100 Days Mission Scorecard

Today’s data to inform tomorrow’s preparedness

January 2024
EXECUTIVE SUMMARY

The 100 Days Mission seeks to accelerate our collective ability to develop and deploy products to combat epidemic diseases. Working with the International Pandemic Preparedness Secretariat, Policy Cures Research has developed a Scorecard to critically assess available data to determine how well we are meeting this challenge. In general, we remain underprepared and reactive in the face of emerging epidemic threats. The Scorecard reveals:

- Funding for epidemic diseases is highly reactive, we have not yet adopted a preparedness approach for Research and Development (R&D).
- The R&D funding ecosystem is upheld by public funders, and dominated by the US government, making it less sustainable and vulnerable to political shifts.
- Medical countermeasures are unavailable for most R&D Blueprint Priority pathogens. COVID-19 and Zaire ebolavirus are the only two pathogens with a full complement of approved products, however, these are not always accessible.
- Pathogens which have had larger outbreaks and were perceived as a greater risk to national biosecurity have more mature pipelines. Aside from COVID-19 and Ebola, the clinical pipeline has few candidates, with the majority in early phases of testing.
- Vaccines R&D is the most advanced space in terms of funding, product R&D and has WHO Target Product Profiles (TPPs) for nearly all pathogens.

- Therapeutics R&D lags behind with few approved products, clinical candidates and only one WHO TPP. There is a lack of unifying leadership to coordinate the sector in the way that CEPI and FIND champion vaccines and diagnostics.
- Funding for platform technologies to support “Disease X” has grown since 2019 and these are being used to develop products for eight priority pathogens. These should benefit R&D for other pathogens, but this is not yet routine.
- Pandemic product development predominately follows a traditional model of R&D but alternative approaches are needed to meet the 100 Days Mission, for example, greater use of the “animal rule” to support and accelerate licensure.
- COVID-19 is an outlier on every level. This reflects its bigger global impact, greater political will and a commercial market that is driving product development. It raises questions about how we right-size our response to pandemic threats.

This first 100 Days Mission scorecard provides a snapshot of the product development landscape for epidemic diseases. However, even when a product has been approved for use this doesn’t equate to access.

This version of the scorecard doesn’t include all the necessary indicators to fully assess the pandemic R&D ecosystem. Our future ambition is to integrate additional indicators to provide a more comprehensive view.

These could include indicators focused on:

- Clinical trials e.g. capacity, location, and inclusion of underserved groups
- Regulation e.g. time between first Stringent Regulatory Authority (SRA) approval and first Low and Middle Income Country (LMIC) product introduction
- Manufacturing e.g. technology transfer agreements, regional manufacturing capacity
- Procurement e.g. LMIC governments with specific budgets dedicated to the purchase of pandemic products, volume guarantees and advance purchase agreements.
- Access e.g. proportion of pipeline candidates with LMIC access plans in place
- Other enablers e.g. prototype libraries

These indicators are drawn from our newly developed “Evidence for Impact” impact indicator framework.

This first 100DM Scorecard highlights areas of deficiency where urgent action is needed to ensure future, global preparedness. The COVID-19 pandemic has shown what is possible when political will backs the epidemic R&D ecosystem, building from these lessons with more targeted and intentional approaches to preparedness we can collectively move forward to meet the goals of the 100DM.

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In partnership with the International Pandemic Preparedness Secretariat (IPPS), Policy Cures Research have developed a Scorecard to support the 100 Days Mission (100DM). This short report contextualises the Scorecard and provides more nuanced analysis of the research and development (R&D) ecosystem to assess how well we are globally prepared to meet the 100DM and highlights areas for further action.

In the aftermath of the COVID-19 pandemic, the 100DM was launched as a pandemic preparedness action plan focused on accelerating product development in the face of new threats. The goal is to have accurate and approved rapid diagnostic tests, an initial therapeutics regimen and vaccines ready to be produced at scale within the first 100 days from an identified pandemic threat. With input from the IPPS Scientific and Technical Expert Group (STEG), Policy Cures Research have developed a Scorecard to assess the health of the diagnostics, therapeutics, and vaccines ecosystem for the 10 current WHO R&D Blueprint Priority diseases.

This first 100DM Scorecard has focused on publicly available data mainly for product development. Primary sources were Policy Cures Research’s G-FINDER R&D funding data (2014-2022) and the Infectious Disease R&D pipeline tracker (as of August 2023). These were supplemented using data sources which can be found in Annexe I.

