health decision making. However, a framework that outlines the data requirements for use of CoP to accelerate licensure is needed.

INNOVATIVE FUNDING APPROACHES

Integrating funding for DTVs presents opportunities to unlock efficiencies and maximise limited resources across aligned stakeholders. For example, supporting tandem test-treatment programmes may garner more traction than diagnostic development on its own, delivering a package of tools that could potentially be procured together (see Spotlight 4: Test-to-Treat). Similarly, supporting development of diagnostics that can expedite clinical trial enrolment in vaccine or therapeutic trials may also accelerate innovative test development. Beyond diagnostics, funding approaches across therapeutic and vaccine programmes can leverage shared scientific learnings - for instance, isolation of potent neutralising human mAbs can support identification of protective epitopes and novel antigen targets for vaccine design. U.S. NIAID's Research and Development of Vaccines for Monoclonal Antibodies for Pandemic Preparedness (ReVAMPP) programme demonstrates this synergistic approach by simultaneously advancing mAb and vaccine candidates for priority pathogens, thus reducing duplication of efforts while accelerating discovery and maximising the impact of limited funding.[19]

Beyond these technical synergies, innovative funding models can further support integration across product types. For instance, Combating Antibiotic-Resistant Bacteria Biopharmaceutical Accelerator (CARB-X)'s funding model in antimicrobial resistance (AMR) shows how coordinated financing and risk-sharing across governments, private sector, and philanthropies can overcome market barriers through strategic use of non-dilutive funding. Their milestone-based approach de-risks early-stage development while ensuring efficient use of resources, helping companies advance promising innovations when traditional investors are most hesitant.[20]

Building on these innovative funding approaches, investors should balance the need for targeted product-specific investment with broader opportunities offered by multi-product platform technologies (e.g., mRNA platforms can be used to encode vaccine antigen or mAb sequences) that may have greater flexibility to pivot between endemic and pandemic response.[21] These investments could be further strengthened through business models and portfolio approaches that create additional value by addressing both infectious and non-communicable diseases.

18 US FDA, Platform Technology Designation Program for Drug Development (2024), https://www.fda.gov/regulatory-information/search-fda-guidance-documents/platform-technology-designation-program-drug-development.
19 National Institute of Allergy and Infectious Diseases, Research and Development of Vaccines and Monoclonal Antibodies for Pandemic Preparedness (ReVAMPP) (2024), https://www.niaid.nih.gov/research/vaccines-and-monoclonal-antibodies-pandemic-preparedness-revampp.
20 CARB-X, Combating Antibiotic-Resistant Bacteria, https://carb-x.org/.
21 CARB-X, Combating Antibiotic-Resistant Bacteria.

Spotlight 2: Behaviour and Community Engagement in Effectively Implementing DTVs

While the rapid provision of safe, effective, and affordable DTVs is essential for pandemic response, their successful implementation is what ultimately saves lives.

The COVID-19 pandemic demonstrated how misinformation can severely undermine pandemic response through its effects on public behaviour. Vaccine conspiracy theories led to reduced uptake, misinformation about therapeutics resulted in dangerous self-medication practices, and unclear guidance caused improper use of home testing kits and unreliable results.[22] This was more prevalent in communities where trust in public health systems was low.[23] To tackle this, governments must provide clear fact-based information and engage with communities to build trust.[24]

A regional listening exercise conducted by IPPS in East Africa also highlighted that engaging with the end users of MCMs is key to improving uptake. Local regulation and product manufacture were also noted an effective means of building trust around these MCMs in communities.[25]

During the Ebola outbreak in West Africa in 2014-2016 implementing behavioural changes with communities was critical in containing the disease. Behavioural interventions were most effective when decision makers understood the cultural context of an area and involved members of the community in efforts. In Ebola, funeral practices can be sources of disease spread and the population initially did not comply with efforts by authorities to remove bodies. Cultural sensitivities were then studied and communicated to responders, leading to safe and dignified burials where community leaders and family members could be involved without risking further transmission of the disease, which increased compliance and built trust within communities.[26,27,28] This community engagement to build trust has laid the foundations for Sierra Leone to begin a targeted nationwide preventative Ebola vaccination campaign.[29,30] An engaged community is also more likely to report unusual health events, enabling earlier detection of outbreaks. In the Democratic Republic of the Congo community-based surveillance was crucial for early Ebola detection.[31]

Decision makers should consider the role human behaviour has in the effectiveness of delivering MCMs. To change behaviour, organisations should engage with local communities to build trust and understand barriers. This is particularly important in an international context where cultural differences may be overlooked. Governments should look to understand the synergies throughout DTVs where behavioural change has worked effectively in their context and begin to build trust in 'peacetime'. In future pandemics, learnings should be drawn from this to effectively deliver a pandemic response.

22 M. M. Ferreira Caceres et al., "The impact of misinformation on the COVID-19 pandemic," AIMS Public Health 9, no. 2 (2022), https://doi.org/10.3934/publichealth.2022018.
23 G. Pennycook et al., "Fighting COVID-19 Misinformation on Social Media: Experimental Evidence for a Scalable Accuracy-Nudge Intervention," Psychol Sci 31, no. 7 (Jul 2020), https://doi.org/10.1177/0956797620939054.
24 Hannah S. Whitehead et al., "A systematic review of communication interventions for countering vaccine misinformation," Vaccine 41, no. 5 (2023/01/27/ 2023), https://doi.org/https://doi.org/10.1016/j.vaccine.2022.12.059, https://www.sciencedirect.com/science/article/pii/S0264410X22015936.
25 IPPS, 100DM Regional Listening Exercises Report: East Africa (2023), https://ippsecretariat.org/publication/rle-east-africa/.
26 BBC, Ebola virus burial teams may have 'saved thousands of lives' (2017), https://www.bbc.co.uk/news/health-40375693.
27 Congressional Research Service, Fostering Behavior Change During Disease Outbreaks: Insights from Ebola Response in Africa (2020), https://crsreports.congress.gov/product/pdf/IN/IN11285.
28 GPMB, The Changing Face of Pandemic Risk: 2024 Report (2024), https://www.gpmb.org/reports/m/item/the-changing-face-of-pandemic-risk-2024-report.
29 The Guardian, Ten years ago Ebola tore through Sierra Leone. Can a vaccine drive stop history repeating itself? (2024), https://www.theguardian.com/global-development/2024/nov/27/ten-years-ago-ebola-sierra-leone-2014-vaccine-drive-stop-history-repeating-itself.
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AI TECHNOLOGIES TO ACCELERATE PANDEMIC COUNTERMEASURES

Table 2. Example uses of AI in development of pandemic countermeasures

Stages of pandemic countermeasure development	Example use of AI
Outbreak identification	Early warning system for pandemics by monitoring social media trends
DTV R&D	Map and predict ability of viruses to evade the immune response
	Immunogen design
	Stable mRNA sequence design
	Antiviral drug discovery
	Bioprocess optimisation to reduce cost of goods
Clinical trials	Predict clinical trial success
	Manage patients, clean data, and produce interoperable datasets
Regulation	Automate regulatory processes
	Process data for pharmacovigilance
DTV delivery	Predict stock shortages
	Improve the accuracy and speed of diagnostics & linkage to care

The relevance of AI in science is ever expanding, highlighted through the award of one half of the 2024 Nobel Prize for an AI program (AlphaFold) that predicts protein structure with remarkable speed and accuracy. The other half of the prize recognises computational protein design which can also be applied to DTV projects. It is clear AI has the potential to vastly accelerate the end-to-end development of MCMs. AI advances have already had an impact across the vaccine and therapeutics pipeline, including contributing to a SARS-CoV-2 vaccine approved in 2023.[32]

AI may enable the design of more effective vaccines, therapeutics, and diagnostics, and has potential to accelerate R&D from early drug discovery through to last mile delivery of countermeasures. Apriori Bio has developed an AI platform Octavia™ which maps virus mutations' ability to evade the immune response. Vaccines could be targeted to proteins with low 'escape potential' to create variant resistant vaccines, or vaccines could be created for concerning variants before they emerge. CEPI has supported partners to develop computational tools to generate immunogen designs for several high-risk viral families, which could be combined with rapid response vaccine platforms (e.g., mRNA, viral vectors) to quickly create vaccine candidates.

32 Science, AI designer proteins could transform medicine and materials (2024), https://www.science.org/content/article/ai-designer-proteins-could-transform-medicine-and-materials.

AI could also be used to make mRNA vaccines more effective and accessible by designing mRNA sequences with shapes and structures more intricate than those used in current vaccines. Creation of more stable and potent mRNA products could vastly improve the ability to deploy mRNA vaccines by reducing dose, administration frequency, and reliance on ultra-low cold chain infrastructure.[33,34]

In therapeutics, the NIH/NIAID-funded antiviral drug discovery (AViDD) centre AI-driven Structure-enabled Antiviral Platform (ASAP), identified a promising small molecule SARS-MERS candidate and is advancing projects targeting flaviviruses and enteroviruses (though notably, this funding is set to be discontinued in 2025).[35] More broadly the use of AI and tools such as digital twins (virtual models of real-world experiments) could reduce the costs associated with DTV development enabling companies to replace many traditional processes with in silico simulations or streamline current processing methods.[36]

AI can support delivering countermeasures at pace. Streamlining the clinical trial process could prove vital in ensuring vaccines and therapeutics can be delivered in 100 days. The use of AI has been explored in clinical trial design where it could be used to predict whether a clinical trial will succeed based on the drug molecule, target diseases and patient eligibility criteria. AI can also be incorporated into the running and reporting of results in the trial including managing patients and cleaning data.[37,38] In 2020, AI was used to clean the data of more than 30,000 patients in Pfizer's COVID-19 vaccine trial.[39]

AI could also play a role in delivering diagnostics. By combining point-of-care testing with AI techniques for test readout, the accuracy and speed of testing can be improved. A team from South Africa and the UK used mobile phones to capture and classify human immunodeficiency virus (HIV) rapid tests which was then used to develop deep learning algorithms which demonstrated high levels of sensitivity (97.8%) and specificity (100%) compared with traditional visual interpretation.[40] Similarly, a South Korean team tested an approach integrating time-series deep learning architecture and AI-based verification for enhanced analysis of lateral flow assays, exceeding human accuracy while delivering faster diagnostic results.[41]

Once countermeasures are developed, AI could also speed up regulation by automating time consuming administrative processes and reducing the requirement for human involvement.[42] This automation could also optimise pharmacovigilance processes.[43] Furthermore, AI is already being used in delivery of countermeasures in Tanzania where the Program for Appropriate Technology in Health (PATH) and partners are using AI to combine vaccines supply chain and logistics management information systems with population and meteorological data to predict stock shortages.[44]

33 Nature, 'Remarkable' AI tool designs mRNA vaccines that are more potent and stable (2023), https://www.nature.com/articles/d41586-023-01487-y.
34 CEPI, Vaccines R&D pro forma.
35 DNDi, pro forma.
36 BioProcess International, Reimagining the Future of Biopharmaceutical Digitalization (2024), https://www.bioprocessintl.com/information-technology/reimagining-the-future-of-biopharmaceutical-digitalization.
37 PR Newswire, Research Grid raises $6.5 million to make clinical trials admin-free (2024), https://www.prnewswire.com/news-releases/research-grid-raises-6-5-million-to-make-clinical-trials-admin-free-302297019.html.
38 PR Newswire, Research Grid raises $6.5 million to make clinical trials admin-free.
39 Nature, How AI is being used to accelerate clinical trials (2024), https://www.nature.com/articles/d41586-024-00753-x.
40 V. Turbé et al., "Deep learning of HIV field-based rapid tests," Nat Med 27, no. 7 (Jul 2021), https://doi.org/10.1038/s41591-021-01384-9.
41 Seungmin Lee et al., "Rapid deep learning-assisted predictive diagnostics for point-of-care testing," Nature Communications 15, no. 1 (2024/02/24 2024), https://doi.org/10.1038/s41467-024-46069-2, https://doi.org/10.1038/s41467-024-46069-2.
42 Ruchika S. Patil, Samruddhi B. Kulkarni, and Vinod L. Gaikwad, "Artificial intelligence in pharmaceutical regulatory affairs," Drug Discovery Today 28, no. 9 (2023/09/01/ 2023), https://doi.org/https://doi.org/10.1016/j.drudis.2023.103700, https://www.sciencedirect.com/science/article/pii/S1359644623002167.
43 Maribel Salas et al., "The Use of Artificial Intelligence in Pharmacovigilance: A Systematic Review of the Literature," Pharmaceutical Medicine 36, no. 5 (2022/10/01 2022), https://doi.org/10.1007/s40290-022-00441-z, https://doi.org/10.1007/s40290-022-00441-z.
44 devex, 5 innovations in global health (2024), https://www.devex.com/downloadables/5-innovations-in-global-health-31.

Alongside DTVs, AI has wider uses across the pandemic preparedness landscape, particularly in surveillance where **AI could help public health systems identify emerging threats.** The AESOP (Alert-Early System for Outbreaks with Pandemic Potential) Early Warning System aims to use AI to track early-stage outbreaks and predict where they might spread rapidly by integrating data collected from Brazil's Unified Health System (SUS) with other health, environmental, and sociodemographic data sources.[45] Researchers at University of California, Irvine (UCI) and the University of California, Los Angeles (UCLA) are also using AI to provide an early warning system for pandemics by monitoring social media trends. This works by training the AI tool on millions of social media posts to identify which ones are meaningful in predicting the early signs of a future pandemic.[46] While such approaches show promise, research funders need to increase their support for developing and validating AI applications across pandemic preparedness, including surveillance, diagnostics, and response.

It must be noted that, as with any new technology, **AI could pose substantial risk** if used maliciously - for example, to design viruses that could evade vaccine-induced immunity. To protect against this threat, government and regulators must take proactive steps for mitigation. This has been highlighted in CEPI's Biosecurity Strategy, WHO's Global Initiative on AI for Health, and multiple expert publications.[47,48,49] Discussions among governments have started on this topic, with the U.S. and UK governments creating new organisations that will carry out evaluations to better understand biological-weapons threats.[50] Other AI organisations with a wider remit have also been established, including the International Network of AI Safety Institutes and the European Union's AI office.[51]

While AI clearly has potential to enhance pandemic preparedness efforts, achieving the 100DM requires a balanced approach that integrates AI alongside other critical technologies and initiatives. Over-reliance on any single approach, no matter how promising, could detract from the comprehensive strategy needed to meet this ambitious goal.

45 The Rockefeller Foundation, Advanced Surveillance Project Using Artificial Intelligence Aims to Anticipate Alerts of Infectious Disease Outbreaks (2023), https://www.rockefellerfoundation.org/news/advanced-surveillance-project-using-artificial-intelligence-aims-to-anticipate-alerts-of-infectious-disease-outbreaks/.
46 U.S. National Science Foundation, PIPP Phase I: An End-to-End Pandemic Early Warning System by Harnessing Open-source Intelligence (2022), https://www.nsf.gov/awardsearch/showAward?AWD_ID=2200274.
47 CEPI, CEPI puts new biosecurity strategy at heart of 100 Days Mission (2024), https://cepi.net/cepi-puts-new-biosecurity-strategy-heart-100-days-mission.
48 WHO, Global Initiative on AI for Health (2023), https://www.who.int/initiatives/global-initiative-on-ai-for-health.
49 Lynda M. Stuart, Rick A. Bright, and Eric Horvitz, "AI-Enabled Protein Design: A Strategic Asset for Global Health and Biosecurity," NAM Perspectives (2024), https://doi.org/https://doi.org/10.31478/202410d; Stuart, Bright, and Horvitz, "AI-Enabled Protein Design: A Strategic Asset for Global Health and Biosecurity."
50 Doni Bloomfield et al., "AI and biosecurity: The need for governance," Science 385, no. 6711 (2024), https://doi.org/doi:10.1126/science.adq1977, https://www.science.org/doi/abs/10.1126/science.adq1977.
51 Nature, AI could pose pandemic-scale biosecurity risks. Here's how to make it safer (2024), https://www.nature.com/articles/d41586-024-03815-2.

Spotlight 3: 100DM in motion - Rwanda's response to Marburg outbreak

On September 26, 2024, Rwanda's Ministry of Health confirmed the country's first Marburg virus disease (MVD) outbreak following the testing of patients with a viral haemorrhagic fever (VHF). Healthcare professionals trained in VHF-preparedness immediately moved to isolate themselves and patients to prevent further spread.[52] On December 20, 42 days after the last confirmed case tested negative, the outbreak was declared over.[53] Over this time, the Rwandan government carried out an effective response across DTVs bolstered by strong cooperation between organisations, clear leadership, and an emphasis on preparedness ahead of the outbreak.

Within 9 days of notifying international health authorities, the first doses of the Sabin Vaccine Institute's viral vector vaccine candidate were administered to healthcare workers—70 days faster than deployment of Sabin's candidate during the 2022 Sudan Ebola outbreak in Uganda.[54] The ongoing phase 2 trials of the Sabin Marburg vaccine in Kenya and Uganda meant there were batches of the vaccine ready for export, enabling the efficient commencement of a new single-arm, open-label trial in Rwanda with an updated protocol. The strong political, healthcare, and regulatory infrastructure in Rwanda, supported by extensive collaborations with regional and international partners, ensured all elements, including compliance with Good Clinical Practice, were in place to begin vaccine rollout.

Healthcare workers along with mine workers (exposed to virus-carrying bats in caves in mining districts), and individuals in contact with confirmed cases received vaccine doses immediately or within 21 days to align with the end of the disease's incubation period. Within six weeks, more than 1,700 people, most of them healthcare workers at highest risk of contracting the disease, had been vaccinated.[55]

Rwandan leadership identified that healthcare workers were at the greatest risk of infection and implemented widespread testing, training, and infection control measures to protect this group through an intensive, door-to-door surveillance, testing and contact-tracing operation, ultimately monitoring more than a thousand family members, carers and friends of infected cases. Monoclonal antibodies were also given to healthcare workers as a preventative measure and remdesivir, a broad-spectrum antiviral medication, was used as an emergency treatment measure. Sadly, this outbreak led to 15 early deaths, however the fatality rate was reduced to 23% dropping from the previously recorded fatality rate of 88%, demonstrating the effectiveness of rapidly implementing MCMs.[56]

While the handling of this outbreak was exemplary, its remarkable speed and effectiveness were the result of years of preparedness work, strong partnerships, and strategic investments, which ensured a swift and coordinated response. There was a stockpile of a phase 1 tested vaccine candidate in vials ready to be exported. CEPI had also recently carried out a tabletop pandemic preparedness exercise with the Rwandan government. Subsequently there was clear political leadership behind the response and strong relationships had been built between the government and international organisations to ensure quick and effective decisions were made. To prepare for future outbreaks countries should ensure they have the capacity to work with international partners quickly and effectively. Governments should place an emphasis on building strong healthcare and regulatory infrastructure to lay the foundations to rapidly roll out therapeutics, vaccines, and diagnostics to effectively contain deadly viral outbreaks.

52 Jean Pierre Sibomana, "Fight or Flight — Facing the Marburg Outbreak in Rwanda," New England Journal of Medicine 0, no. 0, https://doi.org/doi:10.1056/NEJMp2413951, https://www.nejm.org/doi/full/10.1056/NEJMp2413951.
53 Daily Maverick, Crucial lessons for global health in Rwanda's rapid response to Marburg outbreak (2024), https://www.dailymaverick.co.za/article/2024-11-22-crucial-lessons-for-global-health-in-rwandas-rapid-response-to-marburg-outbreak/.
54 WHO, Ebola trial candidate vaccines arrive in Uganda in record '79 days after outbreak declared (2022), https://www.who.int/news/item/09-12-2022-ebola-trial-candidate-vaccines-arrive-in-uganda-in-record-79-days-after-outbreak-declared.
55 The Telegraph, Rwanda's Marburg response is a masterclass in how to prevent pandemics (2024), https://www.telegraph.co.uk/global-health/science-and-disease/partnerships-preparedness-halted-rwanda-marburg-outbreak/.
56 Telegraph, Rwanda's Marburg response is a masterclass in how to prevent pandemics.

Diagnostics R&D

CONTEXT AND AIMS

Diagnostics are a frontline defence against infectious disease spread, enabling timely outbreak response and effective public health interventions. They are critical to the 100DM, serving as essential tools in confirming cases, measuring immune responses, and guiding clinical studies. The 2024 mpox PHEIC clearly demonstrated this need, where limited availability of rapid point-of-care diagnostics significantly hampered case confirmation, clinical care, and contact tracing efforts in affected regions (see Chapter 5: Mpox case study). Despite this clear importance, the diagnostics pillar of the 100DM remains critically underfunded.

According to the data behind the 100DM scorecard, while COVID-19 diagnostics experienced a 44% decline in funding, other pathogens maintained relatively stable funding levels—though these started from a markedly lower base of just $12 million in 2022 compared to other product development areas (Figure 5). Ebola diagnostics saw a notable doubling of funding to $8.3 million, while Zika received marginally over $1 million. However, diagnostic funding for all other pathogens fell below $1 million, representing a strikingly modest investment in new diagnostic development.

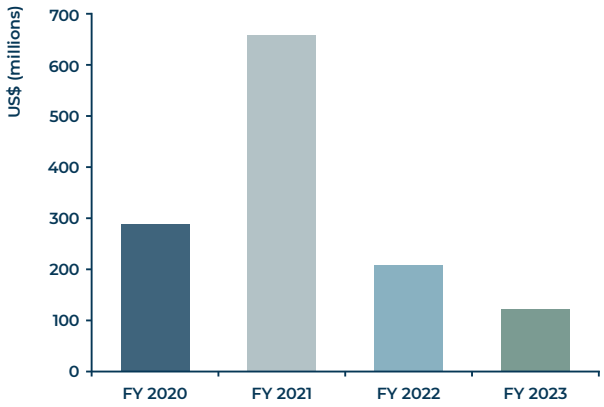


FIGURE 5. DIAGNOSTICS R&D FUNDING

While almost all priority pathogens have approved laboratory-based diagnostics, significant gaps persist in point-of-care testing capabilities. Among the 12 pathogens tracked in the 100DM scorecard, only three—Ebola, SARS-CoV-2, and Zika—have authorised rapid point-of-care diagnostic tests, highlighting a particular challenge for emergency response and rural healthcare settings where such capabilities are essential.[57]

Despite commendable coordination and technical efforts from FIND, Unitaid, PATH, Global Access Diagnostics (GADx), and other partners, the objectives of the 100DM for diagnostics are not on track. To progress this area, sustainable funding and multisectoral coordination is needed. Leveraging resources and synergies across the DTV pillars, in addition to diagnostics specific investment, may accelerate progress toward these goals.

Overarching goals of the 100DM for diagnostics:

Strengthened International Coordination: There is a need for enhanced global collaboration among governments, industry, regulators and international organisations to create a sustainable diagnostics R&D ecosystem.

Development of Diagnostic Libraries: The goal of creating comprehensive diagnostic libraries offering broad coverage for priority pathogen families.

57 FIND, Pathogen Diagnostics Readiness Index (PDxRI).

While this section is focused specifically on Diagnostics R&D, relevant Surveillance updates are in Chapter 4: Strengthening Global Surveillance Systems.

PROGRESS IN 2024

Despite the challenges described above, in 2024 some limited progress has been made in diagnostics R&D toward the 100DM goals, including landscaping efforts by FIND and WHO Interim-MCM-Network (i-MCM-Net) partners to foster coordination in the ecosystem.[58] While a comprehensive overview of progress updates from implementation partners is provided in Annex A, here we highlight several key advances that could have a broader impact on the diagnostics R&D ecosystem and potential for wider adoption in the field. Key developments include FIND's launch of the Pathogen Diagnostic Readiness Index dashboard and the continuous upgrades and updates of the DxConnect test directory, which provide an unprecedented view of gaps and opportunities in diagnostic tool availability to guide future investment priorities.[59,60]

ACCELERATING DIAGNOSTIC DEVELOPMENT FOR PRIORITY PATHOGENS

In 2024, progress was made in **developing diagnostics for priority pathogens**. GADx made significant strides with point-of-care lateral flow test development for CCHF, Nipah, and pandemic influenza, and introduced a multiplexed febrile panel aligned with broader pandemic preparedness goals. GADx also partnered with DiaTROPIX to develop a rapid diagnostic test capable of detecting all Ebola strains, with plans to transfer this technology for manufacture in Senegal.[61] In Brazil, Fiocruz/Bio-Manguinhos advanced molecular tests and wastewater surveillance tools for viruses with pandemic potential and regional priorities like mpox and oropouche.[62] Unitaid, meanwhile, supported late-stage development and expansion of multiplexed molecular diagnostic platforms for surveillance (COVID-19, Influenza, Respiratory Syncytial Virus) and routine clinical screening of endemic diseases.[63] Additionally, BARDA allocated $27 million to support the rapid development and scaled manufacturing of diagnostic tests, including a Marburg virus rapid antigen test, through regulatory approval, using platforms that can be adapted to emerging threats.[64]

Due to the centrality of diagnostics in carrying out efficient clinical trials, delivering therapeutics and developing vaccine strategies, aligning diagnostic development with therapeutics and vaccines R&D may enable **opportunities to link test and treatment together** while leveraging shared resources (see Chapter 2: Synergies).

58 FIND, pro forma.
59 FIND, Pathogen Diagnostics Readiness Index (PDxRI).
60 FIND, DxConnect test directory, https://www.finddx.org/tools-and-resources/dxconnect/test-directory/.
61 GADx, pro forma.
62 Bio-Manguinhos, Estudo de Bio sobre oropouche é publicado na Revista Lancet (2024), https://www.bio.fiocruz.br/index.php/en/noticias/3540-estudo-de-bio-manguinhos-sobre-a-vigilancia-genomica-do-virus-oropouche-no-brasil-e-publicado-na-revista-lancet.
63 Unitaid, pro forma.
64 CIDRAP, HHS ASPR announces new funding to fill gaps in biothreat diagnostics (2024), https://www.cidrap.umn.edu/biosecurity-issues/hhs-aspr-announces-new-funding-fill-gaps-biothreat-diagnostics.

Spotlight 4: Linking rapid diagnostics to care and treatment

Currently, CCHF diagnosis in endemic countries relies on patient samples being sent to reference laboratories, with a turnaround time for results of at least 2-5 days. The diagnostic delay impedes timely treatment and management of this fatal disease. A point-of-care rapid diagnostic for CCHF would facilitate ongoing drug trials, the effective administration of MCMs by coupling diagnostics with treatment, and infection prevention and control measures for better patient outcomes.

GADx has brought a lateral flow test for CCHF from proof-of-concept to readiness for technology transfer to manufacturing developed in partnership with the Liverpool School of Tropical Medicine (LSTM) with pilot phase and development funding from the Pandemic Institute Liverpool and the Medical Research Council (MRC). The proof-of-concept test was evaluated in Turkey and Iraq, with links to reference laboratories and Ministries of Health. GADx is also working with the LSTM team who leads therapeutics trials for CCHF in Turkey, and they are using the lateral flow test in therapeutic clinical trials to accelerate the enrolment process. The test meets the WHO TPP requirements, and full-scale In Vitro Diagnostic Regulation (IVDR)-compliant clinical evaluations of the device in these settings are underway.[65]

Potential enablers for broader adoption of this approach include governments and international procurers providing demand signals for joint packages of tests and treatments. This programme is an exemplar of a collaborative, impact-led approach, bringing together leading reagent development with lateral flow expertise, to bring to market an accurate, affordable, and accessible rapid diagnostic test for an emerging infectious disease.

DIAGNOSTIC PLATFORM INNOVATIONS TO DEMOCRATISE ACCESS TO DECENTRALISED TESTING

Innovative approaches are emerging to enhance diagnostic sensitivity, specificity, and accessibility. Lateral flow-based rapid diagnostic tests (RDTs) serve as valuable point-of-care and self-testing tools. They are low-cost, quick, easy to use, and eliminate the need for advanced laboratory infrastructure or costly equipment. However, while RDTs have improved significantly, their sensitivity remains lower than laboratory-based molecular testing methods. Integrating innovative technologies into test design, such as CRISPR-based target amplification and nanomaterial-based signal amplification, have the potential to bridge the sensitivity and specificity of laboratory-based detection methods with the simplicity of point-of-care readouts.[66,67] Global Health Labs and GADx collaborated on a molecular diagnostic platform that combines highly sensitive and specific nucleic acid amplification with the affordability and accessibility of a lateral flow test strip readout to support equitable access to Polymerase Chain Reaction (PCR) testing, the gold standard for diagnosing many infectious diseases.[68]

Other innovative diagnostic platforms are also being explored, including research on incorporating novel quantum nanomaterials into RDTs for ultra-sensitive virus detection at the point-of-care, and development of devices like Varro Holdings' open-source technology platform to rapidly detect respiratory pathogens directly from human breath with accuracy comparable to PCR.[69,70] However, continued advancements in diagnostic technologies and strategic investments will be critical to transitioning these platforms from the laboratory into real-world use, particularly for point-of-care disease diagnosis and use in resource-limited settings.

65 Caitlin R. Thompson et al., "Development and evaluation of an antigen targeting lateral flow test for Crimean-Congo Haemorrhagic Fever," eBioMedicine 110 (2024), https://doi.org/10.1016/j.ebiom.2024.105460, https://doi.org/10.1016/j.ebiom.2024.105460.

66 Michael M. Kaminski et al., "CRISPR-based diagnostics," Nature Biomedical Engineering 5, no. 7 (2021/07/01 2021), https://doi.org/10.1038/s41551-021-00760-7, https://doi.org/10.1038/s41551-021-00760-7.

67 Sherlock Biosciences, Engineering biology to deliver products so people can access answers to control their health decisions, https://sherlock.bio/.

68 GADx, GHLabs x GADx: PoC innovation in molecular diagnostics (2024), https://www.globalaccessdx.com/ghlabs-x-gadx-poc-innovation-in-molecular-diagnostics/.

69 Q-Biomed, UK Quantum Biomedical Sensing Research Hub, https://www.qbiomed.org.uk/.

70 Business Wire, Varro Receives $20 Million from Vitalik Buterin to Support Development of Cutting-Edge Pathogen Biosensor Technology, https://www.businesswire.com/news/home/20241031135380/en/Varro-Receives-20-Million-from-Vitalik-Buterin-to-Support-Development-of-Cutting-Edge-Pathogen-Biosensor-Technology.

EXPANDING DIAGNOSTIC MANUFACTURING CAPACITY

The manufacturing of diagnostic tests remains concentrated among a small number of companies primarily based in Asia, Europe, and North America. To increase access to affordable, quality-assured diagnostics that meet local and regional needs, sustainable increase and geo-diversification of global manufacturing and distribution ecosystems is essential. PATH has developed an interactive dashboard aggregating information on diagnostics companies with manufacturing presence in Africa, Latin America, and Southeast Asia, increasing visibility of regional manufacturers.[71] Building on efforts to support the regional production of rapid diagnostic tests in Africa during the COVID-19 pandemic, Unitaid, together with partners including FIND, is investing in initiatives to expand the geographical diversity of manufacturing capacity, including through technology transfer, aiming to ensure sustainability and accelerate the availability of quality-assured diagnostics in Africa. This will address persistent public health needs during inter-crisis periods, such as HIV RDTs, while maintaining agility to meet surge demand for priority pandemic products when necessary.[72] TPPs are critical enablers for manufacturers to guide the fast-tracked development of diagnostic products suitable for global use, and to assist in the identification of regulatory requirements based on use cases. However, only a limited number of pathogens have updated TPPs (see Chapter 1: 100DM Scorecard).

STREAMLINE EVIDENCE GENERATION AND DIAGNOSTIC REGULATORY PATHWAYS

Diagnostics face significant regulatory challenges including complex, expensive, and lengthy approval pathways. However, there is a collective willingness to continually learn and improve processes amongst the diagnostics regulatory community as shown by some promising updates in 2024. Unitaid and The Global Fund support the WHO prequalification process and have advanced pathways through the Expert Review Panel for Diagnostics to support an expedited regulatory review process for both internationally and regionally manufactured diagnostics yet to undergo stringent regulatory assessment.[73] The proposed revision to the WHO prequalification assessment process for in vitro diagnostics (IVDs) to address the growing need for increased access to quality-assured IVDs in LMICs, upcoming launch of the Global Benchmarking Tool to create WHO Listed Authorities (WLAs) for medical devices and diagnostics, and ongoing consultations on improving the Emergency Use Listing for Diagnostics, are important steps to more agile and streamlined review processes.[74]

71 PATH, Diagnostic companies across Africa, Latin America, and Southeast Asia, https://www.path.org/who-we-are/programs/diagnostics/diagnostic-manufacturer-in-low-and-middle-income-countries/.
72 Unitaid, Call for Proposals: Regional Manufacturing for Equitable Access: Support to African Manufacturers of Postpartum Hemorrhage (PPH), Malaria and HIV products (2024), https://unitaid.org/call-for-proposal/regional-manufacturing-for-equitable-access-support-to-african-manufacturers-of-postpartum-hemorrhage-pph-malaria-and-hiv-products/#en. org/call-for-proposal/regional-manufacturing-for-equitable-access-support-to-african-manufacturers-of-postpartum-hemorrhage-pph-malaria-and-hiv-products/#en.
73 Unitaid, pro forma.
74 WHO, Public consultation on proposed revisions to the WHO Prequalification of in vitro diagnostics assessment process (2024), https://extranet.who.int/prequal/news/public-consultation-proposed-revisions-who-prequalification-vitro-diagnostics-assessment.

SUMMARY PLANS FOR 2025

The overarching goals of the 100DM for diagnostics are a coordinated and sustainable diagnostics R&D ecosystem and the development of diagnostics libraries to provide broad coverage for priority viral families. To move towards these goals, we propose the following actions should be prioritised in 2025, and IPPS will work with all partners to support their implementation (see Annex A for Planned Partner Commitments and Priority Actions):

- **Implement de-risking strategies to accelerate diagnostic R&D and establish sustainable funding** for the development of rapid point-of-care tests targeting priority pathogen families. Research on both pathogen-agnostic and pathogen-specific platforms should be continued, prioritising multiplexing capability and data connectivity. Target product profiles for point-of-care diagnostics for priority pathogens beyond SARS-CoV-2 need to be developed. Deliberate approaches for leveraging vaccine and therapeutics research to support the identification of diagnostic targets and the development of diagnostic solutions to enable integrated test-and-treat strategies should be promoted and funded.

- **Strengthen robust global biobanking networks** to address critical barriers in access to samples for test development, validation, and regulatory approval processes to support both epidemic and pandemic response. Global biobank networks must be strengthened, with enhanced access to samples through pre-approved material transfer agreements and robust biosecurity measures. Mechanisms to improve pathogen access and facilitate diagnostic evaluations at the country level must be explored, particularly in contexts where the international transfer of samples remains a significant barrier.

- **Expand sustainable capacity for regional production** to ensure that, in case of a pandemic, production of diagnostics at regional level is available to pivot to key products, by supporting the production of RDTs for major public health conditions in interpandemic periods.

- **Simplify and harmonise diagnostic regulatory pathways** to reduce complexity, cost, and approval timeframes. WHO should set out clear technical specifications for rapid point-of-care tests for priority pathogens to enable prequalification in an emergency context. Regulators and WHO should also collaborate through the Global Benchmarking tool to support as many regulators as possible to become WLAs for medical devices, allowing recognition of their approvals. Developers should work closely with relevant regulatory bodies and WHO to determine the most efficient approach to clinical and analytical validations, supported by guidance on streamlining these evaluations to generate the data required for WHO prequalification and Emergency Use Listing. The benefit of independent evaluations conducted by organisations such as FIND, academic institutions, and other experts should be leveraged.

- **Strengthen international coordination** to tackle critical funding, supply chain, regulatory and market challenges through a coordination mechanism across diagnostics partners. In 2025, a consortium of multisectoral diagnostics partners, including FIND, industry, research institutions, governments, regulatory bodies, and international organisations should convene to align on and implement the 100DM diagnostics roadmap, establishing clear deliverables, roles, and responsibilities. Focus on market shaping, developing targeted R&D incentives for priority viral families, and fostering effective partnerships between global health organisations and industry to ensure sustained implementation. Continued support should be given to advocacy around the essential role of rapid point-of-care tests in outbreak response, clinical trials, and integration with vaccines and therapeutics R&D, and coordinated efforts toward the World Health Assembly Resolution to strengthen global diagnostic capacity. The Secretariat is actively engaging industry stakeholders and coordinating a roundtable of multisectoral diagnostics partners to convene in 2025 as part of these efforts.

- **Embed best practices during interpandemic times** with policymakers and health ministries prioritising the procurement and integration of multiplex diagnostics with data connectivity, improve disease surveillance, and link diagnostic testing to treatment pathways. Governments should strengthen market demand signals through mechanisms like Essential Diagnostics Lists to support national procurement. Algorithms developed using evidence from routine surveillance and research should be used to guide development and deployment of the best suited diagnostic options.

Therapeutics R&D

CONTEXT AND AIMS

Safe and effective therapeutics – including directly acting small molecule antivirals and biologics like mAbs – are vital for reducing morbidity and mortality in pandemics, especially for vulnerable populations who may not benefit fully from vaccines. They serve as a critical bridge during the vaccine development and rollout phases, providing lifesaving care when it is needed most.

Therapeutics generally face broader public acceptance than vaccines, as evidenced during the COVID-19 pandemic where antiviral treatments largely avoided the hesitancy and misinformation that hampered vaccine uptake. Antivirals can often maintain effectiveness against evolving viral variants, providing a robust defence against emerging strains. Many therapeutics also offer greater shelf-life and stability, with less stringent cold chain requirements, reducing logistical challenges in resource-limited settings.

Despite lessons learned from COVID-19, the global antiviral pipeline shows major gaps in pandemic preparedness, starting with an alarmingly bare preclinical stage. While COVID-19 and influenza antivirals dominate current research, there is minimal to no development activity for other viral families that pose pandemic risks.[75] The current mpox outbreak highlights these gaps and underscores a critical weakness in antiviral research and development (see Chapter 5: Mpox case study). Advocacy efforts remain piecemeal in the absence of dedicated mechanisms to coordinate and increase strategic investments. Insufficient funding, particularly for early-stage R&D, undermines efforts to create a robust therapeutic arsenal, with industry engagement further discouraged by the absence of clear market incentives for many priority pathogens.

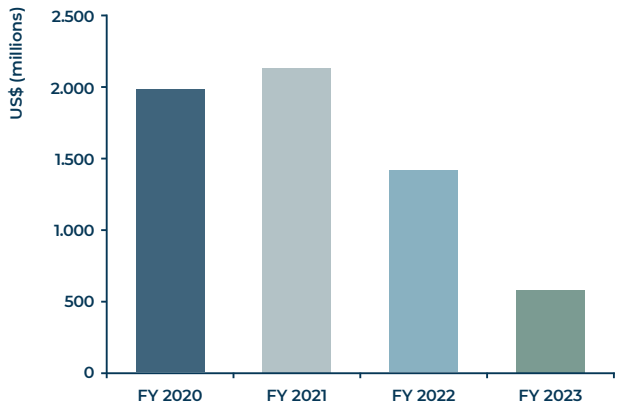


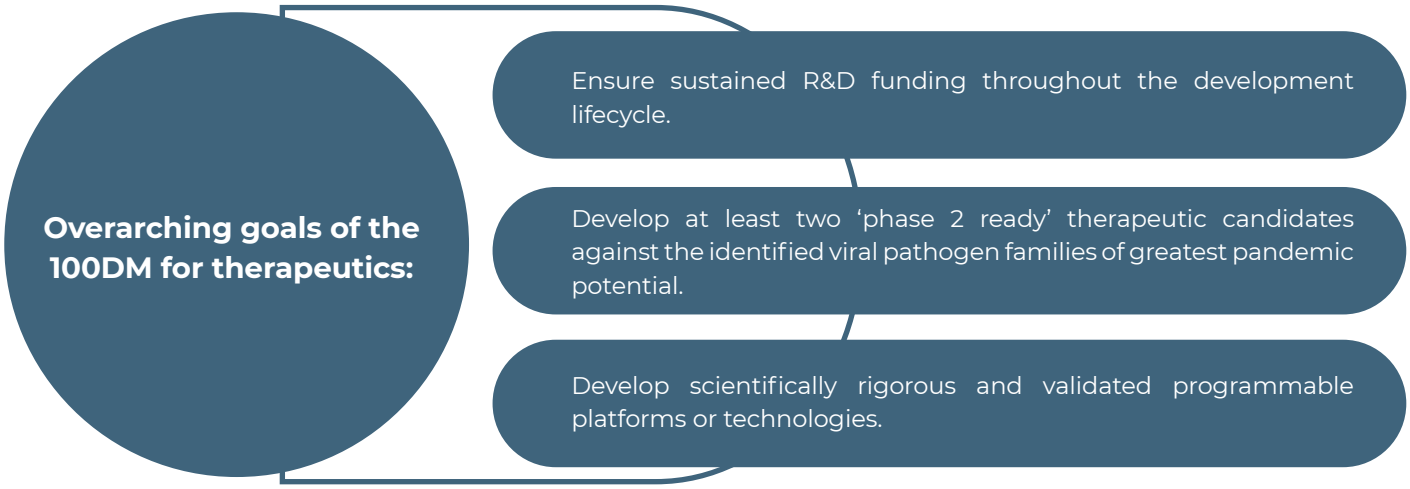
FIGURE 6. THERAPEUTICS R&D FUNDING

According to the data behind the 100DM scorecard, therapeutics funding experienced a dramatic 58% decline in 2023, primarily due to reduced funding from the U.S. NIH (Figure 6). This decline was most pronounced in drug R&D, which saw a 74% reduction, while biologics funding decreased more modestly, mirroring the trend seen in biologic platform investment. While the majority of funding cuts affected COVID-19 research - which could be considered appropriate given the availability of other MCMs - concerning is that these freed-up resources have not been diverted to other priority pathogens. Instead, drug funding declined across every disease, with Zika suffering the most severe cut at 94%, leaving just over $2 million in funding. The decline in biologics funding was less severe, as decreases in COVID-19 investment were partially offset by increased funding for Ebola, Marburg, and Nipah research.

The concentration of both research capabilities and manufacturing capacity in select regions means that even when treatments are developed, their global distribution remains inequitable. Additionally, early-stage R&D often fails to account for genetic diversity across affected populations, potentially limiting treatment efficacy in different communities. These systemic challenges affect not only pandemic response but also the treatment of endemic diseases and the protection of vulnerable populations who may respond less effectively to vaccines.

The 100DM Therapeutics Roadmap, launched in January 2024, aims to provide a framework for action and further collaboration between partners to address these challenges.

75 INTREPID, Antiviral Clinical and Preclinical Development Landscape — 3rd Edition (2024), https://www.intrepidalliance.org/wp-content/uploads/2024/10/Antiviral-Clinical-and-Preclinical-Development-Landscape-3rd-Edition-09Oct2024.pdf.



PROGRESS IN 2024

In response to the challenges and goals outlined in the 100DM Therapeutics Roadmap, progress has been made in 2024 across several key areas. While a comprehensive overview of progress updates from implementation partners is provided in Annex A, here we highlight key advances that could have broader impact on the therapeutics R&D ecosystem and potential for wider adoption in the field.

To address the lack of coordination in the therapeutics ecosystem, stakeholders across sectors recognised the **urgent need for a coordinated, global approach – particularly for early-stage R&D.** The concept of a Therapeutics Development Coalition emerged as a potential solution, aiming to unite diverse partners in a collaborative effort to reinvigorate the antiviral pipeline. This coalition would work to streamline R&D efforts, advocate for sustainable funding, and ensure equitable access to emerging therapeutics for both pandemic and endemic diseases.

In June 2024, IPPS co-organised a workshop with Unitaid, READDI, DNDi, Medicines Patent Pool (MPP), WHO, IFPMA, and the INTREPID Alliance bringing together key international partners from across academia, industry, government, and non-profits. This was followed by the Global Pandemic Preparedness Summit 2024 in Rio de Janeiro in July 2024, which widened consultation with regional partners and highlighted the importance of proof-of-concept projects and developing an operating model. In August 2024, a PLOS Global Public Health article authored by key stakeholders further articulated the case for a Therapeutics Development Coalition.[76] In October 2024, IPPS convened a meeting in Washington, DC, to advance the coalition from concept to incubation phase through structured discussions on proposed operating models and implementation plans (see Chapter 2: Outline for a Therapeutics Development Coalition). These collaborative efforts have established the core framework for the therapeutics development ecosystem, as implementation work advances. As the Coalition develops, lessons from the Tuberculosis and Malaria Drug Accelerators can be leveraged to establish multi-sector partnerships, resource sharing, and structured funding to drive R&D in areas with limited commercial incentives.

76 Shingai Machingaidze et al., "The case for a global therapeutics development coalition: Building a therapeutics pipeline for pandemic and endemic diseases," PLOS Global Public Health 4, no. 8 (2024), https://doi.org/10.1371/journal.pgph.0003654, https://doi.org/10.1371/journal.pgph.0003654.

Outline for a Therapeutics Development Coalition

The 100DM therapeutics roadmap, published alongside the 3rd IPPS annual implementation report in 2024, highlighted the need for increased coordination and investment in end-to-end therapeutics development to reinvigorate the pipeline of candidates against pathogens with pandemic potential. The establishment of a Therapeutics Development Coalition was proposed as a solution, to reinvigorate the therapeutics pipeline for both endemic and epidemic diseases.

Steps were taken throughout 2024 to establish the Therapeutics Development Coalition. Through a series of consultations in the Global North and Global South, stakeholders came together to agree on the Coalition's scope and goals and define key elements of the operating model to support early-stage R&D of therapeutics for viral families.

IPPS TOWARDS A THERAPEUTICS DEVELOPMENT COALITION

END GOALS

- **2x Phase 2 ready therapeutics per priority viral family**
- **Platform technologies to support Disease X response**
- **Pre-agreed pathways for trial, approval, manufacture and procurement with equitable access as focus**
- **Foster sustainable investment in the therapeutics pipeline**

SCOPE

- **Viral threats (not bacterial or fungal)**
- **Treatment for both endemic and epidemic threats**
- **Covering all therapeutic modalities including clinical management considerations**

FUNCTIONS

1st Priority: Early-stage R&D

- **Coordinating strategy for existing R&D efforts in line with WHO blueprint**
- **Regular pipeline analysis**
- **Facilitating partnerships to fill identified gaps**

Trials and Regulation

- **Trial protocol design**
- **Facilitating regulatory awareness of pipeline and pre-agreed emergency pathways**

Market shaping and access

- **Early voluntary licensing support**
- **Identify manufacturing base**
- **Identify access elements to be considered**

In 2025, efforts will be focused on operationalisation of the Therapeutics Development Coalition, including establishment of pre-clinical development teams, clinical development teams, and the virtual antiviral hub. To demonstrate proof-of-concept for the Coalition, two viral families will be selected as the initial focus, with coordinated efforts to collectively develop therapeutic candidates centred around these families. One viral family has already been agreed, flavivirus, and in 2025, the Coalition will identify the second viral family to further demonstrate how it would function to support better coordinated therapeutics development. These coordination activities will also highlight opportunities for funding to maximise the Therapeutics Development Coalition efforts on early-stage R&D of therapeutic candidates.

Parallel to these coalition-building efforts, significant progress has been made in **mapping the antiviral development landscape.** In October 2024, the INTREPID Alliance published its comprehensive Antiviral Landscape Third Edition, covering preclinical and clinical development for 13 viral families aligned closely with the WHO's pathogen prioritisation framework, with the notable addition of poxviruses following the 2022 mpox outbreak.[77] Similarly, READDI, in collaboration with SciVida, developed a comprehensive antiviral landscape assessment database covering seven high-risk viral families, including both active and abandoned R&D efforts.[78] These analyses provide crucial insights into the global antiviral pipeline, highlighting both promising candidates and critical gaps.

Building on this mapping work, there has been progress in both **antiviral small molecule and biologics development.** READDI's AViDD Centre (READDI-AC) is advancing a diverse portfolio of broad-spectrum small molecule antiviral assets with several preclinical studies completed, and several compounds progressing across various viral families.[79] Stanford's SyneRx, another AViDD Centre, is developing outpatient antiviral cocktails targeting both SARS-CoV-2 and other potential pandemic RNA viruses, with a focus on synergistic direct-acting antivirals.[80] The Pandemic Antiviral Discovery (PAD) initiative has further strengthened this momentum, committing $20 million in funding for 11 research projects on novel antivirals for pandemic influenza in May 2024.[81] Meanwhile, the Dengue Alliance demonstrates an innovative South-South partnership, with researchers from Malaysia, Thailand, India, and Brazil collaborating to accelerate development of affordable dengue treatments, including through drug repurposing studies.[82]

In the biologics arena, the National Institute of Allergy and Infectious Diseases (NIAID) has committed up to $100 million annually to its ReVAMPP programme, supporting seven U.S.-based research groups working across nine viral families to develop vaccines and mAbs.[83] CEPI signed an agreement with ServareGMP and Mapp Biopharmaceutical for up to $43.5 million to advance preclinical and clinical studies of the MBP1F5 Nipah mAb in India and Bangladesh[84], while Instituto Butantan made significant strides in developing mAbs against Zika, SARS-CoV-2, and influenza.[85] These diverse but early-phase activities, while promising, face high risks of attrition, underscoring the critical importance of maintaining a portfolio approach to increase the likelihood of successfully developing and deploying new antivirals in communities that are most in need.

2024 also saw a notable focus on **adaptable platform technologies that can be rapidly modified to target multiple pathogens** for therapeutic development. These platforms address gaps in conventional antiviral therapeutics such as product stability, improved formulations, and durability and breadth of protection, and include host-targeted therapies, mAbs, and nucleic acid therapeutics. The Cumming Global Centre for Pandemic Therapeutics invested over $22 million in promising platforms, including antibodies, nanobodies, small molecules with pan-viral potential, host targets such as innate immune activators, and nucleic acid targeting approaches.[86] In 2024, the centre expanded its efforts, initiating a $54 million partnership with the University of Bonn for host-directed pandemic therapeutics research.[87] BARDA's Flexible and Strategic Therapeutics (FASTx) Programme and Wellcome similarly embraced innovative approaches, funding research on low-cost and thermostable nucleic acid-based antiviral antibodies.[88,89] SPRIND is advancing innovative antiviral platforms and broad-spectrum approaches, including gene editing and RNA interference technologies. Notably, SPRIND's "Broad-Spectrum Antivirals" Challenge, which began in 2021, culminated with four winning teams developing unique approaches to tackle current and future pathogens.[90] In addition, SPRIND has been co-investing in the $29 million round of CPTx, one of the Challenge winners who develop novel antivirals based on DNA-origami.[91] However, development of globally accessible TPPs, which do not exist for most pathogens beyond SARS-CoV-2, will be essential in ensuring access is embedded into the design of these next generation approaches.[92]

Alongside these advancements, there has been emphasis on **collaboration and access initiatives** to ensure that the benefits of these innovations reach the populations where they are most needed. IAVI and Impact Global Health recently published a report evaluating mAb R&D and access globally, with a focus on Africa, and calling for scalable solutions to improve equitable access in LMICs. High costs have been a significant barrier to mAbs access in LMICs. However, innovations such as the development of highly potent, long acting mAbs that require lower doses, advances in bioprocess engineering to reduce production costs, and simplified administration methods offer the potential to improve access to these products.

77 INTREPID, Antiviral Clinical and Preclinical Development Landscape — 3rd Edition.
78 READDI, Comprehensive antiviral landscape assessment guides R&D, https://readdi.org/stories/comprehensive-antiviral-landscape-assessment-guides-rd/.
79 READDI, READDI is filling the R&D pipeline for pandemic pathogens, https://readdi.org/stories/readdi-is-filling-the-rd-pipeline-for-pandemic-pathogens/.
80 Stanford Medicine, Development of Outpatient Antiviral Cocktails against SARS-CoV-2 and other Potential Pandemic RNA Viruses, https://virx.stanford.edu/synerx/index.html.
81 DNDi, pro forma.
82 Institute for Medical Research Malaysia, pro forma.
83 National Institute of Allergy and Infectious Diseases, Research and Development of Vaccines and Monoclonal Antibodies for Pandemic Preparedness (ReVAMPP).
84 CEPI, New human trials for novel antibody offer hope for immediate protection against deadly Nipah (2024), https://cepi.net/new-human-trials-novel-antibody-offer-hope-immediate-protection-against-deadly-nipah.
85 Butantan, pro forma.
86 The Cumming Global Centre for Pandemic Therapeutics, pro forma.
87 The University of Melbourne, Cumming Global Centre for Pandemic Therapeutics and University of Bonn announce partnership (2024), https://www.unimelb.edu.au/newsroom/news/2024/september/cumming-global-centre-for-pandemic-therapeutics-and-university-of-bonn-announce-aud$54-million-partnership.
88 Wellcome Trust, pro forma.
89 Medical Countermeasures, BARDA accelerates development of early-stage antiviral platforms with multiple collaborators (2024), https://www.medicalcountermeasures.gov/newsroom/2024/fastx/.
90 SPRIND, Your Challenge: Broad-Spectrum Antivirals, https://www.sprind.org/en/impulses/challenges/antiviral.
91 CPTx, CPTx Secures $29 Million to Advance Breakthrough Antiviral Platform (2024), https://www.cptx.bio/news-resources/cptx-secures-29-million-to-advance-breakthrough-antiviral-platform.
92 James F. Demarest et al., "Antiviral target compound profile for pandemic preparedness," Nature Reviews Drug Discovery (2024/12/02 2024), https://doi.org/10.1038/s41573-024-01102-3, https://doi.org/10.1038/s41573-024-01102-3.

In a step toward addressing manufacturing costs, the Gates Foundation and LifeArc launched a global Grand Challenge initiative in 2024 seeking innovations to produce mAbs at a final drug substance cost of goods of $10 per gram – an ambitious target that could transform access in LMICs.[93] Unitaid has also made significant contributions to these efforts, releasing a call for proposals in December 2023 aimed at demonstrating the feasibility and viability of business models that enable equitable access to mAbs in LMICs.[94,95] As a result, Unitaid is launching three investments in mAbs with viable use cases and access strategies for malaria, respiratory syncytial virus (RSV), and HIV, while considering potential applications for pandemic scenarios. This approach not only addresses current health needs but also builds capacity and infrastructure that could be pivotal in future pandemics. This area presents a great opportunity to expand the use of mAbs into LMICs if market, regulatory and R&D challenges can be overcome.[96] These collaborative efforts and access initiatives are crucial components in building a more equitable and resilient global therapeutic ecosystem.

To strengthen the resilience of Africa's manufacturing ecosystem, Unitaid is making strategic investments in **regional manufacturing capacity** and adaptable platform technologies. Through innovative technologies and value chain collaborations, these initiatives expand manufacturers' capabilities in developing and producing multiple therapeutic formulations, including injectables and paediatric medicines. Working with regional economic communities and institutions like African Union Development Agency - New Partnership for Africa's Development (AUDA-NEPAD) and Africa CDC, Unitaid is supporting African manufacturers to develop cost-competitive, quality-assured therapeutics that address both current healthcare priorities and potential future pandemic needs, ultimately enhancing regional health security and supply chain resilience.[97] Complementing these efforts, MPP approved new initiatives including the use of regionally focused expressions of interest for future MPP-licensed products and the issuance of conditional licences, where companies that show promise but do not yet fully meet requirements can receive a commitment for future licensing once specified standards are met.[98] This creates a pathway for new manufacturers while maintaining quality standards, potentially expanding manufacturing capabilities in LMICs (see Chapter 4: Sustainable Manufacturing).

93 BMGF, Innovations for Exceptionally Low-Cost Monoclonal Antibody (mAb) Manufacturing, https://gcgh.grandchallenges.org/challenge/innovations-exceptionally-low-cost-monoclonal-antibody-mab-manufacturing.
94 Unitaid, Call for Proposals: Establish viable business models for access to monoclonal antibodies in low- and middle-income countries (2023), https://unitaid.org/call-for-proposal/establish-viable-business-models-for-access-to-monoclonal-antibodies-in-low-and-middle-income-countries/#en.
95 Unitaid, pro forma.
96 Shelly Malhotra et al., "Novel approaches to enable equitable access to monoclonal antibodies in low- and middle-income countries," PLOS Global Public Health 4, no. 7 (2024), https://doi.org/10.1371/journal.pgph.0003418, https://doi.org/10.1371/journal.pgph.0003418.
97 Unitaid, Call for Proposals: Regional Manufacturing for Equitable Access: Support to African Manufacturers of Postpartum Hemorrhage (PPH), Malaria and HIV products.
98 Medicines Patent Pool, pro forma.

SUMMARY PLANS FOR 2025

The overarching goals for the 100DM remain the same; sustained R&D funding throughout the development lifecycle; developing at least two 'phase 2 ready' therapeutic candidates against the identified viral families of greatest pandemic potential and developing scientifically rigorous and validated programmable platforms or technologies. To move towards these goals we propose the following actions should be prioritised in 2025 and IPPS will work with all partners to support their implementation (see Annex A for Planned Partner Commitments and Priority Actions):

- **Operationalisation of the Therapeutics Development Coalition** to accelerate product development through coordinated implementation of the therapeutics roadmap, ensuring alignment with the WHO viral family approach and CORCs. This includes establishing coordination structures with clear partner roles to demonstrate proof-of-concept projects across two priority viral families, showcasing how collaborative development can accelerate therapeutic readiness.

- **Mapping of pipeline gaps to identify strategic funding opportunities** for pandemic-ready therapeutics, building on INTREPID and other landscaping efforts in alignment with WHO priorities, to identify critical R&D pipeline gaps where targeted funding could have maximum impact. The assessment will identify promising therapeutic candidates, with detailed evidence-based metrics on their development costs and timelines. TPPs for therapeutic candidates must be defined to guide this work. These efforts should prioritise building and strengthening early-stage R&D capacity in LMICs by leveraging existing centres of excellence, such as H3D in South Africa.[99] A balanced portfolio of push incentives (e.g. grants, tax credits) and pull incentives (e.g. market commitments, prize funds) supported by governments with advocacy from the Coalition, could help address identified gaps and drive innovation while ensuring market viability.

- **Advancement of platform technologies and innovative approaches to therapeutics development**, demonstrating preclinical proof-of-concept for novel antiviral platforms across multiple viral families. Focus on accessible product profiles including broad-spectrum small molecule antivirals, cross-reactive/broadly neutralising mAbs, nucleic acid technologies, and other emerging modalities. Leverage AI and machine learning capabilities to accelerate drug discovery with concrete breakthroughs for priority pathogens.

99 University of Cape Town, H3D, https://h3d.uct.ac.za/.

Vaccines R&D

CONTEXT AND AIMS

The global trajectory for vaccines R&D is robust, driven by advocacy and leadership from key implementing organisations such as CEPI, and supported by the biopharmaceutical industry and vaccine developers as critical contributors to R&D. However, sustained and coordinated efforts among multisectoral partners, along with the continued diversification of vaccine technologies to ensure platforms are appropriately matched to the unique requirements of target pathogens, are needed to translate this progress into equitable global access to vaccines.[100]

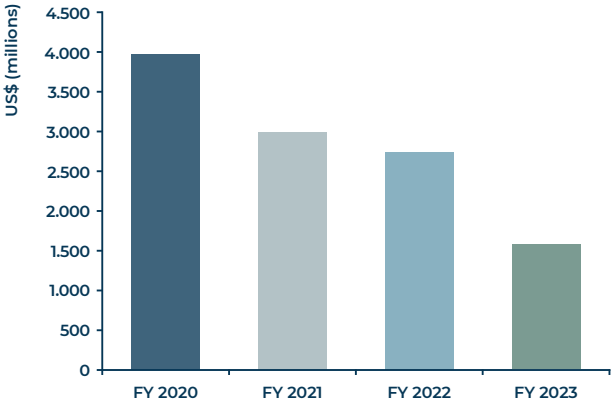


FIGURE 7. VACCINES R&D FUNDING

Despite this momentum, investment in vaccines R&D for emerging infectious diseases fell by 43% in 2023, highlighting the need for renewed global focus (Figure 7). According to the data behind the 100DM scorecard, the vast majority of vaccine R&D (89%) is concentrated in COVID-19 vaccine development, which made up 95% of the $1.2 billion drop that saw funding levels halve – an appropriate measure considering the existing suite of vaccines approved and in late-stage clinical development. Looking at non-COVID pathogens, however, vaccine R&D still fell by 26%. Chikungunya was the only pathogen to experience a notable increase in investment with significant support from CEPI and the European Union, while funding for Marburg virus vaccines remained stable, and all other pathogens saw declining investment.[101]

Considering how to sustain regional vaccine manufacturing capacity during interpandemic periods remains a challenge, particularly in regions where demand for routine vaccines may not be sufficient to maintain a viable commercial base. While this section primarily focuses on vaccines R&D, progress in vaccine manufacturing capacity is addressed separately (see Chapter 4: Sustainable Manufacturing).