There are limitations to the indicators included in this first Scorecard which focuses mostly on product development. Lack of publicly available data hampered our ability to include "ideal" indicators this year. However, we have leveraged Policy Cures Research’s Impact framework to highlight indicators that could be included in future versions. These go beyond product development into access, regulation, human capacity, manufacturing and procurement. We also highlight where data collection, harmonization and interoperability need to be prioritised to enable their future inclusion.

More details on the data sources used, indicator definitions and methodology can be found in Annexe I.

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1. [www.who.int/topics/prioritising-disease-for-research-and-development-in-emergency-contexts](www.who.int/topics/prioritising-disease-for-research-and-development-in-emergency-contexts)
2. [www.ippsecretariat.org](www.ippsecretariat.org)
3. [www.gfinderdata.policycuresresearch.org](www.gfinderdata.policycuresresearch.org)
4. [www.policycuresresearch.org/pipeline-database](www.policycuresresearch.org/pipeline-database)
HIGH-LEVEL FINDINGS

We are not yet prepared to meet an imminent or future threat across several dimensions of the epidemic diseases R&D ecosystem. Our approach remains reactive, there are few approved products or clinical candidates for diseases other than COVID-19 and Ebola and those that are in development don’t possess the desired characteristics to enable global access. For example, most of the COVID-19 vaccines don’t meet the minimum TPP recommendation for broad use in LMICs. The Scorecard highlights key gaps in the Diagnostics, Therapeutics and Vaccines (DTVs) market, clinical pipeline and in the enablers which will accelerate R&D to meet the 100DM.

VACCINES: Vaccines R&D received the most funding compared to other product areas, totalling just under US$11.3bn between 2014 and 2022. Consistently, vaccines R&D makes up more than half (53%-93%) of funding for all but three diseases – SARS, Nipah and Lassa fever. Despite the size of vaccines R&D investment, 89% ($US10bn) comes from just 10 funders, with the US government making up 47% ($US5.3bn) of total funding. For diseases which have had recent large epidemics, like COVID-19, Ebola and Zika, around two-thirds of investment was directed to vaccine development, which has led to 5 successful registrations for Zaire ebolavirus and 35 for COVID-19. Despite Zika matching the trends seen in Ebola and COVID-19 in terms of relative size and reactivity of funding, no vaccine has been approved.

There are 206 vaccine candidates in development for WHO R&D Blueprint Priority pathogens across Phase I (63, 40%), II (59, 29%) and III (64, 31%). For COVID-19, over two-thirds (116, 63%) of vaccine candidates are in Phase II and III, in contrast to other pathogens where there are only 7 vaccines in Phase II and none in Phase III. In the clinical pipeline, at least one vaccine platform technology is being used in all but one of the WHO R&D Blueprint pathogens. Most vaccines in clinical development (108, 52%) use viral vector or protein subunit technology. Vaccines also benefit from the largest number of WHO TPPs to guide product development and the leadership of CEPI which helps coordinate the sector.

THERAPEUTICS: In total, US$6.2bn was invested in therapeutics R&D from 2014 to 2022. This area has grown significantly since 2014, going from just US$2.0bn in 2014 to US$2.0bn in 2021 at the height of the COVID-19 pandemic. Although investment in COVID-19 has bolstered the figures considerably, real growth across diseases has been recorded but funding remains highly concentrated. Almost 90% of investment came from industry and the US government during this period. While investment in COVID-19 has bolstered the figures considerably, the existence of two US government organisations. The unique ecosystem and business model for therapeutics adds further complexity to developing tests but also influences how tests are viewed by decision makers and reimbursed in health systems. These challenges are not unique to the epidemic diagnostics space. The development of TPPs to guide diagnostic development to suit the needs of LMICs will be valuable in achieving the 100DM.

Similar to vaccines, registered therapeutics have emerged from large epidemics as seen with COVID-19 and Ebola. Only these diseases have registered therapeutics, just under half of which are drugs for COVID-19 (6) and the rest are biologics (8). The COVID-19 therapeutics pipeline dwarfs that of all other diseases with 233 candidates in clinical development (54 in Phase I, 109 in Phase II and 70 in Phase III). In contrast, the pipeline for non-COVID priority pathogens shows a total of 12 candidates across Phase I (9), II (2), and III (1). Aside from COVID-19, Ebola has the most mature therapeutics pipeline with six candidates, followed by MERS and Lassa fever with two candidates each, and Marburg and Nipah each with one candidate.

DIAGNOSTICS: Funding for diagnostics R&D, totalled US$1.3bn from 2014 to 2022, just 12% of the funding received by vaccines, 21% of that received by therapeutics. Investment in diagnostics R&D represented an average of 5% of total disease funding. Like the other product areas diagnostics R&D also relies too heavily on a small subset of funders, with 60% of all funding coming from just two US government organisations.