Overarching goals of the 100DM for vaccines focusing on speed, scale, and access:

- **Development of prototype vaccine libraries** for priority viral families, aimed at providing a foundation for rapid vaccine development in response to new or emerging disease threats.
- **Availability of programmable vaccine platform technologies** that can be quickly repurposed to respond to a potential Disease X threat.
- **Optimisation of vaccine platforms and capacities for phase-appropriate production** (e.g., the production of clinical trial materials, alongside sustaining the large-scale capacities needed for outbreak response) and simplified administration, with compliance to WHO TPPs being a key measure.

100 IPPS, 100 Days Mission Scorecard Report (2024), https://ippsecretariat.org/publication/100-days-mission-scorecard-report/.
101 Impact Global Health, G-FINDER data portal: tracking funding for global health R&D.

PROGRESS IN 2024

2024 has seen substantial progress toward the 100DM's goals for vaccines, with key advances in prototype vaccines on platforms aimed at addressing Disease X, in addition to the preclinical and clinical development of vaccines targeting priority pathogens. Here we highlight a few key advances that could have broader impact on the vaccines R&D ecosystem and wider adoption potential in the field; however, a more comprehensive overview of progress updates provided by implementation partners can be found in Annex A.

There have been several significant approvals in 2024 for both new vaccine platforms and candidates for priority pathogens. One significant milestone was the approval of the first self-amplifying RNA (saRNA) vaccine, zapomeran, by Japan's Ministry of Health, Labour and Welfare in late 2023, followed by the EMA's positive opinion recommending its authorisation for COVID-19 prevention in adults in December 2024. The zapomeran COVID-19 vaccine requires much lower titres compared to conventional mRNA vaccines, reducing production costs, and opening up pathways for other saRNA vaccines in the pipeline, including those for influenza.[102] The WHO prequalification of two malaria vaccines—RTS,S/AS01 and R21/Matrix-M—using scalable virus like particle technology marked another milestone, offering insights for both endemic and pandemic response capabilities.[103] Another notable update was Valneva's Ixchiq live attenuated vaccine, the world's only licensed Chikungunya vaccine, which received approvals from the U.S. FDA (November 2023), Health Canada (June 2024) and EMA (July 2024), with additional support from CEPI and European Union for technology transfer to Brazil to facilitate LMIC market access.[104,105] In June 2024, Gavi's Board approved several important vaccine programmes targeting WHO R&D Blueprint priority pathogens. These include dengue, as well as vaccine stockpiles against mpox and hepatitis E, although implementation awaits licensed vaccines becoming available. Since outbreak vaccine markets tend to be small and unpredictable, making them commercially challenging, these approvals provide important market signals. In response to global trends, Gavi has also updated its methodology for considering new vaccines, called the Vaccine Investment Strategy. This revised approach now accounts for vaccines' potential impact on AMR, considers how climate change influences geographical spread, incidence, and severity of disease outbreaks, and incorporates enhanced economic modelling for endemic diseases, including treatment and delivery costs.[106]

102 Nature, Self-copying RNA vaccine wins first full approval: what's next? (2023), https://www.nature.com/articles/d41586-023-03859-w.
103 WHO, Malaria vaccine: WHO position paper – May 2024 (2024), https://www.who.int/publications/i/item/who-wer-9919-225-248.
104 Valneva, Valneva Receives Marketing Authorization in Europe for the World's First Chikungunya Vaccine, IXCHIQ® (2024), https://valneva.com/press-release/valneva-receives-marketing-authorization-in-europe-for-the-worlds-first-chikungunya-vaccine-ixchiq/.
105 CEPI, CEPI expands partnership with Valneva with $41.3 million to support broader access to world's first Chikungunya vaccine (2024), https://cepi.net/cepi-expands-partnership-valneva-413-million-support-broader-access-worlds-first-chikungunya.
106 Gavi, The Vaccine Investment Strategy (VIS) (2024), https://www.gavi.org/news-resources/knowledge-products/vaccine-investment-strategy-vis.

ACCELERATING DEVELOPMENT OF PROTOTYPE VACCINES FOR PRIORITY PATHOGENS

A key goal of the 100DM is the development of prototype vaccine libraries, which would provide globally accessible repositories of scientific knowledge, data, and rapid response vaccine candidates targeting priority pathogens. These foundational elements could be swiftly adapted to address novel pathogens with pandemic potential, significantly accelerating vaccine development. However, alignment among vaccine stakeholders on the vision for a global prototype vaccine library is still needed, and further consultation is essential to define how such materials could be made globally accessible. The WHO's ongoing exploration of CORCs could offer a potential framework to advance technical progress and foster collaboration at the viral family level.

Still, 2024 saw significant progress, including the development of vaccine candidates for priority pathogen families, achievement of preclinical proof-of-concept for rapid response platforms, and generation of correlates of protection data – all critical steps toward future vaccine libraries.

CEPI, along with partners in academia and industry, have advanced multiple candidates across a diversity of vaccine technologies. A few examples include preclinical and early clinical evaluation of vaccines for Lassa Fever (SK Bio, mRNA & Oxford, ChAdOx) and Junín (Oxford, ChAdOx) as exemplars of the Old and New World Arenavirus families, respectively, as well as mRNA-based platform candidates for Japanese Encephalitis (SK Bio) and mpox (BioNTech) as flavivirus and poxvirus prototypes. Moreover, in June 2024, CEPI and the European Commission launched a funding call for broadly protective filovirus vaccines.[107] Additionally, CEPI is supporting later-stage phase 2 trials of viral vector platform vaccine candidates for Lassa Fever (IAVI), Nipah (Oxford), MERS (Barinthus Bio/Oxford), and Rift Valley Fever (Oxford). CEPI's enabling sciences portfolio and networks, including assay harmonisation, animal model development, and epidemiological studies, have been a key enabler for some of this progress, in addition to the use of computational and AI-assisted tools to accelerate vaccine R&D (see Chapter 2: Synergies).

Further efforts to develop vaccine candidates targeting diseases of regional relevance are being driven by the Developing Countries Vaccine Manufacturers Network (DCVMN) and WHO/MPP mRNA Technology Transfer Programme partners, including through regional R&D consortia. Notable candidates include vaccines for COVID 19, Zika (Fiocruz) and influenza (Butantan and Sinergium Biotech) in Latin America; COVID-19, Rift Valley Fever, Gonorrhoea, and Respiratory Syncytial Virus (Afrigen Biologics) in Africa; and Dengue, COVID-19 in Southeast Asia (Government Pharmaceutical Organization Thailand), among others.[108,109,110,111,112] These initiatives not only address urgent endemic health priorities but also build scientific and technical capacity to pivot swiftly to outbreak response, ensuring sustainable R&D that enhances both local and global vaccine development.

In an initiative that could accelerate development and licensure of prototype vaccine candidates, Wellcome and CEPI launched a £38 million funding call to establish correlates of protection. The programme supports projects across 8 diseases that currently lack licensed vaccines, including Lassa, Rift Valley Fever, Nipah, and Marburg virus. Identification of correlates of protection could significantly reduce cost and time taken to develop vaccines for diseases with low incidence or high case fatality rates by serving as alternatives to clinical endpoints, and guiding clinical trial design where efficacy testing would otherwise be unfeasible. In parallel, they are working with regulators and other partners to establish a common framework outlining the data requirements for using correlates of protection biomarkers in licensure pathways.[113]

As prototype vaccine candidates progress through the pipeline, they generate valuable data on antigen designs, platforms, and formulations that elicit robust immune responses against priority viral families. This growing knowledge base will serve as a critical resource that can be adapted and applied to address future outbreaks. However, careful consideration is needed regarding systems for sharing key information safely, openly, and accessibly—such as through a future global vaccine library—to enable broader collaboration, incorporate lessons from past outbreaks, and accelerate future vaccine development.

107 CEPI, CEPI seeks to fund new innovations for broad protection against Ebola and other deadly Filoviruses (2024), https://cepi.net/cepi-seeks-fund-new-innovations-broad-protection-against-ebola-and-other-deadly-filoviruses.
108 NPR, Whatever happened to ... the Brazilian besties creating an mRNA vaccine as a gift to the world (2024), https://www.npr.org/2024/09/09/g-s1-20882/best-friends-mrna-vaccine-covid-brazil.
109 Fiocruz, Centro Pasteur Fiocruz de Imunologia e Imunoterapia é inaugurado no Ceará (2024), https://portal.fiocruz.br/noticia/2024/05/centro-pasteur-fiocruz-de-imunologia-e-imunoterapia-e-inaugurado-no-ceara.
110 PAHO, New initiative launched to advance mRNA vaccine development against human avian influenza (H5N1) (2024), https://www.paho.org/en/news/29-7-2024-new-initiative-launched-advance-mrna-vaccine-development-against-human-avian.
111 Afrigen, pro forma.
112 PATH, PATH congratulates Thailand on granting conditional approval for emergency use to first locally produced COVID-19 vaccine (2024), https://www.path.org/our-impact/media-center/path-congratulates-thailand-on-granting-conditional-approval-for-emergency-use-to-first-locally-produced-covid-19-vaccine/.
113 Wellcome Trust, Seeking predictors of vaccine efficacy: identifying correlates of protection to support vaccine development (2024), https://wellcome.org/grant-funding/schemes/correlates-protection-for-vaccine-development.

PROGRAMMABLE VACCINE PLATFORMS

In 2024, significant progress was made toward scaling programmable vaccine platform technologies that can be rapidly repurposed for future outbreaks, including potential Disease X, through strategic investments and partnerships. In this context, vaccine-related platform technologies encompass both platform development research and process innovation. These include viral vectors (both replicating and non-replicating) and nucleic acid-based platforms (DNA and RNA), as well as innovations in vaccine development processes such as thermostabilisation techniques that can be applied across multiple target vaccines. It also includes research focusing on the administration method of a finished product, such as vaccine microarray patches.[114]

CEPI established partnerships with University of Oxford, BioNTech, and Serum Institute of India to enhance the speed, scalability, and accessibility, of viral vector, mRNA, and protein subunit platforms (see Chapter 4: Sustainable Manufacturing). While continued development of these programmable vaccine platforms is essential for achieving the 100DM by enabling rapid adaptation and scalable production of vaccines against emerging pathogens, greater focus from the global ecosystem is required to expand access to these platform technologies.

VACCINE PLATFORM INNOVATIONS FOR SCALE, AFFORDABILITY, AND ACCESS

Further platform optimisation and innovation is essential to align novel vaccine technologies with TPPs and enable equitable deployment. To advance platform optimisation for large-scale production and simplified administration, BARDA announced up to $500 million in Project NextGen funding in June 2024 for phase 2b trials of novel vaccine delivery methods, such as nasal sprays and pills, aimed at achieving more durable COVID-19 protection.[115] Meanwhile, CEPI allocated $17 million to support proof-of-concept studies for innovative technologies, and are managing ten active projects spanning next generation RNA platforms, alternative delivery systems, and thermostable formulations. Several of these have progressed to early clinical development.[116] For example, Lemonex has initiated phase 1 trials of its thermostable mRNA drug delivery technology, which aims to minimise side effects and enhance accessibility. [117]

114 Policy Cures Research G-FINDER, Emerging Infectious Disease R&D Scope, https://gfinder.policycuresresearch.org/staticContent/pdf/G-FINDER_EID_R%26D_scope.pdf.
115 U.S. Department of Health and Human Services, BARDA awards up to $500 million in Project NextGen funding for vaccine clinical trials (2024), https://www.hhs.gov/about/news/2024/06/13/barda-awards-500-million-project-nextgen-funding-vaccine-clinical-trials.html.
116 CEPI, Regional manufacturing pro forma.
117 CEPI, Vaccines R&D pro forma.

In 2024, the UK Vaccine Network (UKVN) accelerated vaccine development for diseases with epidemic potential in LMICs through an Innovate UK Small Business Research Initiative, awarding £37 million across 25 projects.[118] As part of this initiative, Afrigen Biologics with EnsiliTech, is developing silica-encapsulated thermostable mRNA vaccines to ensure viability in regions with limited cold chain infrastructure.[119] Microarray patches, another thermostable vaccine delivery platform which could simplify vaccine administration, are progressing into clinical development. In April 2024, researchers from the MRC Unit The Gambia at the London School of Hygiene and Tropical Medicine (LSHTM) demonstrated successful phase 1/2 trial results for a measles and rubella microarray patch, achieving over 90% protection rates in infants.[120] Building on this progress, in September 2024, Vaxxas initiated a phase 1 trial of its needle-free avian influenza vaccine microarray patch, which enables lower dose delivery and may improve patient uptake compared to injected vaccines.[121]

There are ongoing wider efforts to create innovative solutions to accelerate mRNA vaccine manufacturing and reduce costs, with Thermo Fisher, DNA Script, and Afrigen Biologics, separately developing enzymatic DNA synthesis technologies and continuous manufacturing processes.[122,123] Since 2021, the Wellcome Leap R3 program, co-funded by CEPI, has advanced dose- and cost-reducing innovations, including self-amplifying RNA products and novel delivery systems, alongside small footprint modular DNA and RNA manufacturing technologies adaptable for diverse products and scales. Clinical GMP demonstrations are ongoing, with pre-IND submissions for low dose saRNA vaccines and mRNA-based mAb therapies targeting respiratory infections and cancer. The program aims to build an economically sustainable global network of biofoundries for innovation and pandemic surge capacity.[124]

Innovative platform products should continue to be developed through preclinical and clinical stages, while platform technologies should advance along Technology Readiness Levels (TRLs) to ensure scalability and readiness for manufacturing.

118 HMG, pro forma.
119 EnsiliTech, EnsiliTech is proud to announce that it has been awarded a highly competitive research contract from the UK Government's Small Business Research Initiative (SBRI) for the development of the world's first thermally stable mRNA vaccine. (2024), https://www.ensilitech.com/news/sbri-contract-awarded.
120 London School of Hygiene & Tropical Medicine, Microarray patches safe and effective for vaccinating children (2024), https://www.lshtm.ac.uk/newsevents/news/2024/microarray-patches-safe-and-effective-vaccinating-children.
121 Business Wire, Vaxxas Initiates Phase I Clinical Trial of Pre-Pandemic Avian Influenza A Virus (H7N9) Vaccine Delivered Using Vaxxas' Novel High-Density Microarray Patch (HD-MAP) (2024), https://www.businesswire.com/news/home/20240911909833/en/Vaxxas-Initiates-Phase-I-Clinical-Trial-of-Pre-Pandemic-Avian-Influenza-A-Virus-H7N9-Vaccine-Delivered-Using-Vaxxas%E2%80%99-Novel-High-Density-Microarray-Patch-HD-MAP.
122 ThermoFisher, pro forma.
123 CEPI, CEPI partners with Afrigen to speed up mRNA vaccine development and access (2024), https://cepi.net/cepi-partners-afrigen-speed-mrna-vaccine-development-and-access.
124 Wellcome Trust, "R3," https://wellcomeleap.org/r3/.

SUMMARY PLANS FOR 2025

To work towards the overarching goals of having vaccines ready for priority pathogens and Disease X, establishing trial-ready investigational stockpiles for certain priority pathogens, advancing platform technologies for rapid outbreak or epidemic response, and optimising vaccine development and production capacity for sustainable manufacturing and equitable access, the following actions should be prioritised in 2025. IPPS will work with all partners to support their implementation (see Annex A for Planned Partner Commitments and Priority Actions):

- **Advancing clinical development of vaccine candidates for priority viral families** through a coordinated coalition of supporting partners including WHO, CEPI, R&D funders, industry, and regulators aligned with the WHO pathogen prioritisation framework and emerging WHO CORCs. As part of this effort, global partners should align to advance a pathogen-specific pilot project to explore the practical implementation of a global vaccine library approach.

- **Sustaining investment in development of a diverse range of existing and novel vaccine platform technologies,** identifying platforms that induce robust immune responses for specific viral families. Continuing progress on **innovations in vaccine thermostability and durability, administration routes** (e.g., transdermal), and cost-effective, adaptable, and scalable manufacturing processes. Efforts should include technology transfer agreements and capacity building with LMIC partners to enhance global access. Planning and implementation must prioritise decisions and approaches that support equitable access. While geo-diversifying manufacturing can enhance vaccine uptake and regional self-sufficiency, it often requires substantial initial investments and may not directly improve access. To address these cost challenges, mechanisms such as the Gavi African Vaccine Manufacturing Accelerator (AVMA) facility play a crucial role.

- **Identifying investment gaps in vaccine candidates and platform technologies** relevant to 100DM around which philanthropic, public, industrial, and other funders can coalesce to advance the most promising technologies into clinical development.

- **Establishing and implementing economic risk-sharing models** to sustain vaccine manufacturing capacity across diverse platform technologies in interpandemic periods through strategic public-private partnerships. Work should encompass support for both routine immunisation programmes and epidemic/pandemic preparedness via mechanisms including advanced purchase commitments, stockpiling arrangements, pooled procurement systems, and surge capacity agreements. This approach should be developed to create sustainable funding models that ensure geographic distribution of manufacturing capabilities while maintaining commercial viability for different market conditions and public health priorities.

Spotlight 5: H5N1 underscores the need for enhanced global preparedness

Throughout 2023-2024, highly pathogenic H5N1 avian influenza has caused widespread mortality in wildlife and poultry, and demonstrated concerning mammalian transmission, particularly in U.S. cattle populations and Finnish fur farms. While human cases remain limited with no confirmed human-to-human transmission, the increasing risk of viral adaptation and spillover highlights critical gaps in our global preparedness.

The recent Finnish experience illustrates both progress and persistent challenges in H5N1 response. Following H5N1 detection in 27 fur farms in July 2023 affecting 485,000 animals, Finnish authorities moved to protect high-risk workers through vaccination. However, despite early planning, regulatory delays postponed the subsequent vaccination campaign of farm workers until June 2024. While Finland's innovative approach of vaccinating high-risk workers within a clinical trial framework offers valuable insights, the delays underscore systemic weaknesses in global response capabilities.

Current H5N1 preparedness mechanisms remain inadequate for an equitable global response. The European Commission has secured options for 40 million vaccine doses and the U.S. for 4.8 million doses, illustrating how vaccine supply is yet again becoming overwhelmingly concentrated in high-income countries.[125] Manufacturing capacity is mainly reliant on traditional egg-based vaccine technology, and the Pandemic Influenza Preparedness (PIP) Framework's 10% reserve of real-time vaccine supply is unlikely to meet equitable global needs in an emergency. [126,127]

Genuine preparedness for H5N1 demands coordinated advancement in three critical areas: modernised vaccine approaches to overcome the limitations of egg-based production – moving toward scalable rapid response platforms, and vaccines with broad spectrum and transmission blocking capability; enhanced global surveillance at the animal–human interface for early detection of viral evolution; and innovative delivery methods—such as mucosal, oral, or transdermal approaches—to improve distribution, particularly in regions with limited cold-chain infrastructure.[128] These technical improvements must be coupled with systemic changes: procurement funding, improved country preparedness, unrestricted trade, and clear triggers for switching between seasonal and pandemic influenza and scaling up production.[129] Without urgent action on these fronts, the world remains extremely vulnerable to a potential H5N1 pandemic.

125 H. Nohynek and O. M. Helve, "One health, many interpretations: vaccinating risk groups against H5 avian influenza in Finland," Euro Surveill 29, no. 25 (Jun 2024), https://doi.org/10.2807/1560-7917.Es.2024.29.25.2400383.
126 CEPI, H5N1 and spillover risk: Is the world ready to tackle zoonotic influenza? (2024), https://cepi.net/h5n1-and-spillover-risk-world-ready-tackle-zoonotic-influenza.
127 WHO, Pandemic Influenza Preparedness (PIP) Framework, https://www.who.int/initiatives/pandemic-influenza-preparedness-framework.
CEPI, H5N1 and spillover risk: Is the world ready to tackle zoonotic influenza?
Nohynek and Helve, "One health, many interpretations: vaccinating risk groups against H5 avian influenza in Finland."
128 CEPI, H5N1 and spillover risk: Is the world ready to tackle zoonotic influenza?
129 Nohynek and Helve, "One health, many interpretations: vaccinating risk groups against H5 avian influenza in Finland."

3

Improvements to clinical trials capability and regulatory processes

CONTEXT AND AIMS

Enhancing clinical trials capability and regulatory processes is vital for rapid pandemic response.

The goals for a clinical trials and regulatory system to enable a 100-day response remain focused on:

- Sufficient clinical trial capacity and capability, especially in areas where outbreaks are most prevalent
- Coordinated clinical pipelines for this global network of trials
- Best practices on trial design embedded across global efforts
- Flexible regulatory procedures, including pre-agreed emergency regulatory procedures during a PHEIC
- Strengthened regulatory capacity in all regions to expedite national approvals
- Adoption of preparatory regulatory approaches such as platform technology master files, harmonised cloud-based data sharing systems and shared risk-benefit frameworks

While there has been notable progress in global clinical trial capabilities and regulatory processes, challenges remain in strengthening coordination and efficiency. Approval processes for clinical trials vary across countries and regions, and the regulatory landscape shows differences across product types - DTVs each have distinct pathways, with some being more established than others, particularly for newer technologies or emergency use authorisations. Clinical trial networks often rely on project-based funding, affecting the sustainability of research capacity, particularly in LMICs where gaps in infrastructure and investment continue to impact research capabilities in both routine and emergency situations. The distribution of research activity relative to disease burden indicates a need to strengthen global research infrastructure and coordination mechanisms to better align research capabilities with public health needs across different regions.

PROGRESS IN 2024

2024 has seen notable progress across the key objectives of improving clinical trial capability and refining regulatory processes, with strides made in both readiness for routine trials and preparedness for emergencies. While a comprehensive overview of progress updates from implementation partners is provided in Annex A, here we highlight key advances that could have broader impact on the clinical trials ecosystem and potential for wider adoption in the field. These developments represent a crucial shift toward more harmonised, efficient, and equitable clinical research practices worldwide.

READINESS: NORMATIVE CLINICAL TRIAL GUIDELINES

Strong normative guidelines for clinical trials are essential for building sustainable research ecosystems that can serve both routine and emergency needs. Efficiently functioning clinical trial capacity for everyday health challenges creates the foundation that can be rapidly pivoted during health emergencies. By establishing clear frameworks for routine research excellence, these guidelines help ensure that when a crisis hits, the necessary infrastructure, expertise, and collaborative networks are already in place and can be quickly adapted rather than built from scratch. This adaptable approach, where research capacity serves both regular and emergency needs, is more sustainable and ultimately more effective than creating emergency-only systems. Major strides toward this goal were made in 2024, with several landmark guidelines and standards published that strengthen trial effectiveness, equity, and adaptability across the global ecosystem:

- **WHO Guidance:** WHO has released comprehensive new guidance on strengthening the global clinical trials ecosystem. Released in September 2024, this framework outlines essential principles for conducting informative trials, emphasising effective trial design, ethical conduct, and inclusion of diverse populations. The guidance places patient and community engagement at the centre of clinical research, from trial design through implementation. It provides practical recommendations for Member States, funders, and researchers to build sustainable national clinical trial capacity that enhances both routine research and emergency response capabilities.[130]

- **U.S. FDA Guidance:** The U.S. FDA published important guidance on conducting trials with decentralised elements, reflecting a growing trend in the use of remote technologies to enhance trial reach and efficiency. Additionally, the FDA released draft guidance on integrating randomised controlled trials (RCTs) into routine clinical practice, further embedding trial practices into day-to-day healthcare operations, and paving the way for smoother integration during pandemics.[131,132]

130 WHO, Guidance for best practices for clinical trials (2024), https://www.who.int/publications/i/item/9789240097711.
131 US FDA, Conducting Clinical Trials With Decentralized Elements (2024), https://www.fda.gov/regulatory-information/search-fda-guidance-documents/conducting-clinical-trials-decentralized-elements.
132 US FDA, Integrating Randomized Controlled Trials for Drug and Biological Products Into Routine Clinical Practice (2024), https://www.fda.gov/regulatory-information/search-fda-guidance-documents/integrating-randomized-controlled-trials-drug-and-biological-products-routine-clinical-practice.

- **African Clinical Trial Ecosystem:** Significant advances have been made in Africa, where the Africa CDC and AUDA-NEPAD are leading efforts to optimise the efficiency and impact of the continent's clinical trial ecosystem and continuing to refine and implement a ten-year execution roadmap.[133] Alongside this the African Vaccine Regulatory Forum (AVAREF) of WHO, as the African Medicines Regulatory Harmonisation (AMRH) technical committee on clinical trial oversight, supports the development of guidelines and joint review at the continental level.[134] Efforts are underway to support countries to domesticate the harmonised guidelines through regional economic communities (RECs).[135] Additionally the AUDA-NEPAD and AVAREF are supporting regulatory and ethics oversight harmonisation and strengthening the capacity of scientific reviewers on regulatory and ethics approval of clinical trials.

EMERGENCIES: RESPONDING TO GLOBAL HEALTH THREATS

While significant progress has been made towards strengthening routine trial capacity, the ability to rapidly adapt these systems during health emergencies remains a critical challenge. Clinical trials during outbreaks face unique pressures - from accelerated timelines to complex ethical considerations - yet structured guidance for these scenarios is still limited. Several key initiatives are working to address these gaps:

- **GloPID-R Living Roadmap:** Since its release in May 2023, 15 GloPID-R members have endorsed the Living Roadmap on Clinical Trial Coordination. This roadmap outlines a strategic approach for funders to support better preparation for coordination of trial networks during emergencies, including the rapid allocation of funds and the harmonisation of data sharing protocols. The roadmap provides a clear framework for aligning grant conditions and promoting an equitable research environment during outbreaks.[136]

- **Pandemic PACT Programme:** Launched in March 2024, the Pandemic Preparedness: Analytical Capacity and Funding Tracking (PACT) programme was designed to coordinate pandemic preparedness and response research investments, ensuring that resources are deployed efficiently during a health crisis. This programme aims to foster stronger collaborations between funders, researchers, and trial networks.[137]

- **University of Oxford pandemic computer simulations to guide future vaccine trials:** With up to $2.4 million funding from CEPI, in May 2024, researchers from University of Oxford are developing a simulation tool that compares vaccine clinical trial designs based on virus, disease, transmission, and outbreak-specific parameters known as 'PREpare using Simulated Trial Optimisation (PRESTO)'. This tool will help identify the most effective trial strategies during an emergency and ensure a rapid response to emerging health threats.[138]

While these recent initiatives represent important steps forward, their concentration in high-income institutions may perpetuate existing systemic vulnerabilities and uneven global research capacity.

INTERNATIONAL AND REGIONAL CLINICAL TRIAL NETWORKS

The development of robust clinical trial networks, with strong representation in geographically diverse regions, remains critical for pandemic preparedness. These networks must be sustainable during routine periods while maintaining the ability to pivot rapidly for emergency responses. Including diverse trial populations is essential, as MCMs must be proven safe and effective across different genetic backgrounds to serve all populations who will need them. Progress in 2024 has focused on building this dual capability, with emphasis on strengthening capacity in LMICs and fostering collaboration between international and regional partners. Key developments include:

- **ADVANCE-ID Network:** Supported by Wellcome, the ADVANCE-ID network with its hub in Singapore is progressing toward conducting registration-standard trials. The network is developing comprehensive capabilities including regulatory compliance, data management, and community engagement, preparing for its first phase 2 trial for a novel antimicrobial drug candidate in 2025. This trial, conducted across multiple sites in Asia, will enhance regional capacity to respond to outbreaks and will provide valuable insights into the capability of networks to pivot in outbreak scenarios.[139]

133 Africa CDC, Meeting Report: Optimizing Efficiency and Impact in the African Clinical Trials Ecosystem (2023), https://africacdc.org/download/meeting-report-optimizing-efficiency-and-impact-in-the-african-clinical-trials-ecosystem/.
134 AUDA-NEPAD, African Vaccine Regulatory Forum Technical Committee (AVAREF-TC), https://amrh.nepad.org/african-vaccine-regulatory-forum-technical-committee-avaref-tc.
135 AUDA-NEPAD, Regional Economic Communities, https://amrh.nepad.org/amrh-recs.
136 Glopid-R, Launch of a new tool for funders: Living Roadmap will support stronger coordination of clinical trial responses to epidemics and pandemics (2023), https://www.glopid-r.org/launch-of-a-new-tool-for-funders-living-roadmap-will-support-stronger-coordination-of-clinical-trial-responses-to-epidemics-and-pandemics/.
137 University of Oxford Nuffield Department of Medicine, New Pandemic PACT research programme launched (2024), https://www.ndm.ox.ac.uk/news/new-pandemic-pact-research-programme-launched.
138 CEPI, University of Oxford pandemic computer simulations to guide future vaccine trials (2024), https://cepi.net/university-oxford-pandemic-computer-simulations-guide-future-vaccine-trials.
139 Wellcome Trust, pro forma.

- **CEPI's East and Central Africa Network:** In March 2024, CEPI launched a $17 million funding call to establish a clinical preparedness network across East and Central Africa. This initiative aims to build sustainable clinical trial capacity in regions most vulnerable to emerging infectious diseases, ensuring these areas are better equipped to respond to future outbreaks. The regional networks and collaborations will incorporate local context, experience, and perspectives while fostering sustainable in-country research partnerships. This approach strengthens regional preparedness, with the goal of enabling the generation of high-quality clinical trial data during disease outbreaks in as little as 100 days.[140]

- **International Severe Acute Respiratory and Emerging Infection Consortium (ISARIC) 3.0:** Launch of phase 3 of ISARIC, a global federation of clinical research networks that aims to prevent illness and deaths from epidemic and pandemic threats. Supported by £16 million in funding from the Foreign and Commonwealth Development Office (FCDO), the Bill and Melinda Gates Foundation (BMGF), and Wellcome, ISARIC 3.0 will establish decentralised LMIC-led research hubs, develop innovative data tools, strengthen clinical research capacity, and conduct collaborative research on priority pathogens including Nipah, dengue, filoviruses, and respiratory infections. This comprehensive approach aims to build sustainable research infrastructure in regions most affected by emerging infectious diseases.[141]

- **The Clinical Trials Community Africa Network (CTCAN):** Launched in 2023 by Science for Africa Foundation and partners, with support from the European and Developing Countries Clinical Trials Partnership (EDCTP) programme, CTCAN establishes a coordinated network of clinical research stakeholders across Africa to sustainably expand clinical trial capacity. Achievements since its inception include a Network Implementation Plan, integrating with national regulatory authorities (Nigerian National Agency for Food and Drug Administration and Control (NAFDAC) and Tanzania Medicines & Medical Devices Authority (TMDA)), and a clinical trial preparedness framework. In 2024, CTCAN held a joint meeting with EDCTP in Nairobi to advance grant management and science communication. The network connects 47 institutions across Africa, and through its Clinical Trials Community platform, CTCAN strengthens regulatory harmonisation, clinical trial preparedness, and knowledge sharing to enable Africa to conduct high-quality clinical trials for diverse populations.[142,143]

- **STRIVE Network:** Operating across 190 sites spanning North America, South America, Europe, Africa, Asia, and Australia, STRIVE is evaluating both licensed and unlicensed treatments for respiratory infections through a master protocol approach. The network is currently conducting a phase 3 trial of the antiviral S-217622 (ensitrelvir) for hospitalised COVID-19 patients, with the master protocol designed to expand to include other respiratory viruses including influenza. This adaptive platform approach strengthens global capacity for both routine and emergency clinical research.[144]

- **ACTIV Network:** The Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV) partnership, coordinated by the U.S. Foundation for the National Institutes of Health, unites NIH, CDC, U.S. FDA, BARDA, DOD, EMA, Department of Veteran Affairs, academia, and industry to accelerate the development of COVID-19 treatments and vaccines through a coordinated research strategy. Partners published a review of key lessons from ACTIV trials which highlights the importance of engaging stakeholders early in trial development, maintaining flexible trial designs, ensuring representative trial populations, leveraging pre-established clinical networks, and using extensive outreach to facilitate timely enrolment, particularly in emergency settings.[145]

140 CEPI, CT & Reg pro forma.
141 ISARIC, Preventing illness and deaths from infectious disease outbreaks through investigator-led clinical research networks., https://isaric.org/.
142 Science for Africa Foundation, Network for Africa's clinical trials community established (2023), https://scienceforafrica.foundation/media-center/network-africas-clinical-trials-community-established.
143 Clinical Trials Community Africa Network (CTCAN), CTCAN 2024 Newsletter (2024), https://www.ctcan.africa/post/ctcan-2024-newsletter.
144 National Institute of Allergy and Infectious Diseases, Strategies and Treatments for Respiratory Infections and Viral Emergencies (STRIVE), https://www.niaid.nih.gov/clinical-trials/strategies-treatments-respiratory-infections-viral-emergencies.
145 Ruxandra Draghia-Akli, Sarah W. Read, and Eric A. Hughes, "Overview of ACTIV trial-specific lessons learned," Journal of Clinical and Translational Science 8, no. 1 (2024), e149, https://doi.org/10.1017/cts.2023.698, https://www.cambridge.org/core/product/D16E76B39F86B95C446438885E489714.

STRENGTHENING GLOBAL REGULATORY CAPACITY

Regulatory harmonisation and capacity building have gained momentum in 2024, with notable progress across Africa, Latin America, and Asia Pacific regions. These regional initiatives are creating more efficient pathways for product development and approval, while building the expertise needed to make informed decisions during health emergencies. Strengthening regulatory capacity in multiple regions simultaneously is critical to ensure that future pandemic products can be approved and distributed more equitably and rapidly. Key developments include:

- **African Medicines Agency:** Africa has made great strides in regulatory harmonisation through the operationalisation of the African Medicines Agency (AMA), and 29 countries have now ratified the treaty.[146] This progress has been bolstered by a $12.3 million grant from Wellcome to support regulatory strengthening, harmonisation, and operationalisation of the AMA.[147] Through the AMRH, AUDA-NEPAD is advancing efforts to streamline regulatory approvals across the continent, ensuring faster access to critical medicines during emergencies, as demonstrated by their August 2024 expedited evaluation process for mpox vaccines and treatments, which offers a rapid screening within 10 days, followed by either a 15-day reliance pathway or 45-day full assessment route.[148] Continental harmonised guidelines, processes and templates for evaluating applications for registration of medicinal products have been adopted and pilot joint assessments and listing is underway. The continental technical committee on Evaluation of Medicinal Products (EMP) has also adopted an Emergency Use Listing (EUL) Procedure which will support countries in strengthening their capacity to respond to emergencies.[149]

- **CEPI's Regulatory Innovation Consortium:** Established in January 2024, CEPI's Regulatory Innovation Consortium focuses on sharing best practices and innovations in regulatory science, including for platform technologies. This consortium brings together industry members, researchers, funders, and regulators to increase collaboration and convergence to improve regulatory processes during health emergencies.[150]

- **Ghana FDA:** Ghana continues to demonstrate regulatory leadership as a WHO Maturity Level 3 National Regulatory Authority with a WHO-Prequalified Quality Control Laboratory status and an AMRH Regional Centre of Regulatory Excellence on registration and evaluation, and clinical trial oversight. In 2024, Ghana continued to provide technical assistance to neighbouring African nations, empowering them to achieve comparable standards, building on achievements like their 2023 regulatory assessment of the R21/Matrix-M malaria vaccine which supported subsequent approval by Nigeria's NAFDAC.[151] This initiative supports a unified continental regulatory environment, promoting regulatory convergence, facilitating expedited approval, access and deployment of vaccines and therapies, ultimately strengthening Africa's healthcare landscape and enhancing the wellbeing of its citizens.[152]

- At the global level, the **International Conference of Drug Regulatory Authorities (ICDRA)** has been instrumental in advancing discussions around regulatory harmonisation. A key component of the ICDRA meeting is the 'pre-ICDRA' session which includes industry participation and allows for engagement with NRAs to move forward on regulatory convergence, reliance and systems strengthening. The main outcomes from the ICDRA 2024 meeting include calls for more aligned global standards in trial design, and preparatory regulatory approaches to streamline approvals during health crises.[153]

- **Correlates of Protection Framework:** CEPI and Wellcome are collaborating with other partners and regulators to establish a common framework for using immune markers to predict vaccine efficacy, aiming to reduce reliance on extensive phase 3 efficacy studies during outbreaks with high case fatality rates. Their joint initiative focuses on addressing gaps in data collection and analysis of these markers, supporting more efficient regulatory pathways for vaccine approval during emergencies.[154,155]

- Significant advancements were made in regulatory pathways with the **refinement of the WHO's Global Benchmarking Tool plus medical devices**, emphasising structured indicators for national regulatory systems. This progress shows the importance of robust legal frameworks and multi-stakeholder engagement required to ensure the quality, safety, and efficacy of medical products.[156]

146 AUDA-NEPAD, African Medicines Agency (AMA), https://amrh.nepad.org/african-medicines-agency-ama.
147 AUDA-NEPAD, Wellcome Commits US $12.3 Million to Support Regulatory Harmonisation and the Operationalisation of the African Medicines Agency (AMA) (2024), https://www.nepad.org/news/wellcome-commits-us-123-million-support-regulatory-harmonisation-and-operationalisation.
148 Africa CDC, Invitation of Expression of Interest to Manufacturers/Developers of mpox diagnotsic tests to a continental faciliated joint review and emergency use listing (2024), https://africacdc.org/opportunity/invitation-of-expression-of-interest-to-manufacturers-developers-of-mpox-diagnotsic-tests-to-a-continental-faciliated-joint-review-and-emergency-use-listing/.
149 EMA, EMA supports pilot for joint African continental assessment procedures (2024), https://www.ema.europa.eu/en/news/ema-supports-pilot-joint-african-continental-assessment-procedures.
150 CEPI, CT & Reg pro forma.
151 Health Policy Watch, Africa to Manufacture New Malaria Vaccine? (2023), https://healthpolicy-watch.news/africa-to-manufacture-new-malaria-vaccine/.
152 Ghana FDA, pro forma.
153 ICDRA, The International Conference of Drug Regulatory Authorities, https://icdra2024.in/ICDRA/Homepage.
154 CEPI, CT & Reg pro forma.
155 Deborah F. King et al., "Realising the potential of correlates of protection for vaccine development, licensure and use: short summary," npj Vaccines 9, no. 1 (2024/04/29 2024), https://doi.org/10.1038/s41541-024-00872-6, https://doi.org/10.1038/s41541-024-00872-6.
156 WHO, WHO Global Benchmarking Tool plus Medical Devices (GBT+ Medical Devices) for Evaluation of National Regulatatory System of Medical Products (2024), https://cdn.who.int/media/docs/default-source/medicines/regulatory-systems/gbt-medical-devices/gbt-md_rev_vi-md_ver_2-3.pdf?sfvrsn=ab243243_3&download=true.

Spotlight 6: African Medicines Regulatory Harmonisation

The AUDA-NEPAD's AMRH initiative is working to drive regulatory coordination across Africa, which has the largest number of countries of any continent in the world. Over the past year, AMRH has carried out significant projects alongside progressing work towards the operationalisation of the AMA, which aims to recruit its Director General by February 2025.[157]

As the AMRH transitions into the AMA, approvals of medicines are underway. A pilot of the continental procedure for the assessment and listing of medicinal products has begun, funded by the BMGF, EMA, European Commission, CEPI, and Wellcome. Manufacturers submitted 64 expressions of interest for product registration, with 24 dossiers now under active review. As the work progresses, the role of the AMA will be to prioritise medicines for diseases affecting the continent, medicines for emergencies, products manufactured in Africa and products that require expertise that may not be available in all countries.

The COVID-19 pandemic provided crucial learnings for the continent, highlighting both the necessity for rapid emergency medicine approvals and the absence of appropriate legal frameworks in many countries to support continental-level approvals. To support countries with their legal frameworks for harmonisation, AMRH has presented an updated African Union Model Law on Medical Products Regulation. This framework includes clauses that will enable National Regulatory Authorities reliance on AMA and Regional Economic Communities recommendations, facilitate emergency use authorisation, and strengthen efforts to combat Substandard and Falsified Medicines. Currently, 18 African Union (AU) member states have adopted the AU Model Law with an additional seven currently being supported by AMRH to review their national laws. The work of the AMRH is to ensure that when emergencies strike, medicines can be assessed swiftly, without compromising on quality and safety. Alongside medicines, there is also a focus on improving regulation for medical devices and in vitro diagnostics through the African Medical Devices Forum (AMDF). This forum has directly supported Africa CDC's mpox diagnostics procurement. The AMDF has established five continental guidelines for medical device regulation and is training countries to implement these guidelines within their National Regulatory Authorities.

The AMRH is maintaining the transparency of this process to build knowledge among manufacturers and countries. A clear set of standards will be defined for manufacturers to follow. Furthermore, once recommendations are made, these will be published to allow countries to make use of the technical output. Digitalisation of regulatory systems at the continental/AMA, regional, and national level will be supported by the Information Management Systems (IMS) technical committee, with four platforms now operational to enhance regulation, harmonisation and digitalisation across the continent while maintaining accountability. Tracking mechanisms for approvals are also being put in place to ensure efficient decision-making timelines.

Driving harmonisation across such a large and diverse continent is a challenging task. The AMRH has mobilised smaller harmonisation projects within the continent based on RECs to move towards continent-wide alignment. Individual countries outside of these RECs are being brought in through a framework which aims to formalise ongoing informal reliance relationships between countries. Increased adoption of the AMRH framework by countries is crucial in advancing continental regulatory processes.

Significant progress has been made by the AMRH over the past year.[158] Some of this work has been supported by the EMA where learnings will be shared between the two organisations. While the EMA is already looking to take stock of the learnings from this process, other regions can look to Africa as a model for achieving harmonisation across a large, diverse territory while maintaining accountability and establishing robust procedures for continent-wide approvals of medicines during emergencies.

157 AUDA-NEPAD, African Medicines Regulatory Harmonization Initiative (AMRH) and the Operationalization of the African Medicines Agency (AMA) Highlights and Achievements December 2024 (2024).
158 AUDA-NEPAD, African Medicines Regulatory Harmonization Initiative (AMRH) and the Operationalization of the African Medicines Agency (AMA) Highlights and Achievements December 2024.

SUMMARY PLANS FOR 2025

To work towards the overarching goals of having sustained clinical trial capacity between outbreaks and pre-agreed regulatory pathways in all regions, the following actions should be prioritised in 2025 and IPPS will work with all partners to support their implementation (see Annex A for Planned Partner Commitments and Priority Actions):

- **Fostering Greater Network Convergence and Integration,** bringing together international and regional trial networks to develop disease-agnostic, multi-functional trial sites capable of adapting to various study types and phases. This will help ensure that trials are conducted in populations most affected by emerging diseases, enhancing both the speed and relevance of research outcomes.

- **Developing Clear Guidelines for Emergency Trials,** establishing structured protocols and coordination mechanisms for clinical trials in emergency settings, including specific procedures for rapidly transitioning from standard to emergency trial operations. Collaboration between pharmaceutical companies, regulators, trial networks, and independent ethics committees is essential to streamline trial processes during pandemics.

- **Adopting Preparatory Regulatory Approaches,** encouraging adoption of innovations such as platform technology master files, harmonised cloud-based data sharing systems, and shared risk-benefit frameworks. This could include regulatory systems strengthening and joint clinical trials monitoring as well as a robust continent-wide post-authorisation safety studies. These approaches will streamline the approval of new MCMs, reducing the time needed to bring critical countermeasures to market during an emergency.

- **Promoting Regulatory Harmonisation,** fostering collaboration between regulatory bodies to share best practices and align approaches. Efforts to harmonise regulatory processes across regions will continue, particularly in Africa and Latin America, where the AMA and other regional bodies are working to align approval processes. This includes developing clear processes for joint regulatory reviews, with defined expedited timelines for decision making and approval to ensure that new MCMs can be approved rapidly in future health emergencies.

- **Advancing Global Regulatory Equity and Inter-regional Recognition**, strengthening inter-regional collaboration and twinning initiatives to support more countries in achieving Maturity Level 3 regulatory status, while encouraging greater parity in the recognition of regional regulatory approvals. This includes exploring ways procurement agencies and donors can recognise diverse regulatory pathways alongside established mechanisms, creating additional market signals for regional production. By supporting the recognition of approvals from different regions that meet rigorous standards, this approach would help cultivate a more equitable global regulatory ecosystem and fosters the sustainable development of regional manufacturing capacities.

4

Enablers

Strengthening Global Surveillance Systems

Disease surveillance is the entry point to launching the 100DM, without which an outbreak cannot be detected. The 2024 report by the Global Preparedness Monitoring Board (GPMB) highlighted the increased pandemic risk associated with increased global movement, and agricultural practices and farming, which underscores the need for integrated disease surveillance through a One Health approach across human, environmental, and animal health.[159] However, bridging the gap between surveillance systems and the diagnostics development ecosystem, and establishing trusted international data and pathogen sharing mechanisms remain critical challenges to address.

The WHO Hub for Pandemic and Epidemic Intelligence continues to lead coordination efforts in this area with a focus on implementation of collaborative surveillance. In 2024, the WHO Pandemic Hub published a technical brief to identify the key research areas that would generate high-quality evidence and methods to better inform decision making in global health emergencies, outlining the priorities for research in pandemic and epidemic intelligence.[160]

PROGRESS IN 2024

In 2024, significant progress was made in enhancing genomic surveillance, particularly in LMICs, and developing innovative surveillance tools and open-source platforms:

- **Africa CDC Pathogen Genomics Initiative (PGI) 2.0:**
  - Strengthened molecular diagnostics, genomics, and bioinformatics capacities in Africa.
  - Launched the Integrated Genomic Surveillance (IGS) and Data Sharing Platform (DETECT), co-funded by the European Union, to enhance outbreak detection, AMR surveillance, and data sharing across member states.[161]
- **Funding for genomics initiatives:**
  - The International Pathogen Surveillance Network (IPSN) launched a catalytic grant fund supported by the Bill & Melinda Gates Foundation, The Rockefeller Foundation, and Wellcome, to scale pathogen genomic surveillance in LMICs and explore new applications such as wastewater surveillance, through grants for ten projects.[162]
- **Innovations in Surveillance Tools:**
  - European Health Emergency Response Authority (HERA) and European Commission Joint Research Centre: Launched GLOWACON, a global consortium focused on wastewater and environmental surveillance, aiming to establish a sentinel system for early detection of epidemic threats.[163] Wastewater surveillance is also being used in the U.S. to monitor zoonotic diseases like H5N1 avian influenza, particularly in areas where the virus has spread to mammalian populations, such as cattle.[164]
  - Epiverse (Data.org): Developed interoperable open-source tools for pandemic preparedness, with a focus on training for global use.[165]
  - Airfinity: Developed predictive models for disease forecasting, including a meteorological model for dengue, providing a potential early warning system for future epidemics.[166]

PRIORITIES FOR 2025

See Annex A for Planned Partner Commitments and Priority Actions:

- Implement **Collaborative Surveillance:** Strengthen data and pathogen sharing mechanisms to support DTV research and development. This should integrate into early outbreak detection systems and rapid response frameworks.
- Adopt a **One Health Approach:** Address the interconnectedness of climate change, agriculture, and emerging infectious diseases.
- **Support Capacity Building in LMICs:** Enhance competencies in pathogen genomic surveillance, bioinformatics, and real-time monitoring to detect outbreaks earlier and more effectively.

159 GPMB, The Changing Face of Pandemic Risk: 2024 Report.
160 WHO, Research prioritization for pandemic and epidemic intelligence: technical brief (2024), https://www.who.int/publications/i/item/9789240094529.
161 Africa CDC, Africa CDC launches initiatives to advance molecular diagnostics and genomic surveillance in Africa (2024), https://africacdc.org/news-item/africa-cdc-launches-initiatives-to-advance-molecular-diagnostics-and-genomic-surveillance-in-africa/.
162 WHO, International Pathogen Surveillance Network launches catalytic grant fund for pathogen genomics (2024), https://www.who.int/news/item/23-02-2024-international-pathogen-surveillance-network-launches-catalytic-grant-fund-for-pathogen-genomics.
163 HERA, 2024 HERA Work Plan, https://health.ec.europa.eu/system/files/2023-12/hera_c_2023_8828_annex_en.pdf.
164 Scientific American, New Bird Flu Spread Patterns Are Revealed in Wastewater (2024), https://www.scientificamerican.com/article/what-bird-flu-in-wastewater-means-for-california-and-beyond/.
165 data.org, pro forma.
166 Airfinity, Biorisk, https://www.airfinity.com/products/airfinity-biorisk.

Sustainable Manufacturing of Diagnostics, Therapeutics, and Vaccines

The 100DM envisions a global health system that can respond swiftly to emerging threats by ensuring sustainable manufacturing capacity for DTVs. A key pillar of this effort is developing flexible and scalable manufacturing systems that can meet routine health needs during interpandemic periods while also being able to rapidly scale up production in times of crisis. To achieve this, regional manufacturing efforts have been prioritised to secure supply chains, reduce reliance on global bottlenecks, and promote equitable access to MCMs.

The Regionalised Vaccine Manufacturing Collaborative (RVMC) plays a critical role in driving these initiatives to support establishing regional production capacity that balances routine and outbreak response needs. In 2024, RVMC published a framework and a strategy outlining their three-year plan for advocating for regionalised manufacturing, aligning regional and global efforts, and offering independent expertise to advance sustainable growth of manufacturing networks globally.[167] RVMC supports existing regional leadership and aims to foster inter-regional collaboration including with Africa CDC, the Platform for Harmonized African Health Products Manufacturing (PHAHM), Pan American Health Organization (PAHO), Association of Southeast Asian Nations (ASEAN) Vaccine Self-Sufficiency and Reliance (AVSSR) initiatives.[168] The DCVMN also continues to support partners to accelerate sustainable regional vaccine manufacturing to advance vaccine candidates for regional priorities.

PROGRESS IN 2024

In 2024, significant progress was made in expanding regional manufacturing capacity, focusing primarily on vaccines while highlighting critical gaps in regional therapeutics and diagnostics production to ensure equitable access to these products:

Africa:

- Africa CDC continues to work towards a target of 60% of local vaccine production by 2040. The AU Member States have agreed to establish a continental pooled procurement mechanism for health products made by African manufacturers.[169]
- Gavi launched the AVMA, committing $1.2 billion over ten years to accelerate the expansion of commercially viable vaccine manufacturing in Africa by offsetting initial costs of process development and production.[170]
- CEPI partnered with BioNTech, funding up to $145 million to establish end-to-end mRNA vaccine R&D and manufacturing capabilities in Kigali, Rwanda, using COVID-19 mRNA vaccine as a blueprint vaccine for initial technology transfer.[171]

Latin America:

- PAHO member states agreed to a resolution to reform the Regional Revolving Funds to encourage local production and innovation projects.[172]
- CEPI partnered with Fiocruz, investing $17.9 million to expand mRNA and viral vector vaccine manufacturing capabilities in Latin America, including support for the region's largest vaccine production centre at the Santa Cruz Campus.[173]
- CEPI and the European Union partnered with Valneva to support broader access to the first licensed Chikungunya vaccine, supporting technology transfer to Instituto Butantan for LMIC market access, funding late-stage studies to support future regulatory approval in Brazil, and securing access to an emergency stockpile.[174]

Asia:

- CEPI partnered with Serum Institute of India, investing up to $30 million to expand their rapid response capabilities as the world's largest vaccine manufacturer.[175]
- Also supported via CEPI's Vaccine Manufacturing Facility Network program, Bio Farma joined the UKVN supported UK-SEA Vax Hub, which is advancing mRNA vaccine technologies in the region.[176]

167 Regionalized Vaccine Manufacturing Collaborative, A Framework for Enhancing Vaccine Access Through Regionalized Manufacturing Ecosystems (2024), https://static.rvmc.net/downloads/2024-07/Regionalized_Vaccine_Manufacturing_Collaborative_2024.pdf
168 Regionalized Vaccine Manufacturing Collaborative, Strategy 2024-2027 (2024), https://static.rvmc.net/downloads/2024-07/RVMC_Strategy_2024-27_290724.pdf.
169 Africa CDC, Africa CDC Spearheads Bold Move to Secure Africa's Health Future by Creating a 50 billion Dollar Medical Market (2024), https://africacdc.org/news-item/africa-cdc-spearheads-bold-move-to-secure-africas-health-future-by-creating-a-50-billion-dollar-medical-market/.
170 Gavi, African Vaccine Manufacturing Accelerator (AVMA) (2024), https://www.gavi.org/programmes-impact/types-support/regional-manufacturing-strategy/avma.
171 CEPI, BioNTech and CEPI expand partnership to strengthen Africa's mRNA vaccine ecosystem, https://cepi.net/biontech-and-cepi-expand-partnership-strengthen-africas-mrna-vaccine-ecosystem.
172 PAHO, CD61/16 - Informe sobre el cargo aplicable para la compra de insumos de salud pública para los Estados Miembros (2024), https://www.paho.org/es/documentos/cd6116-informe-sobre-cargo-aplicable-para-compra-insumos-salud-publica-para-estados.
173 Fiocruz, Fiocruz joins global network of vaccine manufacturers and strengthens the potential of the Global South (2024), https://portal.fiocruz.br/en/news/2024/07/fiocruz-joins-global-network-vaccine-manufacturers-and-strengthens-potential-global.
174 CEPI, CEPI expands partnership with Valneva with $41.3 million to support broader access to world's first Chikungunya vaccine.
175 CEPI, Serum Institute of India joins CEPI global network to boost production of affordable outbreak vaccines (2024), https://cepi.net/serum-institute-india-joins-cepi-global-network-boost-production-affordable-outbreak-vaccines.
176 UKSEA Vax Hub, Our partners in South East Asia, https://ukseavaxhub.org/our-partners/.

Cross-Regional Initiatives:

- Brazil's G20 Presidency proposed creation of the G20 Coalition on Local and Regional Production, Innovation, and Equitable Access.[177]
- WHO and MPP's mRNA Technology Transfer Programme advanced consortia development across South-East Asia, Latin America, and Africa. The initiative aims to establish 11 GMP-certified mRNA manufacturing facilities across 10 countries by 2030. Afrigen Biologics progressed platform validation and implemented technology transfer activities across 15 countries, several of which have partnered with Univercells and Quantoom Biosciences to install modular RNA manufacturing systems.[178,179]
- UKVN funded £33 million for collaborative manufacturing innovation research hubs managed by Engineering and Physical Sciences Research Council (EPSRC), partnering with LMIC organisations across Africa, Asia, and Latin America to address vaccine delivery and manufacturing challenges.[180]
- PATH continues to partner with LMIC vaccine manufacturers, including DCVMN partners, to provide technical assistance and support in achieving WHO prequalification requirements, including for key components for vaccine delivery such as auto-disable syringes.[181]
- Through the Pasteur Network, Fiocruz, Institut Pasteur Dakar, the Institut Pasteur Korea, the Institut Pasteur (Paris), and the Institut Pasteur Tunis signed a Memorandum of Understanding (MoU) for vaccine R&D and capacity building for regional manufacturing, an important initiative involving both North-South and South-South collaboration.[182]
- PAHO and Africa CDC agreed to collaborate on equitable access to vaccines, medicines, and health technologies by strengthening regional regulatory, innovation, and production systems. This partnership supports the African pooled procurement mechanism and promotes local manufacturing for Africa and the Americas.[183]

PRIORITIES FOR 2025

See Annex A for Planned Partner Commitments and Priority Actions:

- Implement **regional coordination:** Establish harmonised approaches and pooled procurement to **provide predictable demand and sustainability** across regions. For endemic diseases, maintain production of clinical trial materials or a portfolio of products, including both infectious and non-communicable diseases, to keep facilities operational in interpandemic periods. For epidemic diseases, integrate flexible manufacturing processes to rapidly respond to sudden shifts in demand.
- Strengthen **operational resilience:** Support multi-purpose production platforms that can maintain routine manufacturing while enabling rapid pandemic response.
- Enhance **technology transfer:** Move beyond fill-and-finish to enable comprehensive drug substance manufacturing capabilities in LMICs.
- Build **supply chain security:** Implement digital monitoring systems and diversify raw material sources to strengthen input supply chain and logistics resilience.
- Secure **government support:** Incentivise and sustain regional manufacturing through procurement preferences, tax policies, and reduced trade barriers where applicable.

177 G20, Sherpa Track Health, https://www.g20.org/en/tracks/sherpa-track/health.
178 Medicines Patent Pool, From Vision to Reality: mRNA Technology Transfer Programme Building Sustainable Vaccine Manufacturing Ecosystems in LMICs (2024), https://medicinespatentpool.org/news-publications-post/from-vision-to-reality-mrna-technology-transfer-programme-building-sustainable-vaccine-manufacturing-ecosystems-in-lmics.
179 Quantoom Biosciences, Quantoom Biosciences' Ntensify™ midi System Adopted by Bio-Manguinhos/Fiocruz Laboratory for Future Groundbreaking mRNA Vaccine Production in Latin America (2024), https://quantoom.com/quantoom-biosciences-ntensify-midi-system-adopted-by-bio-manguinhos-fiocruz-laboratory-for-future-groundbreaking-mrna-vaccine-production-in-latin-america/.
180 HMG, pro forma.
181 PATH, pro forma.
182 Fiocruz, Pasteur Network members unite efforts to accelerate mRNA vaccine research (2024), https://portal.fiocruz.br/en/news/2024/10/pasteur-network-members-unite-efforts-accelerate-mrna-vaccine-research.
183 PAHO, PAHO and Africa CDC strengthen collaboration to address access to essential medicines and vaccines (2024), https://www.paho.org/en/news/20-9-2024-paho-and-africa-cdc-strengthen-collaboration-address-access-essential-medicines-and.

FINANCING, GOVERNANCE, AND MULTILATERAL ENABLERS OF THE 100DM

Pandemic financing and equitable procurement supported by rigorous global health governance form essential foundations of effective pandemic preparedness and response. The GPMB 2024 report highlights trust as one of the key pandemic risk drivers most likely to influence both the emergence and amplification of new outbreaks and epidemics, while significantly impacting response capabilities. There has been a significant decline in trust in governments, public health organisations and the multilateral system since the COVID-19 pandemic. To rebuild this trust, governments must work closely with communities to understand and address fundamental issues of inequity, vulnerability, and risk. Meaningful community engagement, coupled with ensuring timely and equitable access to MCMs, offers a pathway to restore confidence in governance bodies.

Core actions needed to secure funding for preparedness R&D that will enable rapid, scalable responses and broaden access:

- Establish **mechanisms that enable immediate access to pandemic response funding** to promote equitable access to DTVs. (The automatic release of funding should be tied to globally agreed trigger points, whether that be a PHEIC or clear pre-PHEIC milestones)
- Support LMICs in purchasing and distributing DTVs through **equitable allocation and procurement of supplies,** including eliminating trade barriers where applicable.

FINANCING AND GOVERNANCE PROGRESS IN 2024:

Pandemic Response Financing Mechanisms

- **G20 Joint Finance and Health Task Force** (JFHTF) developed a multi-year work plan with a focus on Pandemic Preparedness, Prevention and Response (PPPR) and continues to serve as a platform for enhanced collaboration between the finance and health sectors. It facilitates partnerships between key institutions like WHO and the World Bank. Key deliverables under the G20 Brazil Presidency in 2024 include a policy paper on Debt-for-Health swaps building on the International Financial Architecture (IFA) Working Group discussion on debt for development swaps, a global report on the Framework for Health, Social, and Economic Vulnerabilities and Risks (FEVR) related to pandemics, and an Operational Playbook for Pandemic Response Financing.[184,185] In collaboration with the World Bank and WHO, JFHTF had additional deliverables in response to the mpox outbreak, including a Global mpox Response Financing Tracker to monitor contributions against the pillars of the mpox Continental Preparedness and Response Plan for Africa (see Chapter 5: Mpox case study).[186]

- **G7 Development Financing Institutions (DFIs), MedAccess, the European Investment Bank (EIB), and the International Finance Corporation (IFC)'s Surge Financing Initiative for MCMs:** In September 2024, G7 DFIs, the EIB, and the IFC announced the signing of a memorandum of understanding for the Surge Financing Initiative to focus on the procurement, production, and distribution of DTVs and other MCMs for low-income countries (LICs) and LMICs. This was in accordance with the 2023 G7 Hiroshima Vision for Equitable Access to MCMs which was reaffirmed at the 2024 G7 Apulia Summit.[187]

- **The First Response Fund and Rapid Financing Facility form part of Gavi's Day Zero Pandemic Financing Facility (DZF),** which enables up to $2.5 billion in risk-tolerant, surge, and contingent capital to be quickly mobilised, permitting Gavi to meet urgent demand for vaccines in a PHEIC or other global health emergency.[188]

- **Gavi's First Response Fund (FRF):** In June 2024, Gavi's Board approved the launch of the FRF, a $500 million pool of pre-positioned at-risk capital that can be rapidly deployed when needed. The FRF aims to secure immediate access to vaccines and to protect routine immunisation programmes during major public health emergencies, ensuring lower income countries get earlier access to vaccines in the next pandemic.[189] In September 2024, Gavi was able to draw down from the FRF to secure 500,000 doses of MVA-BN mpox vaccine, as well as to offer $10 million in additional delivery funding to countries receiving donated doses.[190]

- **The U.S. Development Finance Corporation's (DFC's) Rapid Financing Facility with Gavi:** This $1 billion frontloading facility between DFC and Gavi was expanded in 2024, enabling Gavi to access surge financing backed by donor pledges for emergencies beyond COVID-19, as well as for routine immunisation programmes. By enabling liquidity on the basis solely of a public pledge, this facility complements existing pandemic response tools such as the International Finance Facility for Immunisation (IFFIm) and Gavi's liquidity facilities with the European Investment Bank.[191]

- **The Pandemic Fund** initiated funding rounds targeting laboratory capacity, health workforce, and surveillance systems, while also providing accelerated funding for mpox response.[192]

- **Preparedness and Surge Financing Modelling:** WHO, G20 JFHTF and CEPI have undertaken complementary modelling efforts to present the health and economic benefits of investing in preparedness. CEPI launched cost-impact analyses to help policymakers understand the costs, benefits, and trade-offs of different preparedness investments. Initial findings show significant returns on vaccine investments for PPR, and the importance of combining both preparatory investments and surge financing to accelerate pathogen-specific vaccine R&D and at-scale manufacturing.[193] UN Foundation, GPMB and others are also developing pandemic risk models.