Diagnostics have a different R&D pathway to vaccines and therapeutics with 74 tests in early development and 141 in late development (note that only late development candidates are included in the Scorecard). Two-thirds (136, 63%) of diagnostic tests in development are for COVID-19, with the remaining third of pipeline in development for Ebola (27, 13%), CCHF, RVF and Lassa fever (with 13 candidates each, 6%). The remaining pipeline diagnostics are for MERS (7), Nipah (4) and Marburg (2). Half of the candidates in late development are immunosassays and half are molecular tests.

The differences in the diagnostics R&D pathway partly explains the level of funding and approved products. Due to less investment, significant gaps still exist, despite the existence of more targeted investment in multiplex diagnostics, platforms, prototype libraries as well as LMIC manufacturing and linking diagnosis to treatment and care. The link between diagnostics, prevention and treatment is key and mandates that we move away from thinking in product silos to embrace synergies. For example, Zalgen Labs' REALSV Pan-Lassa Antigen Rapid Test is being used to support CEPI vaccine trials in West African countries. The unique ecosystem and business model for diagnostics adds further complexity to developing tests but also influences how tests are viewed by decision makers and reimbursed in health systems. These challenges are not unique to the epidemic diagnostics space. The development of TPPs to guide diagnostic development to suit the needs of vulnerable populations will be valuable in achieving the 100DM. Currently, diagnostic Target Product Profiles (TPPs) have only been developed for COVID-19, Nipah virus and CCHF, although these last two are out-of-date and in draft form.

8 Making the exceptional routine: Embedding diagnostic best practice to improve pandemic preparedness FIND and IPPS November 2023
### Figure 1: 100 Days Mission Scorecard

#### CORONAVIRUSES (COVID-19, MERS-CoV, SARS-CoV-1)

- **COVID-19**: $14.5bn in funding from 2020-2022, involving 64% US government, 25%Aggregate industry, 9% other.
- **MERS-CoV**: $53m in funding from 2019-2020, involving 2% US government, 46% Aggregate industry, 7% other.
- **SARS-CoV-1**: $54m in funding from 2019-2020, involving 5% US government, 17% Aggregate industry, 18% other.

#### FLOAVIRUSES

- **Ebola**: $928m in funding from 2019-2022, involving 75% US government, 19% Aggregate industry, 2% other.
- **Marburg**: $217m in funding from 2019-2022, involving 25% US government, 20% Aggregate industry, 2% other.

#### BUNAVIRUSES

- **Lassa Fever**: $35m in funding from 2019-2022, involving 90% US government, 5% Aggregate industry, 0% other.
- **Rift Valley Fever**: $44m in funding from 2019-2022, involving 70% US government, 5% Aggregate industry, 2% other.

#### ARENAVIRUSES

- **Lymphocytic Choriomeningitis Virus (LCMV)**: $80m in funding from 2019-2022, involving 83% US government, 4% Aggregate industry, 0% other.
- **Nipah**: $53m in funding from 2019-2022, involving 81% US government, 3% Aggregate industry, 2% other.

#### FLAVIRUSES

- **Zika**: $238m in funding from 2019-2022, involving 84% US government, 3% Aggregate industry, 2% other.

#### THERAPEUTIC PLATFORMS

- **Diagnostic Platforms**: $274m in funding from 2020-2022, involving 72% US government, 17% Aggregate industry, 2% other.
- **Therapeutic Platforms**: $415m in funding from 2020-2022, involving 75% US government, 19% Aggregate industry, 2% other.

#### VACCINE PLATFORMS

- **Vaccine Platforms**: $498m in funding from 2019-2022, involving 43% US government, 33% Aggregate industry, 2% other.

### Future Readiness

**Using animal rule to support licensure**
- **Thx**: All targets tested in the laboratory.
- **Vx**: All targets tested in the latest animal models.
- **Dx**: All targets tested in the latest diagnostic technologies.

**Completeness of protection**
- **Thx**: All targets have complete protective immunity.
- **Vx**: All targets have partial protective immunity.
- **Dx**: All targets have no protective immunity.

**Target Product Profiles**
- **Thx**: All targets have approved products.
- **Vx**: All targets have candidates tested in humans.
- **Dx**: All targets have no platform technologies used.