184 G20 JFHTF, pro forma.
185 G20, The final document of the G20 Finance and Health ministerial meeting highlights fighting inequalities and preparing for future pandemics (2024), https://www.g20.org/en/news/the-final-document-of-the-g20-finance-and-health-ministerial-meeting-highlights-fighting-inequalities-and-preparing-for-future-pandemics.
186 G20, G20 Brazil Presidency Press Statement on G20 Joint Finance and Health Ministers' Statement on Mpox Response (2024), https://www.g20.org/en/news/g20-brazil-presidency-press-statement-on-g20-joint-finance-and-health-ministers-statement-on-mpox-response.
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188 Gavi, How day zero financing could help protect the world during the next pandemic (2024), https://www.gavi.org/vaccineswork/how-day-zero-financing-could-help-protect-world-during-next-pandemic.
189 Gavi, How day zero financing could help protect the world during the next pandemic.
190 Ann Danaiya Usher, "Mpox puts Gavi's new pandemic fund to the test," The Lancet 404, no. 10455 (2024), https://doi.org/10.1016/S0140-6736(24)01775-6, https://doi.org/10.1016/S0140-6736(24)01775-6.
191 U.S. DFC, DFC Announces More Than $1.8 Billion in Investments and New Initiatives at U.N. General Assembly (2024), https://www.dfc.gov/media/press-releases/dfc-announces-more-18-billion-investments-and-new-initiatives-un-general.
192 The Pandemic Fund, Pandemic Fund Allocates Second Round of Grants to Boost Pandemic Preparedness in 50 Countries (2024), https://www.thepandemicfund.org/news/press-release/pandemic-fund-allocates-second-round-grants-boost-pandemic-preparedness-50-countries.
193 Barnsley et al., "Impact of the 100 days mission for vaccines on COVID-19: a mathematical modelling study."

Equitable allocation and procurement of supplies

- **African Vaccine Manufacturing Accelerator (AVMA):** AVMA is a strategic financial instrument designed by Gavi in close partnership with Africa CDC that commits up to $1.2 billion over the next decade to strengthen Africa's vaccine manufacturing capacity. It aims to address historical inequities in procurement from geo-diverse manufacturers, support global health vaccine markets, and strengthen Africa's response to outbreaks and pandemics – providing direct benefits to the African continent while also boosting global health security, sovereignty and economic resilience.[194] It is already demonstrating the desired incentive effect, with a number of tech transfer deals between manufacturers for the African continent announced since June.

Coordination of R&D Investments

- **GloPID-R,** a coalition of research funders in pandemic preparedness and response, has launched the Pandemic PACT tool that aims to facilitate coordination amongst public and philanthropic funders.[195] GloPID-R launched a new coordinated funding mechanism, Global Research Improving Pandemic Preparedness (GRIPP), to allow member funders to jointly fund PPR research projects to align resources and prevent duplication. The first GRIPP call, focused on strengthening the clinical research ecosystem in LMICs to improve clinical trial good practices aligned with WHO guidance and GloPID-R Roadmap for Clinical Trial Coordination, will be launched in 2025.

- **MCM R&D Funders Roundtable**, convened by CEPI and the South Africa Medical Research Council (SAMRC) in May 2024 and in December 2024 in collaboration with GloPID-R alongside their assembly, to promote strategic collaboration and discuss how funders can more effectively share information to find synergies.

Multilateral coordination on MCMs and access

- **The WHO-led i-MCM-Net** unites international and regional partners across sectors, including CSOs, facilitating end-to-end coordination on MCMs.[196] This collaboration was demonstrated through the establishment of an mpox access and allocation mechanism during the August 2024 PHEIC (see Chapter 5: Mpox case study).

- **The "XVax Network"** - comprising CEPI, Gavi, UNICEF, WHO and regional organisations - meets regularly to coordinate vaccine preparedness and response for future epidemics and pandemics. The network has established operational frameworks covering triggers, mobilisation stages, governance, information sharing, and risk management, while working to integrate with i-MCM-Net.[197]

- **G20 Coalition on Local and Regional Production, Innovation, and Equitable Access** established at the G20 Health Ministers' Meeting in October 2024. It will strengthen manufacturing capacities for local and regional health products, promote sustainable global production and innovation networks to facilitate better access to DTVs for neglected disease and persons in vulnerable situations, which also could be repurposed for other diseases and health emergencies. The Coalition centres on voluntary cooperation while fostering collaboration and avoiding duplication with multilateral and other relevant initiatives.[198]

Governance

- **International Health Regulations (IHR) and Pandemic Agreement:** The most notable areas of governance progress in 2024 have been passage of the amended IHRs and advancement of the Intergovernmental Negotiating Body (INB)/Pandemic Agreement process, both of which support the 100DM aim of having agreed pre-negotiated pandemic protocols. However, global R&D collaborative mechanisms in support of equitable access remain challenging. This is particularly the case in Pathogen Access and Benefit Sharing (PABS) negotiations within the Pandemic Agreement/INB process, now extended to May 2025. Pandemic Action Network (PAN) has been working with CSOs to stress the critical role of an international agreement to define the rules of the road for coordinated action during pandemic threats and has been advocating to keep governments at the negotiation table.[199]

- **The Lusaka Agenda,** launched in December 2023, aims to establish a coordinated Global Health Initiatives ecosystem, with stronger alignment of an end-to-end approach to R&D, manufacturing, and market shaping.[200] Multisectoral partners have been working together at national, regional, and global levels leading to the establishment of the joint committee working group. Furthermore, the Lusaka Agenda Secretariat, housed at Africa CDC, will work with partners to develop the Lusaka Agenda Monitoring and Accountability Framework and a continental scorecard for timely monitoring and reporting to AU Heads of State and Government.

194 Gavi, African Vaccine Manufacturing Accelerator (AVMA).
195 GloPID-R, GloPID-R announces the launch of Pandemic PACT (2024), https://www.glopid-r.org/glopid-r-announces-the-launch-of-pandemic-pact/.
196 WHO, Interim Medical Countermeasures Network (i-MCM-Net), https://www.who.int/initiatives/i-mcm-net.
197 CEPI, Joint Coordination Group Meeting Summary, 31 January 2024, https://static.cepi.net/downloads/2024-02/PUBLIC_Summary_JCG%2031%20Jan%202024.pdf.
198 G20, Rio de Janeiro Declaration of the G20 Health Ministers (2024), https://www.g20.utoronto.ca/2024/241031-HWG_Ministerial_Declaration_-_Rio_de_Janeiro_ENG.pdf.
199 PAN, pro forma.
200 Future of Global Health Initiatives, The Lusaka Agenda: Conclusions of the Future of Global Health Initiatives Process (2023), https://futureofghis.org/final-outputs/lusaka-agenda/.

- Global South organisations at the Global Pandemic Preparedness Summit in July 2024 signed the **Rio de Janeiro declaration.** The declaration urged global health partners to prioritise research and equitable access policies to focus on end-to-end R&D and support the establishment of the G20 Coalition for Regional and Local Production, Innovation and Access.[201]

PRIORITIES FOR 2025:

See Annex A for Planned Partner Commitments and Priority Actions:

Financing:

- Looking ahead, there is a need for renewed political focus and investment in PPR, as its importance has waned post the COVID-19 pandemic. The mpox PHEIC highlights the urgency of maintaining PPR as a global priority and serves as a pivotal test of solidarity between the Global North and South. Furthermore, there is a critical need to strengthen the connection between preparedness and response financing, with clearly defined operational triggers for organisational mobilisation. These triggers should be structured to enable rapid response and cascade effectively through financing organisations along the MCMs value chain. While surge financing is crucial, it must be balanced with sustained preparedness investments, particularly given the increasing frequency of spillover events driven by climate change. A systematic analysis of stockpiling strategies and advanced market commitments is urgently needed – the 2024 mpox response highlighted how a lack of clear market commitments can become a critical barrier to rapid MCM deployment (see Chapter 5: Mpox case study).

Governance:

- A robust, universally supported Pandemic Agreement has significant potential to improve global pandemic preparedness. This agreement needs to cement core provisions for equity and access, including technology transfer and sustainable manufacturing capabilities, and ensure timely access to pathogen samples and data to support rapid response and innovation. Enhanced coordination mechanisms and participation of regional actors among existing MCM R&D initiatives (i-MCM-Net, XVax Network, RVMC) will be essential to sustain national, regional, and global leadership in PPR.

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Mpox case study - Lessons for future 100DM responses

The 100 Days Mission (100DM) aims to ensure that safe, effective, and affordable diagnostics, therapeutics, and vaccines (DTVs) are ready for scaled production within 100 days of a declared PHEIC, maximizing health impact and saving lives. While the 100DM focuses on the development and availability of medical countermeasures (MCMs), having these tools ready for production does not guarantee their effective deployment and uptake. It is therefore also critical to understand and learn from the persistent unmet needs linked to access and suitability, which ultimately determine whether these interventions reach and benefit those who need them most.

Through stakeholder interviews and analysis of R&D funding, this study examines the 2024 mpox response through a 100DM lens to identify successes and areas for improvement in future health emergencies. These insights will inform actions to strengthen preparedness and response capabilities across all 100DM areas nationally, regionally, and globally.

BACKGROUND

Mpox, a zoonotic disease caused by the monkeypox virus, belongs to the Orthopoxvirus genus, which includes variola virus (smallpox). First identified in 1958 in captive monkeys, human cases of mpox were initially documented in 1970 in the DRC. Historically endemic to Central and West Africa, the disease is caused by two distinct clades: clade I (formerly Central African/Congo Basin clade) and clade II (formerly West African clade).[202]

In 2022, a previously rare outbreak of clade IIb spread globally, marking the first time mpox significantly affected non-endemic regions.[203] The WHO declared mpox a PHEIC in July 2022, sparking a coordinated response concentrated in high-income countries.[204] By May 2023, declining case numbers in non-endemic regions led to the lifting of the PHEIC, although sustained transmission persisted in several African nations where the disease had long been endemic.[205] However, in 2024, a new outbreak driven by clade Ib emerged causing severe outbreaks in Africa, particularly among children.[206] Between January and December 15, 2024, this outbreak resulted in 13,769 confirmed cases and 60 deaths across Africa. The virus demonstrated significant geographic spread, affecting multiple countries across East and Central Africa. This prompted the Africa CDC to declare mpox a PHECS on August 13, 2024.[207] The following day, WHO reinstated the PHEIC status (a status that remains in effect as of printing), underlining the persistent threat posed by evolving strains of the virus.[208]

This qualitative analysis is based on interviews from key stakeholders and comes as the response continues to unfold, reflecting on developments and lessons from the first 100 days since the emergency declarations. We recognise that the response is ongoing and there are best practices that we may not capture at this stage. However, we believe there are lessons learned that may be leveraged from the initial months of the response to inform the next steps within the ongoing response.

EVOLUTION OF MPOX AND ITS CLADES

The evolution of mpox strains underscores the dynamic nature of the virus and its ability to exploit gaps in public health infrastructure. Over decades, clade I dominated outbreaks in Central Africa, characterised by higher case fatality rates than clade II, which was predominantly limited to West Africa.[209] The global 2022 outbreak, fuelled by clade IIb, highlighted the potential for sustained human-to-human transmission outside traditional settings, likely aided by increased global travel and under-recognised reservoirs.[210]

The 2024 outbreak, driven by clade Ib, posed unique challenges due to its higher transmissibility and significant impact on vulnerable populations, particularly children. This clades' emergence in new geographic contexts emphasises the need for enhanced surveillance and sustained investment in research and development beyond emergency situations.[211]

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STATE OF DIAGNOSTICS, THERAPEUTICS, AND VACCINES FOR MPOX

Mpox has approved diagnostics, therapeutics and vaccines. Despite this, there remain important unmet needs linked to access and suitability:

- **Diagnostics:** Of the 177 individual approved tests,[212] most are laboratory-based molecular tests and immunoassays, limiting their use in resource-constrained settings, and lengthening the time to diagnosis during outbreaks. Twenty diagnostics are in late-stage development, including point-of-care solutions that could help meet diagnostic needs in endemic countries. As of publication, however, there are no approved true point-of-care tests available.

- **Therapeutics:** Tecovirimat, originally developed for smallpox, is the sole approved treatment; however, it has not been found to be active against the recent clade Ib.[213] Other experimental candidates such as cidofovir, brincidofovir, and vaccinia immune globulin intravenous (VIGIV) are available for off-label investigational use.

- **Vaccines:** Three vaccines (LC16m8, ACAM2000™, and MVA-BN), originally developed for smallpox, are licensed in high-income countries, but remain unauthorised in the African countries most affected by the outbreak. While MVA-BN received WHO pre-qualification status during the outbreak, access remains uneven.

  There is an urgent need for suitable products to protect paediatric populations. While a phase 2 trial of the approved MVA-BN vaccine among African children aged 2-12 began before the PHEIC, efforts to address this vaccination gap could have started sooner. Since endemic cases of mpox commonly affect children, vaccine efficacy testing should have been conducted during inter-outbreak periods. Moreover, the 2022 WHO PHEIC was a missed opportunity to advance vaccine efficacy testing during an active outbreak, potentially accelerating progress for other clinical candidates.

FUNDING LANDSCAPE

Analysis by Impact Global Health (see Chapter 1: 100DM Scorecard) highlights that the mpox R&D funding landscape is reliant on reactive funding, particularly from the U.S. government. Following the lifting of the 2022 PHEIC, investment in mpox R&D declined sharply, with an 81% reduction in U.S. NIH funding contributing to a more than halving of the overall spend in 2023. The decrease was spread across all product categories. This was slightly offset by other funders, including the French and Canadian governments, as well as industry funding for vaccine development, highlighting the need for a more diversified funding ecosystem. Innovation and access gaps - including challenges of cost, availability, and suitability - persist across DTVs, requiring sustained funding and coordinated action to address.

The 2024 outbreak reignited funding commitments, with additional investments from partners like CEPI and Africa CDC. However, the response remains highly dependent on short-term crisis funding from a limited set of funding sources, lacking the sustained investments from a diversity of funders needed to address inter-epidemic periods and advance preparedness.

212 Based on 100 Days Mission Scorecard data that was sourced from FIND and U.S. FDA on September 30 2024.
213 National Institute of Allergy and Infectious Diseases, The antiviral tecovirimat is safe but did not improve clade I mpox resolution in Democratic Republic of the Congo.

TIMELINE

The resurgence of mpox in 2023–2024, particularly in Africa, led to significant international public health actions. Below is a detailed timeline of key events:

Late September 2023

First mpox case detected in Kamituga, DRC marking the beginning of a large outbreak in October.[214,215]

FEBRUARY 2024

DRC's NITAG recommends LC16m8 and MVA-BN vaccines for emergency response in adults.[216]

11-13 APRIL 2024

Africa CDC holds Emergency Regional Meeting with 11 AU Member States on DRC outbreak.[217]

15 APRIL

New mpox lineage (clade Ib) identified, traced to mid-September in Kamituga.[218]

23 APRIL

DRC declares national mpox epidemic.[219]

22 MAY 2024

WHO updates interim guidance on mpox diagnostic testing.[220]

26 MAY 2024

The DRC reports 7,851 suspected mpox cases across 23 provinces since 1 January.[221]

15 JULY 2024

Uganda confirms the first recorded cases of clade Ib mpox outside the DRC.[222]

24-27 JULY 2024

Rwanda reports first clade Ib mpox cases and declares outbreak.[223]

25 JULY 2024

Burundi confirms 3 clade Ib mpox cases and declares outbreak.[224]

29 JULY 2024

Kenya confirms first clade Ib mpox case.[225]

9 AUGUST 2024

WHO invites vaccine manufacturers to submit for Emergency Use Listing (EUL).[226]

13 AUGUST 2024

Africa CDC declares PHECS.[227]

14 AUGUST 2024

WHO declares PHEIC.[228] **100DM clock starts.**

15 AUGUST 2024

Sweden reports first clade Ib case outside Africa.[229]

16 AUGUST 2024

ECDC raises the risk level of clade Ib mpox to "low".[230]

27 AUGUST 2024

Nigeria receives 10,000 MVA-BN vaccine doses donated by the US.[231]

5-7 SEPTEMBER 2024

DRC receives first batches of MVA-BN vaccine (200,000 total).[232]

13 SEPTEMBER 2024

WHO grants prequalification status to the MVA-BN vaccine.[233]

19 SEPTEMBER 2024

Fifteen African Union member states report mpox cases; Rwanda initiates vaccination campaign.[234]

4 OCTOBER 2024

WHO grants EUL for first molecular mpox diagnostic test.[235]

5 OCTOBER 2024

DRC initiates vaccination campaign in high-priority provinces.[236]

14 OCTOBER 2024

WHO grants prequalification for age-extension of the MVA-BN vaccine (12-17 years).[237]

30 OCTOBER 2024

WHO lists two additional molecular mpox diagnostic tests under EUL.[238]

14 NOVEMBER 2024

DRC receives 100,000 MVA-BN vaccine doses.[239]

18 NOVEMBER 2024

Nigeria initiates vaccination campaign.[240]

19 NOVEMBER 2024

WHO grants EUL for LC16m8 mpox vaccine.[241]

21 NOVEMBER 2024

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METHODS

Case Study Design

This case study employed a qualitative approach to understand the mpox response through the lens of the 100 Days Mission, focusing on key stakeholders' experiences and perspectives. Semi-structured interviews were conducted with key informants from various organisations, including global health bodies, regional agencies, CSOs, and government entities. The participating stakeholders included: Africa CDC (Headquarters, Burundi country office), AMRH, Bavarian Nordic, CEPI, Disability Peoples Forum Uganda, DRC Ministry of Health, Emergent BioSolutions, FIND, GAVI, Health NGO's Network (HENNET) Kenya, SIGA, Uganda Ministry of Health, UNICEF, and WHO Headquarters.

Data Collection and Analysis

Seventeen semi-structured qualitative interviews were conducted remotely by video conferencing. While standardised interview guides provided a framework for discussion topics, questions were tailored to align with each stakeholder's specific expertise. Due to the sensitive nature of the topic, confidentiality measures were strictly upheld to ensure open and honest dialogue.

A thematic analysis was performed to identify recurring themes, opportunities, and areas for improvement in the mpox response. Thematic coding was applied using an inductive approach. The findings from the data analysis do not represent the views of the individual stakeholders or their organisations, but rather the collective themes and subthemes that emerged from the interviews.

FINDINGS

The mpox outbreak provides a critical perspective on the systemic gaps and opportunities in pandemic preparedness and outbreak response. The key themes emerging from data collection include:

1. Competing Local and Global Health Priorities

The mpox outbreak highlighted fundamental tensions between local, regional, and global health priorities. Countries most affected by the outbreak often faced concurrent challenges including cholera outbreaks and urgent needs around routine immunisation coverage, making mpox one among many competing public health demands despite rising case numbers. This exemplifies a broader challenge where countries must carefully weigh emergency declarations against existing health and economic priorities. The political dynamics around emergency declarations created additional complexities - governments needed both domestic public support and clear evidence of urgency to justify redirecting resources, whilst also considering broader international implications. This tension manifested in the timing of declarations, with countries often hesitant to declare emergencies given public perception concerns both domestically and internationally, as well as potential restrictions such as travel, etc. Limited mortality rates in some regions further complicated efforts to build political and public backing for emergency measures, particularly in the wake of COVID-19 response fatigue. The situation highlights how emergency response frameworks must account for competing priorities whilst ensuring sufficient flexibility to mount effective responses when needed. This requires careful consideration of how emergency mechanisms can strengthen rather than strain existing health system capabilities.

2. Institutional Dynamics and Coordination

The 2024 mpox outbreak revealed both progress and persistent challenges in coordinating emergency responses between global and regional institutions. This was highlighted by the initial absence of clear role delineation between WHO (Headquarters and the WHO regional office for Africa) and Africa CDC. This was the first major outbreak where Africa CDC played both political and operational leadership roles. While Africa CDC's proactive declaration of a PHECS demonstrated important regional leadership, it also revealed broader gaps in coordination with global health bodies. This marked a significant shift in regional health governance, creating a new dynamic in global health where regional leaders are taking more independence while requiring realignment of traditional institutional roles.

Future preparedness must build on these lessons by empowering regional organisations like Africa CDC, while fostering collaboration with global entities. Drawing on lessons from previous emergencies, notably COVID-19's "one team, one plan" approach, future preparedness could be enhanced through clearer role definition, pre-agreed coordination frameworks, and trust-building measures between institutions. This would help ensure a more integrated response that leverages the complementary strengths of regional and global health organisations, while acknowledging the complex realities of modern multilateral health governance.

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3. Policy and Regulatory Processes

Regulatory processes presented complexities that impacted the timeliness of the mpox response, affecting the availability and deployment of MCMs. Several of the mpox vaccines already had approval by EMA, FDA and the Ministry of Health, Labour and Welfare/Pharmaceuticals and Medical Devices Agency, but before the declaration of the PHEIC there were limited mechanisms for these approvals to be translated swiftly into approvals in affected countries. The model law now being rolled out by the nascent African Medicines Agency should help expedite reliance processes for translation of approvals in future years. While WHO moved rapidly to issue calls for EUL submissions following the PHEIC declaration, underlying procedural complexities and timing constraints around emergency declarations continued to affect deployment timelines. It should be noted that some companies had submitted dossiers for prequalification before the PHEIC declaration. In future outbreaks it should not necessitate a PHEIC to receive WHO approval, particularly when products have already received approval from Maturity Level 3 (ML3) regulatory authorities. Such ML3 approvals should be considered sufficient evidence of quality, safety, and efficacy for both national and global procurement decisions.

Liability concerns and off-label use for children further complicated matters, particularly as existing vaccines lacked regulatory approval for paediatric use, despite children being significantly affected by the outbreak.

These findings highlight the need to enhance regulatory processes for future outbreaks. Regional regulatory agencies present valuable opportunities for harmonising regulations and expediting approvals across multiple jurisdictions. Through robust preparatory frameworks including pre-established assessment protocols and evidence requirements, countries can maintain rigorous standards whilst enabling swifter emergency responses. Critical to this approach is strengthened collaboration between national and regional regulatory authorities to establish shared standards and facilitate mutual recognition of approvals.

4. Diagnostics and Surveillance Challenges

The mpox response has revealed significant gaps in both diagnostic capabilities and surveillance systems that have severely impacted outbreak containment. At the core of these challenges lies the absence of rapid diagnostic tests for clade I mpox, exposing systemic gaps in diagnostic preparedness. The heavy reliance on centralised laboratories has created significant barriers in sample access and transportation, whilst these facilities struggle with competing demands from routine testing for other endemic diseases. As a result, only a small proportion of suspected cases undergo testing, falling far below Africa CDC's established target of 80%. Despite FIND and Africa CDC identifying several promising tests, essential validation studies and the deployment of new diagnostic tools have been stalled by critical funding gaps, alongside challenges in accessing appropriate samples for diagnostic development.

These diagnostic limitations compound broader surveillance challenges in establishing accurate case definitions and data collection mechanisms across different healthcare settings and contexts. The challenge is particularly acute at the community level, where frontline workers struggle with case identification, as mpox symptoms closely mirror those of endemic conditions such as measles and chickenpox. This difficulty is exacerbated by limited familiarity with proper case presentation. Community-level surveillance has proved especially weak across several regions, as traditional surveillance structures have failed to adapt to the outbreak's distinct characteristics. The situation is further complicated by cross-border surveillance challenges, where multiple unofficial entry points and limited screening capacity create significant blind spots in disease tracking. Moreover, laboratory-surveillance data linkages present persistent difficulties, as countries struggle to maintain effective contact tracing and sustain community health worker engagement.

Addressing these diagnostic and surveillance gaps requires tackling fundamental research and development obstacles, particularly the missed opportunities for diagnostic test development and limited investment during inter-epidemic periods. These findings highlight the necessity of increased coordination and funding for diagnostic research and development, especially for rapid true point-of-care tests in rural communities where these pathogens are endemic. Achieving this will require a coordinated action across multiple fronts: establishing biobanking networks for test validation, securing sustained funding for evaluation studies, and building long-term cross-sector commitments to create viable markets. Given the limited demand for single-pathogen diagnostics, investment in multiplex diagnostics that combine testing for multiple endemic diseases offers a more sustainable solution. When integrated into broader surveillance systems, this approach not only ensures reliable market demand but also strengthens early detection and response capabilities through routine disease monitoring.

5. Evidence Gaps in Vaccine and Therapeutic Efficacy

Evidence generation has also faced substantial challenges. Critical gaps exist in clinical evidence, particularly regarding vaccine effectiveness in children, while the therapeutics pipeline remains limited and existing therapeutics lack robust efficacy data. Careful consideration is needed regarding trial design and objectives, particularly how these align with both scientific inquiry and the generation of evidence suitable for regulatory decision-making. The research infrastructure has shown systemic weaknesses, including limited capacity to conduct trials during outbreaks and insufficient biobanking capacity for future research. These gaps have directly impacted the response, making it difficult to target interventions effectively, evaluate their impact, and develop evidence-based policies. The situation highlights the pressing need for sustained investment in clinical trial networks and research capabilities between outbreaks, ensuring robust evidence generation during both routine operations and emergencies.

6. Vaccine Resource Allocation and Accessibility

Despite the availability of vaccines, the mpox response highlighted stark inequities in the allocation of doses. While political considerations influenced distribution decisions, uncoordinated vaccine supply chains and fragmented donation pathways complicated efficient deployment. Clear, capacity-based allocation criteria are essential for equitable and effective MCM deployment - a role that could be effectively played by promising frameworks such as the Access and Allocation Mechanism, which brings partners from around the world for the development, manufacturing, allocation, and delivery of MCMs.

The response further highlighted that availability of MCMs does not guarantee effective access. Limited absorption capacity and implementation challenges have resulted in significant disparities between doses shipped and administered. This has been further compounded by affected countries' need to balance the mpox response against other pressing health priorities. Effective outbreak control requires comprehensive investment in country-level systems, from healthcare worker training to logistics infrastructure, alongside sustained community engagement. This underscores the need to move away from vertical, single-disease approaches towards holistic health system strengthening that can maintain capabilities between outbreaks.

7. Community Engagement and Trust

The mpox response has revealed significant gaps in community engagement and trust-building efforts. A critical disconnect exists between technical communication approaches and community-level understanding, emphasising the need for more nuanced, culturally appropriate communication strategies. Post-COVID-19 vaccine hesitancy has emerged as a major challenge in many regions, highlighting the need for careful navigation of community concerns and misconceptions.

Multiple communities have faced barriers to meaningful inclusion in response planning and implementation. Disabled communities, for instance, have encountered significant challenges around information accessibility, appropriate communication channels, and physical access to services - issues that exemplify broader systemic gaps in community engagement. Language barriers, cultural considerations, and varying information needs across different population groups have often been overlooked in the rush to deploy interventions. The importance of establishing effective community feedback mechanisms is evident, as is the need to engage more meaningfully with civil society organisations that have deep and trusted community connections and understanding of local contexts.

8. Pre-Emergency Actions and Preparedness

Despite a previous mpox PHEIC in 2022, R&D funding dropped off when it ended, stockpile plans were not finalised, and again the affected areas were dependent on donations from high-income countries who had secured doses for their own needs. As a result, the current mpox outbreak highlighted critical gaps in preparedness and the limitations of reactive approaches to emerging health threats. While there were some preliminary discussions around accurate demand forecasting, purchase commitments and monitoring of outbreak patterns, these efforts lacked both the coordination and urgency needed to prevent escalation to an emergency.

Countries that maintained and adapted infrastructure from previous health emergencies, particularly those established during COVID-19 and polio eradication efforts, as well as those that regularly conducted outbreak simulation exercises and emergency preparedness drills, were better positioned to respond effectively. This underscores the value of sustained investment in health systems during non-emergency periods, while also revealing the challenges of maintaining these capabilities and ensuring their adaptability for diverse future health threats.

Several key areas require attention to enhance preparedness. These include strengthening early warning systems, advancing research and development for therapeutics and point-of-care diagnostics, strategically pre-positioning MCMs in high-risk areas, and developing master clinical trial protocols for rapid deployment during outbreaks. The establishment of sustainable laboratory networks has emerged as particularly vital, requiring consistent investment and capacity-building between outbreaks. Crucially, these efforts must be integrated into routine health services rather than existing as standalone emergency measures.

The key challenge lies in maintaining sufficient capacity during non-emergency periods while ensuring systems can be rapidly scaled up when needed. This requires sustainable funding mechanisms and political commitment to long-term health system strengthening. The mpox experience, as with all major outbreaks, shows that such investments, though costly in the short term, are ultimately more cost-effective than mounting emergency responses without pre-existing infrastructure and capabilities. The cost of the COVID response is well documented and yet, it remains a constant challenge for national governments to balance investment between response and preparation for multiple societal priorities.[242]

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In Summary

The analysis reveals a complex interplay of governance, technical, and operational challenges in the mpox response. While progress has been made in regional leadership and coordination mechanisms, significant work remains in areas such as regulatory harmonisation, community engagement, and sustainable response infrastructure. The lessons learned provide valuable insights for strengthening future outbreak responses and implementing the 100DM effectively.

Proposed priority actions to strengthen current and future mpox responses from the interviews include:

Short-term	Medium - Long-term
Address liability issues for paediatric vaccine deployment.	**Develop clear frameworks for global-regional cooperation.**
Strengthen ground-level implementation support.	**Establish sustainable funding mechanisms for MCM development in an outbreak response.**
Enhance point of care diagnostic validation and deployment.	**Strengthen regulatory harmonisation and emergency use pathways.**
	Build sustainable and geo-diversified research and clinical trial infrastructure to advance R&D for DTVs.
	Enhance community engagement and accessibility in health systems.

Mpox Response and the 100 Days Mission

The mpox outbreak highlights both the urgency and opportunity to advance the ambitions of the 100DM. While progress was evident, critical gaps in preparedness became apparent, emphasising the need for a robust framework to deliver DTVs within 100 days of a declared global health emergency. The lessons learned offer valuable insights not just for the ongoing response to mpox, but for future outbreak responses globally.

Several key themes emerge from the case study that have broader implications for the 100DM. The response demonstrated persistent gaps in diagnostic and therapeutic preparedness. Despite having existing products, their adaptation for the current clade proved challenging, and no rapid diagnostic tests or effective therapeutics were available within the first 100 days. This emphasises the need for sustained investment in R&D, particularly in MCMs for priority pathogens and platforms that can be rapidly adapted to respond to emerging variants, and improved coordination across stakeholders - from research organisations and industry partners to regulatory bodies - elements that were notably lacking after the 2022 mpox outbreak subsided.

Perhaps most significantly, the case study reveals that even when MCMs exist, regulatory and liability barriers can impede their deployment, particularly for vulnerable populations like children. The experience with paediatric vaccination demonstrates that technical availability alone is insufficient; pre-agreed frameworks for emergency use, liability protection, and regulatory harmonisation are all key to achieving the 100DM. These access considerations, including robust demand forecasting based on well-defined scenarios and identification of priority populations, must be integrated from the earliest stages of R&D. An end-to-end approach should be adopted that includes early regulatory engagement and planning for effective last-mile delivery. Similarly, advanced market commitments are crucial to derisk R&D for diagnostics, therapeutics, and vaccines.

While the 100DM focuses on the development and availability of MCMs, the mpox response brings to light a crucial reality: having tools available does not guarantee their uptake. Community engagement emerged as a critical factor in successful MCM acceptance and uptake. Hesitancy, misinformation, and lack of culturally appropriate communication strategies significantly hinder the uptake of products even where they are available. This suggests that, while the 100DM's technical focus is vital, parallel investment in community trust-building and engagement frameworks is essential for translating availability to real-world impact.

While the mpox response showed some improvements from the 2022 outbreak, particularly in regional coordination and leadership, it ultimately reveals that many foundational elements of the 100DM remain unrealised. This experience underlines the importance of maintaining focus and investment between outbreaks while highlighting several critical areas for strengthening future preparedness, specifically around sustainable financing for diagnostics and therapeutics development, regulatory harmonisation, and the integration of community perspectives.

6

Afterword & Acknowledgements

Afterword- South African G20 Presidency

Afterword from **Dr Anban Pillay**, Deputy Director General at the National Department of Health, Government of South Africa

In recent years, the G20 has made strong strides towards building and strengthening resilient health systems globally. South Africa's 2025 G20 presidency will enhance this work, aligning efforts with the targets of the Sustainable Development Goals. Underpinned by the theme of solidarity, equality and sustainability, South Africa will bring the African continent and the Global South's priorities more firmly onto the agenda of the G20.

Given the scale of global health challenges, and the complexity of the health value chain, no single institution, intervention or approach will be adequate to address them effectively. A multi-sectoral and multi-faceted approach must be taken in order to address this. South Africa will continue to focus on improving Pandemic Prevention, Preparedness and Response amongst other pressing issues in the G20 health priorities.

South Africa will build on the progress made by Brazil's G20 presidency and the Coalition on Local and Regional Production, Innovation, and Equitable Access. Geographically diversified research and development (R&D), and national and regional production of diagnostics, therapeutics and vaccines (DTVs) have the potential to improve equity and access as part of universal health coverage whilst protecting populations from health emergencies.

Not only does this require sufficient capacity and capability from early-stage R&D through to clinical trial capacity, regulation, manufacture, and distribution, but also a full complement of drugs, therapeutics and vaccines for priority pathogens and a harmonised approach to regulatory processes. However, as the findings in this report highlight, there is still a need to develop essential medical countermeasures (MCMs), particularly for diagnostics and therapeutics, for priority pathogen families and Disease X.

South Africa will work with WHO and partners to lead the G20 to take a strategic, end-to-end approach to MCM development to fill these gaps in our collective health security. This includes training and retaining the MCM product development workforce; continental coordination on end-to-end MCM product development; and filling the gaps in research and development, to ensure we are ready to respond effectively to the next pandemic threat. South Africa stands ready to seize the opportunity presented by its G20 presidency and work with partners, including the G7, to secure an equitable, sustainable and responsive product development ecosystem, moving the world closer to achieving the 100 Days Mission, and collective health security for citizens across the world.

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 Impact Global Health for their contributions to the 100DM Scorecard, the mpox case study and review of the report, and implementation partners for their input provided through interviews and pro formas. A full list of contributors is listed at Annex C.

Annex A

Summary of Recommendations

NOTE:
- Progress summarised is not exhaustive but seeks to highlight updates of international relevance
- Recommendations have been grouped by theme rather than original numerical order
- Information in the table below has been collated from pro formas and interviews with the named implementation partners.

Topic	Recommendation	2024 Summary progress update	Planned partner commitments and recommended priority actions for 2025
Diagnostics R&D	2. Build prototype [vaccines and] diagnostic libraries applicable to representative pathogens of pandemic potential. 6. Strengthen the role of the international system in R&D capability and coordination for [therapeutics and] diagnostics. Note that progress against this recommendation has been broadened to diagnostics R&D coordination more broadly, beyond a potential CEPI role.	FIND has created a dashboard that tracks the availability of diagnostics for the WHO R&D priority pathogens and the Africa CDC priority list.[243] WHO i-MCM-Net is landscaping the diagnostic ecosystem with partners focusing on Pandemic Influenza, Novel Coronavirus and Disease X.[244] Instituto Butantan has been working in collaboration with Brazil's regulatory agency (ANVISA) to conduct testing across multiple viruses with pandemic potential and is working on developing antibodies for viral diagnostic tests.[245] Bio-Manguinhos/Fiocruz is continuing to develop molecular tests for viruses with pandemic potential including mpox, and in 2024 it started the development of an oropouche molecular test.[246] Global Health Labs (GHL) and GADx collaborated to support the development of a molecular diagnostic tool aimed at making diagnostic testing more affordable and equitable termed NAATOS (Nucleic Acid Amplification Test on a Strip). Designed for ease of use with minimal training, it can be easily distributed while maintaining high-performance standards. This is a significant step towards revolutionising point-of-care testing with molecular diagnostics, ensuring broader access to vital diagnostics in LMICs.[247] GADx has active programmes on developing tests for CCHF, Ebola (all strains), Nipah, Avian and pandemic influenza. GADx is also working with Bioaster to develop a triplex test for febrile disease. GADx is collaborating with multiple agencies and organisations across the world, including UK Health Security Agency (UKHSA), the Pirbright Institute, Liverpool School of Tropical Medicine (LSTM), the University of Oxford, and Institut Pasteur de Dakar.[248] BARDA allocated $27 million to support the rapid development and scaled manufacturing of diagnostic tests, including a Marburg virus rapid antigen test, through regulatory approval, using platforms that can be adapted to emerging threats.[249] Unitaid is supporting the late-stage development and expansion of multiplex molecular diagnostic platforms both for use in surveillance and for the routine clinical screening of ongoing endemic diseases.[250]	**Planned partner commitments** FIND and other partners will continue to work towards the 100DM through investment and collaboration, including working with CEPI to leverage investments and innovations in early R&D for pathogen libraries for test development and align their response strategy with the new WHO viral family approach as outlined in the WHO R&D pathogen prioritisation framework.[257] GADx aims to develop a multiplexed Nipah test that will include an additional test line for Pan-Henipavirus or Paramyxoviridae. GADx aims to build on their experience from partnerships with regional manufacturers in Senegal and Tunisia to establish a similar model of technology transfer, manufacturing, and commercialisation in ASEAN.[258] **Recommended Priority Actions for 2025:** · R&D funders, FIND, and diagnostic developers should coordinate around the WHO pathogen prioritisation framework to develop **point-of-care tests for at least two priority pathogens.** · Governments should allocate sustained funding for diagnostic R&D. · WHO, FIND and other partners should support **expansion of Target Product Profiles** for priority pathogens (currently limited to SARS-CoV-2 with Lassa Fever tests under review), with a focus on point-of-care tests to support rapid and early detection. · WHO should set out clear technical specifications for rapid point-of-care tests for priority pathogens to enable **prequalification in an emergency context.** · Diagnostic developers should work closely with the relevant regulatory bodies, WHO, and the Expert Review Panel for Diagnostics early in R&D process to determine the most efficient and relevant clinical and analytical validations.

243 FIND, Pathogen Diagnostics Readiness Index (PDxRI).
244 FIND, pro forma.
245 Butantan, pro forma.
246 Bio-Manguinhos, Estudo de Bio sobre oropouche é publicado na Revista Lancet.
247 GADx, pro forma.
248 GADx, pro forma.
249 CIDRAP, HHS ASPR announces new funding to fill gaps in biothreat diagnostics.
250 Unitaid, pro forma.
257 FIND, pro forma.
258 GADx, pro forma.

Topic	Recommendation	2024 Summary progress update	Planned partner commitments and recommended priority actions for 2025
Diagnostics R&D		Singapore Ministry of Health continues to support the Programme for Research in Epidemic Preparedness and Response (PREPARE) initiative including the Diagnostic Cooperative Programme which supports funding opportunities for point-of-care molecular diagnostic platforms, real-time biosensing platforms, sample collection to facilitate decentralised testing, and multiplexed protein detection platforms.[251,252] In December 2024, the EPSRC-funded Quantum Biomedical Sensing Research Hub launched, with a focus area on incorporating novel quantum nanomaterials into RDTs for ultra-sensitive virus detection at the point-of-care.[253] Varro has developed a nanobody-based electrochemical biosensor designed to rapidly detect respiratory pathogens from human breath with accuracy comparable to PCR, and the platform is also being adapted for use in environmental surveillance. Varro is moving towards an open-source approach to enhance accessibility and foster collaborative innovation, and is targeting commercialisation by 2025-2026.[254] Unitaid and FIND are investing in initiatives to expand the geographical diversity of manufacturing capacity to produce diagnostic tests, including a partnership with Institut Pasteur de Dakar. Unitaid is investing in regional manufacturing capacity (including through technology transfer) to accelerate the availability of quality-assured diagnostics and sample collection materials in Africa.[255] Unitaid and Global Fund support the WHO prequalification process and have advanced pathways through the Expert Review Panel for Diagnostics (ERP-D) to support an expedited regulatory review process for both internationally and regionally manufactured diagnostics yet to undergo stringent regulatory assessment.[256]	· WHO should lead on harmonising diagnostic regulatory pathways · Regulators and WHO should collaborate through the **Global Benchmarking tool to support as many regulators as possible to become WHO Listed Authorities (WLAs) for medical devices,** allowing recognition of their approvals. · National and regional authorities should actively **enhance the visibility of virtual biobank networks** to ensure that researchers and developers can access resources. · National authorities should implement robust biosecurity measures, ensuring that access to shared biological resources is both secure and efficient. · IPPS should support a consortium of multisectoral diagnostics partners, including FIND, industry, research institutions, governments, regulatory bodies, and international organisations to convene to align on and implement the 100DM diagnostics roadmap, establishing clear deliverables, roles, and responsibilities. As part of this effort, IPPS is coordinating a roundtable of multisectoral diagnostics partners to convene in 2025 to discuss challenges and barriers to industry engagement, including bottlenecks in R&D for pathogens with pandemic potential and regulatory hurdles impacting the 100DM for diagnostics. · FIND and partners should **publish the 100DM Diagnostics Roadmap.** · Policymakers and health ministries should prioritise the procurement and integration of multiplex diagnostics with data connectivity and link diagnostic testing to treatment pathways. · Governments should strengthen market demand signals through mechanisms like Essential Diagnostics Lists to support national procurement.
Therapeutics R&D	3. Develop prototype antiviral therapeutics, including antibody therapies, for pathogens of pandemic potential. Note that progress against this recommendation has been broadened from respiratory to all pandemic pathogens (e.g., skin-to-skin, blood-borne)	INTREPID published the third edition of their Antiviral Landscape report, covering the 13 priority families in WHO's pathogen prioritisation framework and specific analysis of compounds in development for influenza and mpox.[259] In December they examined the landscape of animal models for flaviviruses, to identify opportunities for standardisation. READDI, in collaboration with SciVida, developed a comprehensive antiviral landscape assessment database covering seven high-risk viral families, including both active and abandoned R&D efforts.[260]	**Planned partner commitments** The Cumming Global Centre will continue to establish research partnerships. Discussions are underway to create a global network of partnerships able to amplify the mission of the centre. The centre also plans to establish a fund to support translational research and the incubation of aligned start-ups.[278]

251 Singapore MOH, pro forma.
252 PREPARE, 3. Diagnostics (2024), https://www.prepare.gov.sg/funding-opportunities/diagnostics.
253 Q-Biomed, UK Quantum Biomedical Sensing Research Hub.
254 Business Wire, Varro Receives $20 Million from Vitalik Buterin to Support Development of Cutting-Edge Pathogen Biosensor Technology.
255 Unitaid, pro forma.
256 Unitaid, pro forma.
259 INTREPID, Antiviral Clinical and Preclinical Development Landscape — 3rd Edition.
260 READDI, Comprehensive antiviral landscape assessment guides R&D.
278 The Cumming Global Centre for Pandemic Therapeutics, pro forma.

Topic	Recommendation	2024 Summary progress update	Planned partner commitments and recommended priority actions for 2025
Therapeutics R&D	5. Invest in simplified cheaper routes for producing mAbs and other new therapeutic modalities. 6. Strengthen the role of the international system in R&D capability and coordination for therapeutics [and diagnostics] Note that progress against this recommendation has been broadened to therapeutics R&D coordination more broadly, beyond a potential CEPI role.	In June 2024, IPPS co-organised a workshop 'Towards building a Therapeutics coalition' with Unitaid, READDI, DNDi, Medicines Patent Pool, WHO, IFPMA, and INTREPID Alliance. This workshop brought together diverse stakeholders from different sectors and geographies, to discuss how to collaboratively reinvigorate the pipeline and ensure global access to lifesaving products. There was broad agreement on the need for an independent and inclusive development coalition. Rather than creating a new entity, there was most appetite for a genuine coalition of existing partners working towards these shared goals, ensuring complementarity with WHO's ongoing work on priority pathogen families and the structures being established under the i-MCM-Net.[261] The PAD initiative is funding up to $20 million to 11 research projects around the world to facilitate early-stage development of novel antiviral drugs to treat potential future outbreaks of pandemic influenza. This is the second year that grants have been awarded within the PAD initiative, a global philanthropic collaboration between the Novo Nordisk Foundation, Open Philanthropy, and the BMGF. PAD has a focus on antiviral drug candidates for coronaviruses, paramyxoviruses, and orthomyxoviruses.[262] The Dengue Alliance, initiated by DNDi and led by Global South researchers, exemplifies a South-South partnership aimed at expediting the development of therapeutics for a priority flavivirus. As part of the Dengue Alliance, partners in dengue-endemic countries including the Ministry of Health (Malaysia), Faculty of Medicine Siriraj Hospital Mahidol University (Thailand), Translational Health Science and Technology Institute (India), Fiocruz and the Federal University of Minas Gerais (Brazil) are collaborating to share knowledge and accelerate development of affordable and accessible treatments for dengue, including testing repurposed drugs.[263] In September 2024, National Institute of Allergy and Infectious Disease (NIAID) of the U.S. NIH announced plans to commit up to $100 million a year to the ReVAMPP programme (Research and Development of Vaccines and Monoclonal Antibodies for Pandemic Preparedness). One of the ReVAMPP awardees is James Crowe, Chief Scientist of AHEAD100; his team at Vanderbilt University Medical Center is launching 30 new antibody discovery programmes against pathogenic viruses in collaboration with three network partners.[264, 265]	One of Butantan's priorities is the development of a comprehensive therapeutic library that offers broad coverage for priority viral families. Over the coming year it will drive this forward through enhancing therapeutic capabilities and R&D and strengthening collaboration with academic institutions, industry partners, and global health organisations.[279] **Recommended Priority Actions for 2025:** · IPPS in collaboration with Unitaid, READDI, DNDi, MPP, IFPMA, and the INTREPID Alliance, and other industry, government, and funding partners, should **support operationalisation of the Therapeutics Development Coalition** to accelerate product development through coordinated implementation of the therapeutics roadmap, ensuring alignment with the WHO viral family approach and CORCs. The Coalition should establish coordination structures with clear partner roles to demonstrate proof-of-concept projects across two priority viral families, showcasing how collaborative development can accelerate therapeutic readiness. · INTREPID Alliance and partners should **continue mapping of pipeline gaps to identify strategic funding opportunities for pandemic-ready therapeutics,** to identify critical R&D pipeline gaps where targeted funding could have maximum impact. · WHO should support **development of TPPs for therapeutic candidates.** · Therapeutics developers should **advance platform technologies** and innovative approaches to therapeutics development, demonstrating preclinical proof-of-concept for novel antiviral platforms (e.g., broad-spectrum small molecule antivirals, cross-reactive/ broadly neutralising mAbs, and nucleic acid technologies) across multiple viral families with a focus around accessible product profiles.

261 Machingaidze et al., "The case for a global therapeutics development coalition: Building a therapeutics pipeline for pandemic and endemic diseases."
262 BMGF, pro forma.
263 Institute for Medical Research Malaysia, pro forma.
264 Research and Development of Vaccines and Monoclonal Antibodies for Pandemic Preparedness (ReVAMPP).
265 VUMC joins national effort to prevent another pandemic (2024), https://news.vumc.org/2024/09/13/vumc-joins-national-effort-to-prevent-another-pandemic/.
279 Butantan, pro forma.

Topic	Recommendation	2024 Summary progress update	Planned partner commitments and recommended priority actions for 2025
Therapeutics R&D		Several organisations are progressing work on mAbs targeting viruses of pandemic potential.[266, 267,268] With support from CEPI, Mapp Bio and ServareGMP are advancing a Nipah mAb into clinical trials in India and Bangladesh. Renbio, with support from Wellcome, is developing low-cost DNA mAbs for Zika and Influenza, increasing the accessibility of these therapeutics in LMICs.[269] The U.S. Department of Defence has sponsored a programme at Vanderbilt University Medical Center to discover neutralising antibodies against hantaviruses for which there are currently no approved specific treatments or vaccines.[270] Unitaid released a call for proposals in December 2023 aimed at demonstrating the feasibility and viability of business models that enable equitable access to mAbs in LMICs. As a result, Unitaid is poised to launch three investments in mAbs with viable use cases and access strategies, focusing on malaria, RSV, and HIV while considering potential applications for pandemic scenarios.[271] READDI's AViDD Centre (READDI-AC) screened over half a million chemical compounds across various viral families and is advancing a diverse portfolio of broad-spectrum small molecule antiviral assets. As of early 2024, 1,433 compounds have been sent to 22 labs and four contract research organisations to validate and advance hits. READDI-AC has also completed 14 in vivo efficacy studies and two in vivo pharmacokinetic-pharmacodynamic studies across seven preclinical lead assets.[272] Professor Dame Angela McLean (UK CSA) chaired a roundtable on broad-spectrum antivirals in August 2024. The roundtable explored the potential effectiveness of broad-spectrum antivirals and how they could form part of a pre-prepared panel of therapeutics against priority viruses.[273] The Drugs for Neglected Diseases initiative (DNDi) are working with partners on broad-spectrum antivirals including for SARS-CoV-2, SARS-MERS, flaviviruses and enteroviruses, and influenza.[274] SPRIND's "Broad-Spectrum Antivirals" Challenge, which began in 2021, culminated with four winning teams developing unique platform approaches to tackle current and future pathogens.[275] The Cumming Global Centre for Pandemic Therapeutics is focusing research on platform technologies which can rapidly give rise to new therapeutics candidates. In September 2024, the centre announced a $54m Bonn-Cumming Host-Directed Pandemic Therapeutics Research Programme with the University of Bonn to fund research into early immunity to develop novel targets for therapeutics for pathogens of pandemic potential, and began a two-year pilot phase in October.[276]	

266 CEPI, New human trials for novel antibody offer hope for immediate protection against deadly Nipah.
267 Butantan, pro forma.
268 Wellcome Trust, pro forma.
269 Wellcome Trust, pro forma.
270 JPEO-CBRND, JPEO-CBRND and VUMC Vaccine Center Collaborates to Discover New Antibodies for Viral Defense (2024), https://www.jpeocbrnd.osd.mil/Media/News/Article/3852012/.
271 Unitaid, Call for Proposals: Establish viable business models for access to monoclonal antibodies in low- and middle-income countries.
272 READDI, READDI is filling the R&D pipeline for pandemic pathogens.
273 Government Office for Science, Broad-spectrum antivirals (2024), https://www.gov.uk/government/publications/broad-spectrum-antivirals/broad-spectrum-antivirals.
274 DNDi, pro forma. DNDi, pro forma.
275 SPRIND, Your Challenge: Broad-Spectrum Antivirals.
276 The Cumming Global Centre for Pandemic Therapeutics, pro forma.

Topic	Recommendation	2024 Summary progress update	Planned partner commitments and recommended priority actions for 2025
Therapeutics R&D		BARDA have awarded contracts to industry and academic partners to advance the progression of adaptable therapeutic platforms. These have the potential advantage of being able to pivot quickly against new threats and be effective against a range of viral families.[277]	
Vaccines R&D	2. Build prototype vaccines [*and diagnostic*] libraries applicable to representative pathogens of pandemic potential. 4. Invest in modernising vaccine technology by targeting vaccine preventable diseases. 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.	Japan's Ministry of Health, Labour and Welfare have approved the first self-amplifying RNA (saRNA) vaccine at the end of 2023. The zapomeran COVID-19 vaccine, which allows for much lower titres compared to conventional mRNA vaccines, reducing production costs, opens pathways for other saRNA vaccines in the pipeline, including those for influenza.[280] WHO have prequalified two malaria vaccines, RTS,S and R21 which use virus like particle technology.[281] Valneva has received marketing authorisation for their Chikungunya vaccine, IXCHIQ, from the European Medicines Agency (EMA), U.S. FDA and Health Canada. This is the first vaccine to be authorised for this disease.[282] CEPI and the European Union will provide up to $41.3 million to expand access to this vaccine including clinical trials in vulnerable groups. The partnership will also support technology transfer to an additional manufacturer to supply Asian LMICs.[283] CEPI continues to support prototype vaccines and diversified portfolio investments across a range of viral pathogens with epidemic or pandemic potential, for example the Junín and Lassa viruses in the Arenaviridae family. This includes work with University of Oxford, optimising Lassa virus ELISA testing in the field for vaccine developer partners and producing additional preclinical infection models.[284] In June 2024, CEPI and European Union launched a funding call on the development of broadly protective Filovirus vaccines, including funding for designing and testing several immunogens against a wide range of viruses with outbreak potential to support building a Filovirus vaccine library.[285] The Oxford Vaccine Group and the Pandemic Sciences Institute have partnered with Univercells to develop RNA vaccines targeting flaviviruses. The collaboration will also explore the production of these vaccines at Oxford's Clinical Biomanufacturing Facility, streamlining and accelerating the development and testing processes.[286]	**Planned partner commitments** In 2025, CEPI plans to launch the GS LEARN initiative (Global South Leaders in Epidemic Analytics and Response Network) to develop leaders in epidemic analytics and response by advancing technical expertise and knowledge in infectious disease modelling across the Global South. The initiative also aims to foster interdisciplinary collaborations within and across regions through the creation and fostering of key global partnerships. CEPI is supporting a predictive modelling project led by Harvard Medical School to develop a computational tool that ranks viral sequences based on the predicted vaccine escape potential of SARS-CoV-2 variants. In 2025 this will expand to include HPAI H5N1, Lassa, and Nipah. This modelling could ensure vaccines are designed to be effective against future strains.[319,320] The UK government's 10-year strategic partnership with Moderna has progressed with the build programme of its UK vaccine manufacturing facility advancing, with the facility's first mRNA vaccine for use in the NHS expected in 2025.[321] **Recommended Priority Actions for 2025:** · While significant technical progress has been achieved in enhancing 100DM response capabilities, greater coordination among global health partners is essential to **advance the vaccine library concept.** This includes fostering a shared understanding of the approach, identifying knowledge gaps, and piloting a pathogen-specific project to explore its practical implementation. · A coordinated coalition of partners including WHO, CEPI, R&D funders, industry, and regulators should advance clinical development of vaccine candidates for priority viral families aligned with the WHO pathogen prioritisation framework and emerging WHO CORCs.

277 Medical Countermeasures, BARDA accelerates development of early-stage antiviral platforms with multiple collaborators.
280 Nature, Self-copying RNA vaccine wins first full approval: what's next?
281 WHO, Malaria vaccine: WHO position paper – May 2024.
282 Valneva, Valneva Receives Marketing Authorization in Europe for the World's First Chikungunya Vaccine, IXCHIQ®.
283 CEPI, CEPI expands partnership with Valneva with $41.3 million to support broader access to world's first Chikungunya vaccine.
284 CEPI, Vaccines R&D pro forma.
285 CEPI, CEPI seeks to fund new innovations for broad protection against Ebola and other deadly Filoviruses.
286 Oxford Cancer, University of Oxford unveils new vaccine development partnership (2024), https://www.cancer.ox.ac.uk/news/university-of-oxford-unveils-new-vaccine-development-partnership.
319 CEPI, Vaccines R&D pro forma.
320 Nicole N. Thadani et al., "Learning from prepandemic data to forecast viral escape," Nature 622, no. 7984 (2023/10/01 2023), https://doi.org/10.1038/s41586-023-06617-0, https://doi.org/10.1038/s41586-023-06617-0.
321 HMG, pro forma.

Topic	Recommendation	2024 Summary progress update	Planned partner commitments and recommended priority actions for 2025
Vaccines R&D		With funding from CEPI, PATH is working with clinical and regulatory stakeholders, developing a study protocol that could be implemented to evaluate available vaccine candidates (or approved vaccines) during a Nipah virus outbreak.[287] PATH will also generate and scale up standardised SARS-CoV-1 and SARS-CoV-2 antibody reagents to support vaccine development.[288] Afrigen Biologics has validated its mRNA platform with AfriVac 2121, a COVID-19 vaccine candidate, and prepares for Good Manufacturing Practices (GMP) inspection in early 2025. Afrigen Biologics is also selecting its own mRNA vaccine candidates for Rift Valley Fever, Gonorrhoea, and Respiratory Syncytial Virus.[289] The Native Antigen Company produces antigens including for nine viral families that are classed as possessing a high PHEIC risk (according to the 2024 update to the WHO Blueprint). They have the capacity to respond rapidly to new pandemic threats, this was recently demonstrated by production of H5N1 hemagglutinin in less than 5 weeks.[290] Thailand's Government Pharmaceutical Organization, with partners from Vietnam, Brazil, U.S., and PATH, received approval for a COVID-19 vaccine based on a Newcastle virus platform, which uses advanced egg-based technology to provide an affordable locally produced booster option.[291] The DCVMN has also been instrumental in both accelerating sustainable regional vaccine manufacturing and supporting partners in advancing vaccine candidates for regional priorities. Notable achievements include Fiocruz's new Brazilian immunology centre and development of preclinical Zika vaccine candidates, while Butantan and Sinergium Biotech are advancing H5N8 and H5N1 influenza vaccine candidates, respectively, as part of the WHO mRNA Tech Transfer Programme.[292,293,294] HERA launched a Call for Proposals on the European Hub for Vaccine Development in May 2024 as part of the EU4Health 2024 work programme, aiming to support vaccine development for priority pathogens with epidemic and pandemic potential, linking vaccine development with clinical trials and activities for scaling manufacturing.[295] Wellcome and CEPI have launched a £38 million funding call to establish or validate CoP for up to 11 diseases lacking licensed vaccines. In parallel they are also working with regulators and other partners to establish a common framework outlining the data requirements for use of a CoP biomarker to support licensure.[296]	• Philanthropic, public, industrial, and other funders should continue to **support development of a diversity of existing and novel vaccine platform technologies**, and innovative technologies for vaccine thermostability and durability, administration routes (e.g., mucosal delivery), and cost-effective, adaptable, and scalable manufacturing processes, and coordinate to advance the most promising technologies into clinical development. • Governments and private and public sector partners, including G7 DFIs, should collaborate with vaccine developers to **establish and implement economic risk-sharing funding models** to leverage and maintain vaccine manufacturing capacity across diverse platform technologies to support both routine immunisation programmes and epidemic/pandemic preparedness via mechanisms including advanced purchase commitments, stockpiling arrangements, pooled procurement systems, and surge capacity agreements.

287 CEPI, CEPI and PATH strengthen partnership to accelerate development of vaccines against diseases with epidemic or pandemic potential (2023), https://cepi.net/cepi-and-path-strengthen-partnership-accelerate-development-vaccines-against-diseases-epidemic-or.
288 CEPI, New project aims to bolster global vaccine preparedness against SARS-CoV-1 and SARS-CoV-2 (2024), https://cepi.net/new-project-aims-bolster-global-vaccine-preparedness-against-sars-cov-1-and-sars-cov-2.
289 Afrigen, pro forma.
290 TNAC, pro forma.
291 PATH, PATH congratulates Thailand on granting conditional approval for emergency use to first locally produced COVID-19 vaccine.
292 Fiocruz, Centro Pasteur Fiocruz de Imunologia e Imunoterapia é inaugurado no Ceará.
293 PAHO, New initiative launched to advance mRNA vaccine development against human avian influenza (H5N1).
294 Butantan, pro forma.
295 ERRIN, Call for proposals on the European Hub for vaccine development (HERA) - CP-g-24-10 (2024), https://errin.eu/calls/call-proposals-european-hub-vaccine-development-hera-cp-g-24-10.
296 Wellcome Trust, Seeking predictors of vaccine efficacy: identifying correlates of protection to support vaccine development.

Topic	Recommendation	2024 Summary progress update	Planned partner commitments and recommended priority actions for 2025
		Since 2021, the Wellcome Leap R3 program, co-funded by CEPI, has developed modular, cell-free DNA and RNA manufacturing technologies deployable in <35 m^2, capable of producing diverse pre-clinical products and millions of vaccine doses daily. Clinical GMP demonstrations are underway, with pre-IND submissions for two saRNA vaccines, a therapeutic mRNA mAb for respiratory infections, and an mRNA T-cell engager for multiple myeloma. The programme aims to create a global network of sustainable biofoundries for innovation and pandemic response.[297] As of November 2024, the R3 program was collaborating with several international partners to scale these advances, including A*STAR which will launch Singapore's non-GMP Nucleic Acid Therapeutics Initiative, integrating automation to improve RNA production efficiency and positioning Singapore as one of the potential future regional hubs.[298] CEPI have been working with several partners on mRNA vaccine development, including BioNTech, SK Bio, and Moderna.[299] They are supporting BioNTech to establish mRNA vaccine R&D, clinical and commercial-scale manufacturing capabilities of a facility in Kigali, Rwanda to support building a sustainable and resilient end-to-end African vaccine ecosystem using COVID-19 mRNA vaccine as a blueprint vaccine for initial technology transfer.[300] CEPI also expanded its partnership with the University of Oxford to enhance the ChAdOx platform's speed and scalability. Similarly, they have signed an agreement with Fiocruz that will strengthen R&D capabilities in viral vectors and mRNA technologies in South America.[301] CEPI launched funding calls for chemistry, manufacturing and controls (CMC) innovations: $17 million has been awarded to fund proof-of-concept studies for innovative technologies, including thermostable mRNA presentations, rapid protein production processes, and enablers such as synthetic DNA.[302] One of the awardees, Lemonex has initiated phase 1 trials of its thermostable mRNA drug delivery technology, which has the potential to both minimise post-mRNA vaccination side effects and improve access to future mRNA vaccines.[303] BARDA have announced up to $500 million in Project NextGen funding for phase 2b trials of novel vaccine delivery methods for COVID-19 including nasal sprays and pills.[304] PATH, CEPI, and ThermoFisher Scientific are all separately carrying out work that supports the development of new vaccines for viruses of pandemic potential including research into novel nucleic acid technologies and delivery platforms.[305,306,307] PATH has been working to improve the market resilience, the local production and sustainability of auto disable syringes.[308]	

297 Wellcome Trust, R3.
298 Technology and Research Agency for Science, Singapore Advances mRNA Manufacturing Capabilities With Opening Of Non-GMP NATi mRNA BioFoundry (2024), https://www.a-star.edu.sg/News/astarNews/news/press-releases/singapore-advances-mrna-manufacturing-capabilities.
299 CEPI, Vaccines R&D pro forma.
300 CEPI, BioNTech and CEPI expand partnership to strengthen Africa's mRNA vaccine ecosystem.
301 CEPI, Mobilising Brazil's manufacturing might to support vaccine production in the Global South (2024), https://cepi.net/mobilising-brazils-manufacturing-might-support-vaccine-production-global-south.
302 CEPI, Regional manufacturing pro forma.
303 CEPI, Vaccines R&D pro forma.
304 U.S. Department of Health and Human Services, BARDA awards up to $500 million in Project NextGen funding for vaccine clinical trials.
305 PATH, pro forma.
306 CEPI, Vaccines R&D pro forma.
307 ThermoFisher, pro forma.
308 PATH, pro forma.

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		The UKHSA has advanced a Hantavirus vaccine candidate and is addressing the global BSL4 capacity shortage through development of pseudo virus assays for Crimean-Congo Haemorrhagic Fever, Sudan Ebola virus, Lassa, and Marburg virus to support clinical trial sample analysis. In partnership with CEPI's Centralised Laboratory Network, UKHSA developed live virus neutralisation assays for mpox, MERS, and SARS-CoV-1, with the mpox assay being transferred to the Uganda Virus Research Institute in July 2024 to strengthen regional research capacity.[309] The UKVN has ongoing work supporting vaccine development in LMICs, this includes work through Innovate UK to develop vaccines and vaccine technologies for epidemic diseases in LMICs and the expansion of a programme of collaborative manufacturing innovation research hubs managed by the EPSRC.[310] An example project includes Afrigen Biologics' collaboration with EnsiliTech on silica-encapsulated thermostable mRNA vaccines, addressing cold chain challenges in resource-limited settings.[311] In September 2024, Vaxxas initiated a phase 1 trial of its needle-free avian flu vaccine microarray patch, which enables lower dose delivery and may improve patient uptake compared to injected vaccines.[312] ThermoFisher is currently developing an enzymatic DNA synthesis technology as an alternative to traditional plasmid DNA scale-up. This process will significantly shorten the production time compared to fermentation-based scale-up by several weeks.[313] CEPI also supports Afrigen Biologics in collaboration with Syngoi to develop synthetic DNA and continuous manufacturing processes to speed up mRNA vaccine development and access.[314,315] Use of computational and AI-assisted tools have been critical to progress CEPI's Disease X Programme and Vaccine Library. CEPI funded Apriori Bio to advance its biology-informed artificial intelligence platform Octavia™, aimed at protecting humanity against rapidly evolving viruses by designing variant-resilient vaccines.[316,317] PATH is also piloting the use of AI for mRNA process development, and comparative lipid nanoparticle (LNP) formulation and analytical characterisation.[318]	
Improvements to Clinical Trials Capability and Regulation Processes	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. 18. Explore the creation of regional mechanisms to coordinate and prioritise clinical trials of DTVs.	In September 2024, WHO launched new guidance for best practices for clinical trials. It aims to enhance clinical research efficiency and provide guidance on sustained clinical trial capacity that is always functional and active for endemic conditions and can pivot in time of emergency or pandemics.[322] In September 2024, the U.S. FDA published final guidance on conducting trials with decentralised elements and draft guidance on integrating RCTs into routine clinical practice. Both sets of guidance aim to promote opportunities to innovate in and streamline clinical trial design.[323]	**Planned partner commitments** WHO will drive actions from their new guidance for best practices for clinical trials. Different parties will be engaged in actions under the umbrella of the WHO clinical trials framework. One example of this is Wellcome's collaboration with WHO to strengthen funder policies and establish best practices for community engagement within clinical trials to ensure meaningful community participation throughout the research process.[341] In 2025 WHO will develop all these actions and stakeholder groups into a global action plan.

309 HMG, pro forma.
310 HMG, pro forma.
311 EnsiliTech, EnsiliTech is proud to announce that it has been awarded a highly competitive research contract from the UK Government's Small Business Research Initiative (SBRI) for the development of the world's first thermally stable mRNA vaccine.
312 Business Wire, Vaxxas Initiates Phase I Clinical Trial of Pre-Pandemic Avian Influenza A Virus (H7N9) Vaccine Delivered Using Vaxxas' Novel High-Density Microarray Patch (HD-MAP).
313 ThermoFisher, pro forma.
314 CEPI, CEPI partners with Afrigen to speed up mRNA vaccine development and access.
315 Afrigen, pro forma.
316 CEPI, Apriori receives funding boost from CEPI to advance AI platform to protect against viral threats (2024), https://cepi.net/apriori-receives-funding-boost-cepi-advance-ai-platform-protect-against-viral-threats.
317 CEPI, Vaccines R&D pro forma.
318 PATH, pro forma.
322 WHO, Guidance for best practices for clinical trials.
323 GCTC, pro forma.

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Improvements to Clinical Trials Capability and Regulation Processes	10. Develop a common regulatory framework that better defines criteria and standards for effectiveness, quality and use cases for diagnostics. 11. Transform the approach to clinical trial regulation, shortening the time to authorise trials and streamlining the requirements and guidelines relating to trial conduct. 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. 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.	GloPID-R continues to drive the implementation of its Roadmap for Clinical Trial Coordination for research funding organisations. GloPID-R also hosts a Clinical Trial Working Group of funders and researchers which supports pandemic preparedness and response by aiming to ensure the clinical trial infrastructure can mount an efficient and coordinated trial response globally. The GloPID-R regional hubs have been effective in coordinating research and clinical trials, the GloPID-R Africa Hub has been working with the GloPID-R Central Secretariat to organise highly specialised mpox meetings with GloPID-R members and other key stakeholders such as Africa CDC and WHO.[324] The Good Clinical Trials Collaborative (GCTC) continues to run 'Good Trials Prism', a capacity strengthening collaboration supporting clinical trials in low-resource settings which is funded by Wellcome and co-led by ADVANcing Clinical Evidence in Infectious Diseases (ADVANCE-ID), Africa Health Research Institute (AHRI), Oxford University Clinical Research Unit (OUCRU), The Global Health Network (TGHN). The ADVANCE-ID network, supported by Wellcome, is building capabilities to conduct its first phase 2 trial for a novel antibiotic drug candidate in 2025 across multiple sites in Asia, and developing their community engagement capabilities and practise.[325] CEPI launched a clinical research preparedness network in West Africa in 2023 to support large-scale clinical trials against priority pathogens. In March 2024 a second funding call was launched to form an East and Central Africa clinical preparedness network. CEPI is continuing to collaborate with existing organisations and networks across Africa (EDCTP), South-East Asia (WHO Coalition of Interested Parties efforts in the South-East Asia Regulatory Network) and Latin America (MoU and Joint Action Plan with PAHO).[326] The African Vaccine Regulatory Forum (AVAREF) of WHO, as the African Medicines Regulatory Harmonisation (AMRH) technical committee on clinical trial oversight, supports the development of guidelines and joint review at the continental level.[327] Efforts are underway to support countries to domesticate the harmonised guidelines through regional economic communities (RECs).[328] Additionally the AUDA-NEPAD and AVAREF are supporting regulatory and ethics oversight harmonisation and strengthening the capacity of scientific reviewers on regulatory and ethics approval of clinical trials. There is a move towards greater regulatory harmonisation in the African region through the operationalisation of the AMA.[329] This work has been driven by AUDA-NEPAD and has recently received a $12.3 million grant from Wellcome.[330] African harmonised guidelines, processes, and templates for evaluating applications for registration of medicinal products have been adopted and pilot joint assessments and listing is underway.	GloPID-R will update their scoping review on 'Addressing challenges for clinical research responses to emerging epidemics and pandemics: a scoping review'. This review aims to synthesise and update solutions to the political, economic, administrative, regulatory, logistical, ethical, and social (PEARLES) barriers affecting the implementation of clinical research (including trial) responses during new, emerging, or re-emerging diseases of pandemic and epidemic potential, to further inform strategies that would enhance pandemic and epidemic preparedness and response.[342] GloPID-R plan to publish a progress report on their Roadmap for Clinical Trial Coordination for research funding organisations. Pandemic PACT are integrating International Clinical Trials Registry Platform data into their platform and also launching their 'living' Rapid Research Needs Assessments platform, whereby existing published research is mapped against a set of emerging infectious diseases research priority domains to identify gaps in the evidence base. Identifying critical knowledge and evidence gaps will inform research prioritisation and coordination of effective, equitable research responses, and generate data to inform the response to improve epidemic and pandemic outcomes.[343] **Recommended Priority Actions for 2025:** • **International and regional clinical trial networks should coordinate** to develop disease-agnostic, multi-functional trial sites capable of adapting to various study types and phases. • WHO should work with regulators, pharmaceutical companies, and trial networks to **develop clear guidelines for emergency trials,** establishing structured protocols and coordination mechanisms for clinical trials in emergency settings. • Regulators and WHO should collaborate to **promote regulatory harmonisation at the regional level,** developing clear processes for joint regulatory reviews, with defined expedited timelines for decision making and approval to ensure that new MCMs can be approved rapidly in future health emergencies. AMA should continue to align regional approval processes.

341 Wellcome Trust, pro forma.
342 GloPID-R, pro forma.
343 GloPID-R, pro forma.
324 GloPID-R, pro forma.
325 Wellcome Trust, pro forma.
326 CEPI, CT & Reg pro forma.
327 AUDA-NEPAD, African Vaccine Regulatory Forum Technical Committee (AVAREF-TC).
328 AUDA-NEPAD, Regional Economic Communities.
329 AUDA-NEPAD, African Medicines Agency (AMA).
330 AUDA-NEPAD, Wellcome Commits US $12.3 Million to Support Regulatory Harmonisation and the Operationalisation of the African Medicines Agency (AMA).

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Improvements to Clinical Trials Capability and Regulation Processes		The continental technical committee on Evaluation of Medicinal Products (EMP) has also adopted an EUL procedure which will support countries in strengthening their capacity to respond to emergencies.[331] In 2024, Ghana has utilised its knowledge as a WHO Maturity Level 3s National Regulatory Authority to support regulatory functions in other African countries.[332] In January 2024 CEPI set up their Regulatory Innovation Consortium which focuses on sharing best practices and innovations in regulatory science. The consortium brings together industry members, researchers, funders, and regulators to increase collaboration and convergence to improve regulatory processes during health emergencies.[333] The NISH, the National Immunisation Technical Advisory Groups (NITAGs) Support Hub, continues to actively support the work of NITAGs in Africa; and EVIDA, the WHO-PAHO initiative on Strengthening Evidence-informed Vaccine & Immunisation Decision making and Appraisal in LMICs initiative, with funding support from Wellcome, has begun to support the work of NITAGs in the Americas and encourage them to collaborate with African NITAGs.[334] The International Conference of Drug Regulatory Authorities (ICDRA) has been instrumental in progressing discussions around regulatory harmonisation, outcomes of the 2024 meeting include calls for more aligned global standards in trial design, particularly in integrating platform technology master files and leveraging cloud-based data platforms.[335] The International Coalition of Medicines Regulatory Authorities (ICMRA) have two groups working on pandemic preparedness measures. The real-world evidence (RWE) working group with representatives from 15 agencies has a focus on preparedness for public health emergencies through collaborative studies. The ICMRA Vaccines Pharmacovigilance Network focuses on COVID-19 but will pivot if another global pandemic arises.[336] Pandemic PACT launched an interactive funding tracker for diseases with pandemic potential and active outbreak trackers that aims to foster stronger collaborations between funders, researchers, and trial networks.[337] CEPI has funded a study at University of Oxford to develop a computational tool and graphical interface to compare suitable clinical trial designs based on virus-, disease-, transmission- and outbreak-specific parameters. This will allow evidence generation and trial design to be quickly selected for a future disease outbreak. CEPI is investing in the Global Vaccine Data Network (GVDN) to deliver safety and pharmacovigilance networks for CEPI priority pathogens and/or vaccine platform techniques in the Global South.[338]	• ICMRA, regulators, and developers should collaborate to adopt **preparatory regulatory approaches,** including platform technology master files, cloud-based data platforms, and shared risk-benefit frameworks to streamline the approval of new MCMs. • **WHO, G7 and G20, should support advancing inter-regional recognition processes,** strengthening inter-regional collaboration and twinning initiatives to support more countries in achieving Maturity Level 3 regulatory status, while encouraging greater parity in the recognition of regional regulatory approvals. • Procurement agencies and donors should recognise diverse regulatory pathways alongside established mechanisms, creating additional market signals for regional production.

331 MA, EMA supports pilot for joint African continental assessment procedures.
332 Ghana FDA, pro forma.
333 CEPI, CT & Reg pro forma.
334 Wellcome Trust, pro forma.
335 ICDRA, The International Conference of Drug Regulatory Authorities.
336 ICMRA, ICMRA Working Group on Real-World Evidence for public health emergencies
337 Nuffield Department of Medicine, New Pandemic PACT research programme launched.
338 CEPI, CT & Reg pro forma.

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Improvements to Clinical Trials Capability and Regulation Processes		CEPI is supporting development of controlled human infection models (CHIM) at Imperial College London through the Mucosal Immunity in human Coronavirus Challenge (MUSICC) consortium, to support the development of virus transmission-blocking coronavirus vaccines and develop standardised assessment approaches of mucosal immunity.[339] CEPI supported generation of evidence on mpox vaccines to inform regulatory decision making, including preparation of a dossier of available data on existing licensed vaccines. The goal of these activities is to enable access to vaccines, to build regional capacity, and to inform the definition of a TPP for next generation pan-orthopox vaccines for use in future outbreaks. CEPI also supported complementary clinical trials aiming to close the evidence gaps in COVID-19 vaccination policy.[340]	
Strengthening Global Surveillance	7. Governments should normalise the use of accurate diagnostics for coronavirus and influenza in point-of-care and nonclinical settings. 8. WHO should support an enhanced role for diagnostics in the surveillance of pandemic threats. 21. Explore the scope for a system that enables biological samples to be collected and shared immediately and unhindered in a pandemic. 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.	WHO published a technical brief to identify the key research areas that would generate high-quality evidence and methods to better inform decision making in global health emergencies. This technical brief outlines the priorities for research in pandemic and epidemic intelligence identified through the prioritisation process.[344] Africa CDC launched the IGS and Data Sharing Platform (DETECT), co-funded by the European Union, to enhance outbreak detection, AMR surveillance, and data sharing across member states.[345] The African Bioinformatics Institute (ABI), supported by Wellcome and the Chan Zuckerberg initiative, was launched aiming to support and develop sustainable genomics research and infrastructure on the African continent, including a focus on pathogen genomics.[346] The IPSN network launched a catalytic grants fund to support scaling up pathogen genomics projects across the world, particularly in LMICs.[347] Wellcome launched a funding call to generate evidence on where dengue and Zika viruses co-circulate and investigate the implications this has on host immune responses and clinical outcomes. Funded projects will also help to design and implement future interventions to reduce dengue and Zika's growing burden and impact on health.[348] Wellcome and FCDO have committed £5 million to co-fund the 'Mpox-GECIVO Africa' study through the African-led MpoxReC consortium. This research will explore genomics, epidemiology, clinical, immunological, and virological outcomes across sites in Nigeria, DRC, and Cameroon, addressing top priorities in the Africa CDC/ WHO mpox R&D plan and showcasing coordinated regional leadership in responding to emerging health threats.[349]	**Planned partner commitments** IPSN plan to launch a second round of catalytic grant funds in 2025 to support partners from LMICs to build capacities in pathogen genomic analysis.[356] Butantan, data.org and PATH will continue to build on their work to advance global surveillance of viruses with pandemic potential.[357,358,359] **Recommended Priority Actions for 2025:** · WHO Hub for Pandemic and Epidemic Intelligence should continue to support national and regional authorities to **implement Collaborative Surveillance** to strengthen data and pathogen sharing mechanisms to support DTV R&D, in collaboration with governments, academia, foundations, CSOs, and international organisations.

339 CEPI, Global consortium plans coordinated human challenge studies in hunt for transmission-blocking coronavirus vaccines (2024), https://cepi.net/global-consortium-plans-coordinated-human-challenge-studies-hunt-transmission-blocking-coronavirus.
340 CEPI, CT & Reg pro forma
344 WHO, Research prioritization for pandemic and epidemic intelligence: technical brief.
345 Africa CDC, Africa CDC launches initiatives to advance molecular diagnostics and genomic surveillance in Africa.
346 Wellcome Trust, We're establishing a new institute to advance genomics in Africa (2024), https://wellcome.org/news/were-establishing-new-institute-advance-genomics-africa.
347 WHO, International Pathogen Surveillance Network launches catalytic grant fund for pathogen genomics.
348 Infectious Disease Award: Understanding dengue and Zika spread, immunity and clinical outcomes (2024), https://wellcome.org/grant-funding/schemes/infectious-disease-award-understanding-dengue-and-zika-spread
349 Wellcome Trust, pro forma.
356 News-Medical.Net, WHO and partners announce grants to boost pathogen genomic surveillance (2024), https://www.news-medical.net/news/20241126/WHO-and-partners-announce-grants-to-boost-pathogen-genomic-surveillance.aspx.
357 Butantan, pro forma.
358 data.org, pro forma.
359 PATH, pro forma.

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		The 7-1-7 Alliance, a country-led initiative championed by Resolve to Save Lives (RTSL) continues to promote a target of detecting outbreaks within 7 days, reporting them in 1 day, and responding within 7 days.[350] ISARIC has received funding for its third phase (ISARIC 3.0) which will focus on establishing decentralised, LMIC-led research hubs, developing innovative data tools, strengthening clinical research capacity, and conducting collaborative research on pathogens like Nipah, dengue, filoviruses, and respiratory infections as determined by high priority needs by member networks.[351] Data.org have been working to create interoperable open-source tools for pandemic preparedness; in the last year they have put an increased focus on training to increase the use of these tools globally, with a programme in collaboration with WHO to roll out free-to-use open-source R-based pandemic and epidemic intelligence analytics tools and training in ten African countries starting in 2025.[352] HERA, in cooperation with the European Commission Joint Research Centre (JRC), has launched the Global Consortium for Wastewater and Environmental Surveillance for Public Health (GLOWACON) which led to the Global Wastewater Sentinel System for the early detection, prevention, and real-time monitoring of epidemic threats and outbreaks. HERA is using this system to develop the ATHINA system (Advance Technology for Health Intelligence and Action), ensuring its interoperability with other existing platforms.[353] PATH is working with the UK Medicines and Healthcare products Regulatory Agency (MHRA) to create internal process controls for diseases with pandemic potential for optimisation and harmonisation of sampling methods for wastewater surveillance.[354] Airfinity have developed predictive models for disease forecasting, including a meteorological model for dengue, providing a potential early warning system for future epidemics.[355]	• Governments should adopt a **One Health Approach** to address the interconnectedness of climate change, agriculture, and emerging infectious diseases, and support feeding digitally connected diagnostics into the surveillance system. • **Funders should continue to support capacity building in LMICs:** Enhance competencies in pathogen genomic surveillance, bioinformatics, data science, and real-time monitoring to detect outbreaks earlier and more effectively. • The INB should set out a **framework for Access and Benefit Sharing** that enables equitable R&D efforts for DTVs.
Regionalised manufacturing of DTVs	16. Governments and industry should share risk to maintain vaccine manufacturing capacity. Note: Recommendation 16 extended to cover manufacturing capacity across DTVs	In January 2024, the RVMC Secretariat published their framework for regionalised vaccine manufacturing, and in June they published their strategy. The framework lists eight areas where focus and development are needed while the strategy outlines the roles of the collaborative for the next three years.[360,361] PAHO, USAID, and RVMC held a workshop to assess regional capabilities and explore collaboration opportunities for strengthening vaccine innovation and production, including a comprehensive analysis of existing research on these capacities.[362]	**Planned partner commitments** CEPI have initiated due diligence to potentially onboard a further two facilities in Latin America and the Western Pacific region to the CEPI Vaccine Manufacturing Facility Network to join Aspen, IPD, BioFarma, SII, Fiocruz-BM. [385]

350 RTSL, 7-1-7 Alliance (2024), https://717alliance.org/.
351 Wellcome Trust, pro forma.
352 data.org, pro forma.
353 HERA, 2024 HERA Work Plan.
354 PATH, pro forma.
355 Airfinity, Biorisk.
360 Regionalized Vaccine Manufacturing Collaborative, A Framework for Enhancing Vaccine Access Through Regionalized Manufacturing Ecosystems.
361 Regionalized Vaccine Manufacturing Collaborative, Strategy 2024-2027.
362 PAHO, PAHO leads regional collaboration to analyze strategic information on vaccine innovation and production capacities in Latin America and the Caribbean (2024), https://www.paho.org/en/news/14-10-2024-paho-leads-regional-collaboration-analyze-strategic-information-vaccine-innovation.
385 CEPI, Regional manufacturing pro forma.

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Regionalised manufacturing of DTVs		PATH have developed a dashboard of information on diagnostics and vaccine manufacturing companies with a presence in Africa, Latin America and South-East Asia to increase their visibility within the regions and provide an overview of their product portfolios and quality systems.[363] In October 2024 at the G20 Health Minister's meeting, the G20 Coalition on Local and Regional Production, Innovation, and Equitable Access was established. This aims to strengthen manufacturing capacities for local and regional health products, promote sustainable global production and innovation networks to facilitate better access to DTVs for neglected disease and persons in vulnerable situations, which could also be repurposed for other diseases and health emergencies. The Coalition centres on voluntary cooperation while fostering collaboration with, and avoiding duplication of multilateral and other relevant initiatives.[364] BioPhorum is a community of companies across the full value chain of the biopharmaceutical manufacturing operations and ancillary support activities. The membership of the collaboration includes 125 major industry companies and their key suppliers. In 2024 they published a Pandemic Timeline to understand how industry responded to the COVID-19 pandemic and understand any gaps that would need to be filled ahead of the next pandemic.[365] They also have a number of workstreams ongoing that are focused on increasing manufacturing robustness and resilience at the time of a crisis.[366] The mRNA Technology Transfer Programme continues to make progress on the objective to develop sustainable capabilities for the development of mRNA technologies in regions that are looking to expand this. With support of WHO, MPP and PAHO, Sinergium Biotech, a partner in the mRNA Technology Transfer Programme, has been working to develop candidate H5N1 vaccines.[367,368] Fiocruz Bio-Manguinhos and MPP signed an MoU to support establishing a pipeline of RNA-based vaccines for both epidemic and pandemic threats, improving the formulation of RNA-based vaccines, and testing new lipids synthesised as part of the mRNA Programme's new Lipids Discovery Initiative, and technology transfer from Afrigen Biologics.[369] To support regionalised manufacturing, the MPP supported the use of regionally focused expressions of interest for future MPP-licensed products and the issuance of conditional licences, where companies that show promise but do not yet fully meet requirements can receive a commitment for future licensing once specified standards are met.[370]	Over the coming year RVMC plan to publish/develop the following: global vision document for regionalised manufacturing, initial analysis of relevant facts for rational decision making, including a publicly accessible dashboard and a baseline report across the framework and regions. Alongside this they will work with partners to deliver support packages, understand preferences for an inter-regional supply chain convening mechanism, map funders interests and build foundations for a first sustainable markets global gathering to further inter-regional collaboration around predictable demand to sustain regionalised vaccine manufacturing efforts.[386] PATH plans to continue providing technical assistance to LMIC vaccine manufactures working to advance high-quality vaccines to the global market through the Gates Foundation supported Sustaining Vaccine Manufacturer's project.[387] **Recommended Priority Actions for 2025:** • RVMC, DCVMN partners, CEPI, G20 Coalition on Local and Regional Production, Innovation, and Equitable Access, and partners should **promote sustainable practices in manufacturing globally and support regional coordination:** Establish harmonised approaches for facilities and pooled procurement to provide predictable demand and sustainability across regions. Enhance technology transfer: Move beyond fill-and-finish to enable **comprehensive geo-diversified drug substance manufacturing capabilities** in LMICs. • Funders and developers should support **development of multi-purpose production platforms** that can maintain routine manufacturing while enabling rapid pandemic response. • Industry stakeholders, governments, and international organisations should collaborate to **strengthen supply chain security and resilience** by implementing digital monitoring systems, diversifying raw material sources, and fostering global cooperation. • Governments should **incentivise local manufacturing through equitable procurement preferences** and support for existing initiatives such as RVMC and the G20 Coalition on Local and Regional Production.

363 PATH, Diagnostic companies across Africa, Latin America, and Southeast Asia.
364 G20, Rio de Janeiro Declaration of the G20 Health Ministers.
365 BioPhorum, Pandemic timeline: supply chain disruptions (2024), https://www.biophorum.com/download/pandemic-timeline-supply-chain-disruptions/.
385 CEPI, Regional manufacturing pro forma.
386 CEPI, Regional manufacturing pro forma.
387 PATH, pro forma.
366 BioPhorum, pro forma.
367 Medicines Patent Pool, mRNA Technology Transfer Programme, https://medicinespatentpool.org/what-we-do/mrna-technology-transfer-programme.
368 PAHO, New initiative launched to advance mRNA vaccine development against human avian influenza (H5N1).
369 Medicines Patent Pool, Fiocruz Bio-Manguinhos and MPP Sign MoU to Enhance mRNA Vaccine Production (2024), https://medicinespatentpool.org/news-publications-post/fiocruz-bio-manguinhos-and-mpp-sign-mou-to-enhance-mrna-vaccine-production.
370 Medicines Patent Pool, pro forma.

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Regionalised manufacturing of DTVs		PAHO and Africa CDC have signed an agreement to collaborate on access to MCMs; each organisation will leverage their specific expertise to strengthen regionalised manufacturing, innovation and regulation.[371] In June, Gavi launched the AVMA, a financing instrument that will make up to $1.2 billion available over ten years to support the sustainable growth of Africa's manufacturing base.[372] Africa CDC, the Clinton Health Access Initiative (CHAI), and PATH updated mapping of African vaccine manufacturers current capacity and capabilities to support coordinated efforts.[373] CEPI and European Union partnered with Valneva to support broader access to the first licensed Chikungunya vaccine, supporting technology transfer to Instituto Butantan for LMIC market access, funding late-stage studies to support future regulatory approval in Brazil, and securing access to an emergency stockpile.[374] PAHO, Fiocruz, and Butantan collaborated to deliver vaccine development and manufacturing training for Mercosur states parties and associates.[375] Vaxthera has completed the construction of its vaccine facility in Colombia and is collaborating with Univercells to develop mRNA vaccines using automated equipment, strengthening health sovereignty and positioning Vaxthera as a scientific research hub for Latin America. Fiocruz are also collaborating with Univercells and Quantoom Biosciences on the development of self-amplifying RNA vaccines.[376,377] PATH's Centre for Vaccine Innovation and Access (CVIA) is continuing to improve access to vaccines by working in partnership with vaccine manufacturers globally and providing technical assistance to manufacturers in LMICs.[378] CEPI CMC teams have co-developed templates and guidance for technology transfer, process development, and a CMC framework to support vaccine developers working with industry partners and organisations like PATH and PAHO.[379] CEPI signed agreements with vaccine manufacturing facilities in Latin America (Fiocruz), Africa (BioNTech) and South Asia (Serum Institute of India). They also support regionalised manufacturing through technical consultation, supplying access to materials and building implementing partnerships to enable projects globally.[380] The Malaysian Genome and Vaccine Institute (MGVI) is progressing plans to deliver on the National Vaccine Development Roadmap for local vaccine manufacturing.[381]	• MPP should work with partners to **expand to expand preparatory voluntary licensing** systems. • Developers should explore synergies between Pandemic Preparedness and One Health by leveraging livestock vaccines as a pathway to establish biomanufacturing ecosystems in resource-limited settings, fostering sustainable economic models while reducing the risk of zoonotic spillover to humans.

371 PAHO, PAHO and Africa CDC strengthen collaboration to address access to essential medicines and vaccines.
372 Gavi, African Vaccine Manufacturing Accelerator (AVMA).
373 Africa CDC, The change in African vaccine manufacturing landscape (2024), https://africacdc.org/news-item/the-change-in-african-vaccine-manufacturing-landscape/.
374 CEPI, CEPI expands partnership with Valneva with $41.3 million to support broader access to world's first Chikungunya vaccine.
375 PAHO, PAHO - FIOCRUZ - Butantan Vaccine Development and Production Course ends (2023), https://www.paho.org/en/news/17-11-2023-paho-fiocruz-butantan-vaccine-development-and-production-course-ends.
376 Vaxthera, Colombia avanza en la búsqueda de su soberanía sanitaria, gracias a la construcción de la planta de vacunas de VaxThera (2024), https://www.vaxthera.com/en/w/colombia-avanza-en-la-b%C3%BAsqueda-de-su-soberan%C3%ADa-sanitaria-gracias-a-la-construcci%C3%B3n-de-la-planta-de-vacunas-de-vaxthera
377 The Pharma Letter, Belgium and Brazil join forces to advance RNA-based therapies (2024), https://www.thepharmaletter.com/belgium-and-brazil-join-forces-to-advance-rna-based-therapies.
378 PATH, pro forma.
379 Anna Särnefält et al., "A Strategic Guide to Improve and De-Risk Vaccine Development: CEPI's CMC Framework," PDA Journal of Pharmaceutical Science and Technology 78, no. 5 (2024), https://doi.org/10.5731/pdajpst.2023.012912, https://journal.pda.org/content/pdajpst/78/5/613.full.pdf.
380 CEPI, Regional manufacturing pro forma.
381 Institute for Medical Research Malaysia, pro forma.

Topic	Recommendation	2024 Summary progress update	Planned partner commitments and recommended priority actions for 2025
Regionalised manufacturing of DTVs		In 2024 BioFarma became a member of UK-SEA Vax Hub initiated by University of Sheffield which aims to share knowledge related to vaccine development, especially mRNA vaccines in South-East Asia.[382] Regional pooled procurement was reaffirmed as a key priority for vaccine security by the ASEAN, a meeting was held in September 2024 on vaccine security and self-reliance where a steering committee was established to drive this.[383] WHO Eastern Mediterranean Regional Office (EMRO) is exploring how to use pooled procurement mechanisms to improve LMIC access to medicines in the region while enhancing regional production capacities.[384]	
Sustainable Pandemic Financing & Procurement for Equitable Access	13. The International Monetary Fund (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. 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. 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.	There were three G20 JFHTF priorities this year: (i) unpacking the centrality of financing initiatives designed to tackle the social determinants of health; (ii) increasing resource mobilisation to the health sector through assessing "debt for health" (DfH) swap arrangements; and (iii) improving the assessment of global health, and social and economic vulnerabilities.[388] These priorities were chosen in recognition of the significant inequities exposed by the pandemic, with the poorest and most vulnerable suffering both the highest risks and experiencing the worst health, social, and economic outcomes. This also acknowledges the severe pressure on health and social spending budgets, exacerbated by high levels of debt and debt servicing costs. Over the past year there have been several key deliverables under the JFHTF priorities: A social determinants of health policy note on the selection of indicators that are relevant for the framework of health, social and economic vulnerabilities to pandemics building on the Presidency Side Event held in June 2024; a policy paper on Debt for Health swaps building on the IFA Working Group discussion on debt for development swaps; an operational playbook for response financing to health emergencies and pandemics; and a global report on the framework for health, social, and economic vulnerabilities and risks (FEVR) related to pandemics.[389] In collaboration with the World Bank and WHO, JFHTF responded to the mpox outbreak with a statement announcing a financial tracking mechanism that tracks contributions against the pillars of the mpox Continental Preparedness and Response Plan for Africa.[390]	**Planned partner commitments** CEPI will leverage Imperial College London's SARS-X model to further investigate the optimisation options for PPR investments. This will be coordinated with and complementary to the modelling work undertaken by WHO and the G20 JFHTF. Initial findings from the modelling demonstrate significant returns on vaccine investments for pandemic preparedness and response, and the importance of combining both preparatory investments (R&D, enabling technologies and adaptable/ scalable manufacturing capacity) and surge financing to accelerate pathogen-specific vaccine R&D and at-scale manufacturing. Pandemic Action Network will continue to champion, and hold leaders accountable for implementing the policies and investments needed to ensure the world is better prepared for pandemic threats, including advancing the 100DM, including: • Pushing for the completion of a meaningful Pandemic Agreement that cements agreements on core issues for equity and access, such as technology transfer. • Championing continued and increased investments in pandemic preparedness– domestically, regionally, and globally– including those that will support an equitable R&D ecosystem.

382 BioFarma, pro forma.
383 Bangkok Post, NVI and Partners Take Major Step Toward ASEAN Vaccine Security (2024), https://www.bangkokpost.com/thailand/pr/2872037/nvi-and-partners-take-major-step-toward-asean-vaccine-security.
384 WHO, High-level panel discussion on health in Eastern Mediterranean Region explores ways to move from crisis to opportunity, https://www.emro.who.int/media/news/high-level-panel-discussion-on-health-in-eastern-mediterranean-region-explores-ways-to-move-from-crisis-to-opportunity.html.
385 CEPI, Regional manufacturing pro forma.
386 CEPI, Regional manufacturing pro forma.
387 PATH, pro forma.
388 G20, G20 Joint Finance and Health Ministerial Meeting: Chair's Statement (2024), https://g20.utoronto.ca/2024/241031-finance-and-health.html#:~:text=As%20a%20contribution%20towards%20this,DfH)%20swap%20arrangements%3B%20and%20(
389 G20 JFHTF, pro forma.
390 G20, G20 Brazil Presidency Press Statement on G20 Joint Finance and Health Ministers' Statement on Mpox Response.

Topic	Recommendation	2024 Summary progress update	Planned partner commitments and recommended priority actions for 2025
Sustainable Pandemic Financing & Procurement for Equitable Access	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 high-income countries (HICs) are supplied. 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.	CEPI launched the Preparedness and Surge Financing Modelling Project to guide policy discussions on pandemic preparedness and surge financing. CEPI engaged experts from Linksbridge SPC, the University of Chicago, Dartmouth College, and Imperial College London to conduct a set of cost-impact analyses to help policymakers understand the costs, benefits, and trade-offs of different preparedness investments.[391] Gavi set up a DZF for Vaccines that can mobilise up to $2.5 billion in risk-tolerant surge and contingent capital to enable Gavi to quickly meet the demand for vaccines in a PHEIC. As part of the DZF, Gavi also launched the First Response Fund in June 2024, a $500 million pool of immediately available, at-risk capital designed to be deployed in public health emergencies.[392] In September 2024, Gavi used the newly established First Response Fund to secure 500,000 doses of MVA-BN mpox vaccine.[393] Gavi also expanded its $1 billion frontloading facility with DFC, enabling Gavi to access surge financing backed by donor pledges for emergencies beyond COVID-19, as well as for routine immunisation programmes, complementing the European Investment Bank's existing EUR 1 billion facility and the access to capital markets provided by the International Finance Facility for Immunisation.[394] The Pandemic Fund has allocated rounds of funding to boost pandemic preparedness to increase laboratory capacity, health workforce, and surveillance systems. It also provided accelerated funding for the mpox response.[395]	• Continued development and funding to support a MCM platform, prepositioned to be able to act quickly during an emergency. • Elevating and sustaining political will and attention needed to maintain pandemic PPR as a high-level, whole-of-government, whole-of-society priority. **Recommended Priority Actions for 2025:** • Governments should work with Gavi, G7 DFIs, G20 JFHTF, and partners to **support and implement recommendations on the Surge Financing Initiative, stockpiling strategies, and advanced market commitments.** • GloPID-R funders should launch a joint call to fund pandemic preparedness research projects to align resources and prevent duplication, demonstrating a coordinated funding approach. • Pandemic Fund should expand and diversify funding sources, and ensure regional bodies are involved in setting priorities and funding decisions.

391 CEPI, sustainable financing pro forma.
392 Gavi, How day zero financing could help protect the world during the next pandemic.
393 Usher, "Mpox puts Gavi's new pandemic fund to the test."
394 U.S. DFC, DFC Announces More Than $1.8 Billion in Investments and New Initiatives at U.N. General Assembly.
395 The Pandemic Fund, Pandemic Fund Allocates Second Round of Grants to Boost Pandemic Preparedness in 50 Countries.

Annex B:

Secretariat Governance detail

STEERING GROUP

The Secretariat is led by a small Steering Group which provides oversight, accountability, and strategic direction. The Steering Group meets on a quarterly basis and comprises representatives from the following organisations:

Select governments, including representatives from current, past, and incoming G7 and G20 presidencies
World Health Organization (WHO)
Wellcome Trust
Bill and Melinda Gates Foundation (BMGF)
International Federation of Pharmaceutical Manufacturers & Associations (IFPMA)
Science and Technology Expert Group (STEG) Co-Chairs
Dr Mona Nemer, Chief Science Adviser for the Canadian Government

SCIENCE AND TECHNOLOGY EXPERT GROUP

The STEG provides technical input to the Secretariat. Reporting to the Steering Group, it delivers an assurance function for the annual report against the 100DM recommendations and galvanises support from the scientific community on pandemic preparedness through meetings, working groups, and assessments. It has subgroups focusing on specific issues, including diagnostics, therapeutics, manufacturing, clinical trials and regulatory matters, and R&D coordination.

Dr Victor Dzau	President of the National Academy of Medicine	U.S. (Co-chair)
Shingai Machingaidze	Head of Africa Strategy and Engagement at CEPI	South Africa (Co-chair)
Dr Rick Bright	Bright Global Health, Former Director of BARDA	U.S.
Hala Audi	Chief Alliance Officer at Univercells & CEO of Unizima	UK
Dr Kelly Chibale	Professor of Organic Chemistry at the University of Cape Town	South Africa
Professor Tan Chorh Chuan	Chief Health Scientist, Ministry of Health, Singapore Executive Director, MOH Office for Healthcare Transformation	Singapore
Dr Delese Mimi Darko	Chief Executive, Food and Drugs Authority Ghana	Ghana
Dr Ruxandra Draghia-Akli	Executive Vice-President, Head of Research and Development at Novavax	U.S.
Dr Ranna Eardley-Patel	Senior External Stakeholder and Project Lead, Manufacturing & Supply Chain, Division CEPI	UK
Professor George Gao	Dean of the Savaid Medical School of the University of Chinese Academy of Sciences	China
Professor Ken Ishii	Director of the International Research and Development Centre for Mucosal Vaccines, University of Tokyo	Japan
Dr Yenew Kebede	Head, Division of Laboratory Systems & Networks at Africa CDC	Ethiopia
Professor Teresa Lambe OBE	Professor of Vaccinology and Immunology at the University of Oxford	UK
Dr Amadou Sall	CEO of Institut Pasteur de Dakar	Senegal
Dr Umesh Shaligram	Executive Director, Serum Institute of India Private Limited	India
Dr Mariângela Simão	Former WHO Assistant Director-General for Drug Access Vaccines and Pharmaceuticals	Brazil
Dr Lynda Stuart	Executive Director of the Institute for Protein Design at the University of Washington School of Medicine	U.S.
Dr Renu Swarup	Former Secretary of the Department of Biotechnology, Ministry of Science & Technology, Government of India	India
Dr Jean-Francois Toussaint	Head of Research and Development at Sanofi Vaccines	France
Dr Niteen S Wairagkar	Founder and CEO, Vaccines for All, Consultant for Africa CDC Partnership for Africa Vaccine Manufacturing, Consultant in Vaccine Development at CEPI	India
Dr Haruko Yamamoto	Director of the Department of Data Science, National Cerebral & Cardiovascular Center	Japan

IPPS SECRETARIAT

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Colleen Loynachan	Senior Technical Adviser
Cornelius Self	Science Policy Officer
Heulwen Philpot	Head of Secretariat
Pippa McCarthy	Team Coordinator
Sheila Mburu	Deputy Head of Secretariat
Thomas Collin-Lefebvre	Strategic Planning and Monitoring Manager (CEPI secondee)

Annex C:

Additional Contributors

The Secretariat would like to extend their thanks to representatives of all organisations listed below who have contributed to the 2024 100DM implementation report and ongoing efforts to prepare MCMs for pandemic response. The Secretariat would like to thank colleagues at Impact Global Health, including Dr Lindsay Keir and Juliette Borri, for their contributions to the 100DM Scorecard, the mpox case study and review of the report.

- **Africa CDC**
- **African Union Development Agency - New Partnership for Africa's Development (AUDA-NEPAD)**
- **Afrigen Biologics**
- **Airfinity ltd**
- **Bill & Melinda Gates Foundation (BMGF)**
- **Bio Farma**
- **Bio-Manguinhos/Fiocruz**
- **Biophorum**
- **Coalition for Epidemic Preparedness Innovations (CEPI)**
- **Cumming Global Centre for Pandemic Therapeutics (CGCPT)**
- **Data.org**
- **Developing Countries Vaccine Manufacturers Network (DCVMN)**
- **Drugs for Neglected Diseases initiative (DNDi)**
- **European Commission, Health Emergency Preparedness and Response (HERA)**
- **European Medicines Agency (EMA)**
- **FDA Ghana**
- **Foundation for Innovative New Diagnostics (FIND)**
- **G20 Joint Task Force on Finance and Health (JFHTF)**
- **Gavi The Vaccine Alliance**
- **Global Access Diagnostics (GADx)**
- **Global Research Collaboration for Infectious Disease Preparedness (GloPID-R)**
- **Good Clinical Trials Collaborative (GCTC)**
- **Government of Japan**
- **Impact Global Health**
- **Instituto Butantan**
- **International AIDS Vaccine Initiative (IAVI)**
- **International Coalition of Medicines Regulatory Authorities (ICMRA)**
- **International Federation of Pharmaceutical Manufacturers and Associations (IFPMA)**
- **INTREPID Alliance**
- **Malaysia, Ministry of Health**
- **Medicines Patent Pool (MPP)**
- **Moderna**
- **Native Antigen Company**
- **Pan American Health Organization (PAHO)**
- **Pandemic Action Network (PAN)**
- **Pandemic Sciences Institute, University of Oxford**
- **Program for Appropriate Technology in Health (PATH)**
- **Rapidly Emerging Antiviral Drug Development Initiative (READDI)**
- **Regionalised Vaccine Manufacturing Collaborative (RVMC)**
- **Serum Institute of India Private Limited**
- **Singapore Government**
- **SPRIND**
- **Thermo Fisher Scientific**
- **UK Government: UKHSA, DHSC**
- **Unitaid**
- **Varro Life Sciences**
- **Wellcome**
- **World Health Organisation (WHO)**

Annex D:

Methodology

This report provides detailed coverage of progress against the 100DM and each of the 25 recommendations (from January to December 2024), based on three data sources, collected in Q4 of 2024:

- **Desk research for relevant documents and datasets**
- **Structured interviews with key global health and PPR stakeholders**
- **40+ pro forma surveys from key stakeholders (**listed in contributors)

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 fora
Annual reports and press releases from relevant private sector organisations
Peer reviewed research literature from academic institutions

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 2024
Plans to take forward 100DM and proposed milestones
Alignment of 100DM with ongoing priorities and approach to implementation
Organisations identified as collaborators and engagement framework
Barriers, risks, and enablers to achieving 100DM
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 and STEG.

Annex E:

Definition of 100DM Scorecard Indicators

	INDICATORS	CATEGORY	DEFINITION	SOURCE
	R&D funding for diagnostics, vaccines and therapeutics (DTV)	Now	This indicator shows the total R&D funding invested by disease broken down by donor over a rolling 4-year period. For Scorecard 2.0, published in January 2025, this was financial years 2020-2023. This indicator is based on the scope of the G-FINDER project. G-FINDER tracks and analyses global investment in the research and development of new health technologies for global health issues such as neglected diseases, emerging infectious diseases, and sexual & reproductive health issues. G-FINDER does not, and is not intended to, capture investment in the entire spectrum of global health research. Many research activities that are extremely important for global health are excluded from this project because they are not related to the development of new tools for the diseases included in the scope.	Impact Global Health's (IGH) G-FINDER R&D funding data.[396]
	Approved products	Now	This indicator shows where vaccines, diagnostics and therapeutics have been approved for use for each disease. Approved products were defined as finished pharmaceutical products, drugs, vaccines, biologics, or diagnostics that had been granted a marketing authorisation by a medicines regulatory authority or had obtained WHO prequalification. A preliminary list of approved products was identified through a normative literature review of treatment guidelines, WHO position papers, and essential medicines and diagnostic list databases. This preliminary list was then cross-referenced against regulatory authority databases.[397] The outer section of the visualisation also shows where products have been approved for use in LMICs. LMIC approval was defined as a product being approved by a National Regulatory Authorities (NRAs) of vaccine producing countries of maturity level 3 or above (as defined by WHO Listed Authorities framework) or has WHO prequalification.[398] For Scorecard 2.0, published in January 2025, the data was updated for the period 30 August 2023 to 30 September 2024.	IGH's infectious disease R&D tracker data,[399] FIND,[400] and additional data sources for COVID-19[401,402,403,404] MERS,[405] Ebola,[406] and SARS-CoV-1.[407,408]

396 Impact Global Health, G-FINDER data portal: tracking funding for global health R&D.
397 Impact Global Health, Infectious Disease R&D Tracker.
398 Impact Global Health, Infectious Disease R&D Tracker.
399 Impact Global Health, Infectious Disease R&D Tracker.
400 FIND, FIND maintains a searchable directory of diagnostic tests for various diseases under the DxConnect umbrella., https://finddx.shinyapps.io/testdirexplorer_beta/.
401 Biotechnology Innovation Organisation, Vaccines & Biodefense, https://www.bio.org/policy/human-health/vaccines-biodefense.
402 WHO, The selection and use of essential in vitro diagnostics - TRS 1031 (2021), https://www.who.int/publications/i/item/9789240019102.
403 US FDA, At-Home OTC COVID-19 Diagnostic Tests, https://www.fda.gov/medical-devices/coronavirus-covid-19-and-medical-devices/home-otc-covid-19-diagnostic-tests.
404 FIND, FIND maintains a searchable directory of diagnostic tests for various diseases under the DxConnect umbrella.
405 Jaime Castillo-León, Ramona Trebbien, John J. Castillo, and Winnie E. Svendsen, "Commercially available rapid diagnostic tests for the detection of high priority pathogens: status and challenges," 10.1039/D0AN02286A, Analyst 146, no. 12 (2021), https://doi.org/10.1039/D0AN02286A, http://dx.doi.org/10.1039/D0AN02286A.

INDICATORS	CATEGORY	DEFINITION	SOURCE
Clinical candidates tested in humans	Future Readiness	This indicator shows the number of candidates for each disease that are being tested in humans. These are broken down by R&D stage and include phase 1, 2, 3 for vaccines and therapeutics and late-stage development for diagnostics. Candidates were defined as potential drugs, vaccines, vector control products, diagnostics, or platform technologies, currently under investigation that had yet to be approved by a medicines regulatory authority.[409] For Scorecard 2.0, published in January 2025, the data was updated for the period 30 August 2023 to 30 September 2024.	IGH's infectious disease R&D tracker data,[410] FIND,[411] ICTRP,[412] CT.gov,[413] Linksbridge,[414] GHTC[415] and additional data sources for COVID-19.[416]
Platform technologies	Future Readiness	This indicator shows if platform technologies are being used to develop clinical candidates. The outer section shows where multiple technologies (i.e., >3) are being applied to the pipeline. The platform technology category includes vaccine, drug, and biologics platforms; adjuvants and immunomodulators; and general diagnostic platforms.	IGH's infectious disease R&D tracker data, and additional data sources for COVID-19.[417]
Use of animal rule to support licensure	R&D enablers	This indicator shows where the animal rule, has been used to support product licensure. The animal rule is a principle for an alternative licensure pathway to allow for the approval of drugs and biological products when human efficacy studies are not feasible and is instead based on well-controlled animal studies, when the results of those studies establish that the drug or biologic product is reasonably likely to produce clinical benefit in humans. For Scorecard 2.0, published in January 2025, the data was updated for the period 30 August 2023 to 30 September 2024	U.S. FDA[418] and EMA.[419]

406 Hokkaido University, Democratic Republic of the Congo approves "QuickNavi™-Ebola" kit for the detection of Ebola virus antigens (2024), https://www.global.hokudai.ac.jp/blog/democratic-republic-of-the-congo-approves-quicknavi-ebola-kit-for-the-detection-of-ebola-virus-antigens/.
407 Eiken Genome Site, https://loopamp.eiken.co.jp/product/loopamp-ivd/sars-cov.html.
408 https://www.mhlw.go.jp/houdou/2003/12/h1218-1.html409 Impact Global Health, Infectious Disease R&D Tracker.
409 Impact Global Health, Infectious Disease R&D Tracker.
410 Impact Global Health, Infectious Disease R&D Tracker.
411 FIND, FIND maintains a searchable directory of diagnostic tests for various diseases under the DxConnect umbrella.
412 WHO, International Clinical Trials Registry Platform (ICTRP), https://www.who.int/clinical-trials-registry-platform.
413 National Library of Medicine, ClinicalTrials.gov, https://clinicaltrials.gov/.
414 Linksbridge, News, https://linksbridge.com/news.
415 Global Health Technologies Coalition, News, https://www.ghtcoalition.org/news.
416 WHO, The selection and use of essential in vitro diagnostics - TRS 1031.
417 WHO, The selection and use of essential in vitro diagnostics - TRS 1031.
418 US FDA, CDER DRUG AND BIOLOGIC ANIMAL RULE APPROVALS, https://www.fda.gov/media/150191/download?attachment.
419 EMA, List of medicinal products under additional monitoring, https://www.ema.europa.eu/en/documents/additional-monitoring/list-medicinal-products-under-additional-monitoring_en.pdf.

	INDICATORS	CATEGORY	DEFINITION	SOURCE
	Generally accepted correlates of protection	R&D enablers	This indicator shows where there are generally accepted correlates of protection as defined by CEPI.	Wellcome- and CEPI[420] and Wellcome Vaccine Ecosystems.[421]
	WHO TPPs	R&D enablers	This indicator shows which diseases have active WHO Target Product Profiles for vaccines, diagnostics and therapeutics.	IGH's infectious disease R&D tracker data[422] and WHO TPP directory.[423]
	R&D funding for platform technologies	Disease X	This indicator shows total R&D funding invested into platform technologies broken down by donor over a rolling 4-year period. For Scorecard 2.0, published in January 2025, this was financial years 2020-2023. WHO recognises Disease X as an unknown pathogen that could cause a serious international epidemic. In G-FINDER this is captured as non-disease-specific R&D, for this indicator it includes the following categories: Therapeutic platforms include drug and biologic delivery platforms; Vaccines include vaccine platforms and adjuvants and immunomodulators.	G-FINDER R&D funding data.[424]

420 Wellcome Trust, Seeking predictors of vaccine efficacy: identifying correlates of protection to support vaccine development.
421 Wellcome Trust, Effective Vaccine Ecosystem (2020), https://cms.wellcome.org/sites/default/files/2021-10/effective-vaccine-ecosystem-equipped-to-meet-challenges-of-future-infectious-disease-threats.pdf?_gl=1*ykx9jc*_gcl_au*NTY2NDQxMzA5LjE3MzE5MzQ4MDc.
422 Impact Global Health, Infectious Disease R&D Tracker.
423 WHO, Target product profile directory, https://www.who.int/tools/target-product-profile-database.
424 Impact Global Health, G-FINDER data portal: tracking funding for global health R&D.

Annex F:

Table of Abbreviations

Abbreviation	Definition
100DM	100 Days Mission
ABI	African Bioinformatics Institute
ACTIV	Accelerating COVID-19 Therapeutic Interventions and Vaccines
AESOP	Alert-Early System for Outbreaks with Pandemic Potential
Africa CDC	Africa Centres for Disease Control and Prevention
AHRI	Africa Health Research Institute
AI	Artificial Intelligence
AMA	African Medicines Agency
AMR	Antimicrobial Resistance
AMRH	African Medicines Regulatory Harmonisation
ASAP	AI-driven Structure-enabled Antiviral Platform
ASEAN	Association of Southeast Asian Nations
ATHINA	Advance Technology for Health Intelligence and Action
AU	African Union
AVAREF	African Vaccine Regulatory Forum
AViDD	Antiviral Drug Discovery Centers for Pathogens of Pandemic Concern
AVMA	African Vaccine Manufacturing Accelerator
AVSSR	ASEAN Vaccine Self-Sufficiency and Reliance
AUDA-NEPAD	African Union Development Agency - New Partnership for Africa's Development
BARDA	Biomedical Advanced Research and Development Authority
BMGF	Bill and Melinda Gates Foundation
CARB-X	Combating Antibiotic-Resistant Bacteria Biopharmaceutical Accelerator
CCHF	Crimean-Congo Haemorrhagic Fever
CEPI	Coalition for Epidemic Preparedness Innovations
CHAI	Clinton Health Access Initiative
CHIM	Controlled human infection models
CMC	Chemistry, manufacturing and controls
CoP	Correlates of protection
CORC	Collaborative Open Research Consortium
CSO	Civil Society Organisations
CTCAN	Clinical Trials Community Africa Network
CVIA	Centre for Vaccine Innovation and Access
DCVMN	Developing Countries Vaccine Manufacturers Network
DFC	U.S. Development Finance Corporation's
DfH	debt-for-health swap
DFI	Development Financing Institutions

Abbreviation	Definition
DOD	Department of Defence
DRC	Democratic Republic of Congo
DTV	Diagnostics, therapeutics, and vaccines
DZF	Day Zero Pandemic Financing Facility for Vaccines
EC	European Commission
EDCTP	European and Developing Countries Clinical Trials Partnership
EIB	European Investment Bank
ELISA	Enzyme-linked immunosorbent assay
EMA	European Medicines Agency
EMRO	Eastern Mediterranean Regional Office
EPSRC	Engineering and Physical Sciences Research Council
EUA	Emergency Use Authorisation
EUL	Emergency Use Listing Procedure
EVIDA	Evidence-informed Vaccine & Immunisation Decision making and Appraisal
FCDO	Foreign and Commonwealth Development Office
FDA	Food and Drug Administration
FIND	Foundation for Innovative New Diagnostics
FRF	First Response Fund
GCP	Good Clinical Practice
GCTC	Good Clinical Trials Collaborative
GHL	Global Health Labs
GMP	Good Manufacturing Practices
GPMB	Global Preparedness Monitoring Board
GVDN	Global Vaccine Data Network
HERA	European Health Emergency Response Authority
HIC	High-income countries
HIV	Human Immunodeficiency Virus
IAVI	International AIDS Vaccine Initiative
ICDRA	International Conference of Drug Regulatory Authorities
ICMRA	International Coalition of Medicines Regulatory Authorities
IFA	International Financial Architecture
IFC	International Finance Corporation
IGS	Integrated Genomic Surveillance
IHR	International Health Regulations
i-MCM net	interim medical countermeasures network
IMF	International Monetary Fund
INB	Intergovernmental Negotiating Body

Abbreviation	Definition
IP	Intellectual property
IPPS	International Pandemic Preparedness Secretariat
IPSN	International Pathogen Surveillance Network
JFHTF	Joint Finance and Health Task Force
JRC	Joint Research Centre
KII	Key Informant Interviews
LIC	Low-income countries
LMIC	Low- and Middle-income countries
LNP	Lipid nanoparticle
LSHTM	London School of Hygiene and Tropical Medicine
LSTM	Liverpool School of Tropical Medicine
mAbs	Monoclonal Antibodies
MCM	Medical Countermeasures
MGVI	Malaysian Genome and Vaccine Institute
MHRA	Medicines and Healthcare products Regulatory Agency
MoU	Memorandum of Understanding
MPP	Medicines Patent Pool
MRC	Medical Research Council
MUSICC	Mucosal Immunity in human Coronavirus Challenge
MVA-BN	Modified Vaccinia Ankara–Bavarian Nordic
MVD	Marburg virus disease
NAATOS	Nucleic Acid Amplification Test on a Strip
NAFDAC	National Agency for Food and Drug Administration and Control
NIAID	National Institute of Allergy and Infectious Disease
NIH	National Institutes of Health
NISH	National Immunisation Technical Advisory Groups (NITAGs) Support Hub
NITAG	National Immunisation Technical Advisory Groups
NRA	National Regulatory Authoritiesw
OUCRU	Oxford University Clinical Research Unit
PABS	Pathogen Access and Benefit Sharing
PACT	Pandemic Preparedness: Analytical Capacity and Funding Tracking
PAD	Pandemic Antiviral Discovery
PAHO	Pan American Health Organization
PAN	Pandemic Action Network
PATH	Program for Appropriate Technology in Health
PCR	Polymerase Chain Reaction

Abbreviation	Definition
PEARLES	Political, economic, administrative, regulatory, logistical, ethical, and social
PHECS	Public Health Emergency of Continental Security
PHEIC	Public Health Emergency of International Concern
PIP	Pandemic Influenza Preparedness
PPPR	Pandemic Preparedness, Prevention and Response
PPR	Pandemic preparedness and response
PREPARE	Programme for Research in Epidemic Preparedness and Response
PRET	Preparedness and Resilience for Emerging Threats
PTMF	Platform Technology Master File
R&D	Research and development
RCT	Randomised controlled trials
RDT	Rapid diagnostic tests
ReVAMPP	Research and Development of Vaccines for Monoclonal Antibodies for Pandemic Preparedness
RSV	Respiratory syncytial virus
RTSL	Resolve to Save Lives
RVMC	Regionalised Vaccine Manufacturing Collaborative
RWE	Real-world evidence
SAMRC	South Africa Medical Research Council
STEG	Science and Technology Expert Group
TGHN	The Global Health Network
TPOXX	Tecovirimat
TPP	Target Product profile
TRL	Technology Readiness Levels
UCI	University of California, Irvine
UCLA	University of California, Los Angeles
UKHSA	UK Health Security Agency
UKVN	UK Vaccine Network
VHF	Viral haemorrhagic fever
WHO	World Health Organisation
WLA	WHO Listed Authorities

100DM

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