**Notes:** Funding amount colour scales. Approved product - Product approved. Approved product in AMC - Product approved in AMC. Approved products see only for Zika ebolavirus, not human ebolavirus.
R&D FUNDING LANDSCAPE

INDICATOR 1.0: R&D funding for diagnostics, therapeutics & vaccines (DTVs) (2019-2022)

Since funding data was first tracked by G-FINDER in 2014, over US$18.7bn has been invested in DTV R&D for WHO R&D Blueprint diseases. R&D funding for these epidemic diseases has historically been highly reactive; it increases and decreases in response to outbreaks as seen in the Ebola outbreaks (both 2014-2016 and 2018-2020), Zika (2016-2017) and COVID-19 pandemic (2020-2022). This reactivity is exemplified in Figure 2, prior to the pandemic (2016-2019) only US$154m had been invested in R&D for any coronavirus, while from 2020-2022 over US$14bn was invested for COVID-19 DTV R&D. Currently we are funding in a way to respond to, rather than prevent outbreaks.

R&D funding from 2019 to 2022 shows large differences in total investment between COVID-19 and the other WHO R&D Blueprint pathogens – COVID-19 is in a different ballpark. This is partially reflective of the reactive funding landscape but also that diseases which are perceived as lesser risks to national biosecurity get less funding. COVID-19 also benefits from a commercial market driving product development. Despite that, funding in 2022 saw historical increases for Lassa fever, RVF and Nipah which suggests that some funders are starting to invest more before an outbreak, perhaps an indication that things are changing as a response to the COVID-19 pandemic that caught the world off guard. While we do not yet know what the right-size funding for each pathogen is, COVID-19 R&D stands out as an dominant area. Not only when compared to investment in other pathogens in the same period, but also when compared to other large-scale outbreaks, for example total funding for Ebola (with two major multi-year outbreaks) totals US$2.8bn, half of what COVID-19 received in 2020 alone. This level of response reflects not only the global nature of COVID-19 but also its commercial market – which of which have not been seen in other epidemic diseases. To meet the 100DM and move away from reacting to outbreaks, we need appropriate benchmarks for priority pathogens during preparedness periods as well as funding gap estimates for response.

Overall, there is also a lack of diversity of funders. Public funders dominate the landscape, providing just under three-quarters of the US$18.7bn invested between 2014-2022. Private industry represents the remaining quarter of investment, while philanthropics represent less than 3%. Sector concentration is a concern, but a major vulnerability is that 50% of all investment was contributed by the US government, namely the US National Institutes of Health (NIH), Biomedical Advanced Research and Development Authority (BARDA) and DOD, making this landscape very sensitive to country political environments and shifts. While concerning, this highlights opportunities for governments, foundations and private companies to get involved – there is space for more players.

INDICATOR 1.1: Disease X R&D funding (2019-2022), Future readiness

Funding for platform technologies applicable to WHO R&D Blueprint diseases has increased dramatically over the past seven years, rising about 7-fold from 2016 to 2022. Much of this growth happened in recent years, with a significant funding jump occurring from 2019 to 2020 (up US$102m, 44%), following the WHO’s addition of ‘Disease X’ – representing unknown pathogens with pandemic potential – to its R&D Blueprint Priority list which had the desired effect of increasing focus on platform technologies. This also reflects a change in thinking around pandemic pathogens, with a move towards tackling viral families rather than individual pathogens.

Funding by platform technology type mirrors the product landscape, where we see more funding for vaccine platforms (US$4.98bn) followed by therapeutic platforms (US$4.15bn) and then diagnostic platforms (US$2.74bn). While therapeutic platforms experiencing a funding peak in 2020 due to pandemic preparedness-related biologic platform projects, this has not been sustained. The decline is largely linked to reduced investment by the US Department of Defense (DOD). A more diverse funding landscape is needed to support progress with therapeutics platforms. Diagnostic platforms have received lower overall funding with decline in investment since 2019. In contrast, vaccine platforms have seen steady, progressive growth since 2016 reaching a peak in 2022, with a slightly broader and less concentrated funding base. Philanthropy features more readily in the top funders of platform technologies than for individual pathogens, accounting for almost a quarter (23%) of total funding. Both the Bill & Melinda Gates Foundation and Open Philanthropy feature in the top funders, for vaccine and diagnostic platforms, respectively. Investment in disease-agnostic platforms that are applicable across priority pathogens will be key to securing future readiness and needs to be achieved with a diverse and stable funding base.
 APPROVED PRODUCTS AND CANDIDATES

INDICATOR 2.0: Approved products

As of September 2023, there are 40 market approved vaccines (35 for COVID-19 and 5 for Ebola), 14 licensed therapeutics made up of 8 biologics (6 for COVID-19 and 2 for Ebola) and 6 drugs (all for COVID-19) as well as 2043 individual, approved diagnostic tests for COVID-19 and 44 diagnostics for non-COVID diseases. COVID-19 and Ebola are the only two priority pathogens to have a full complement of approved products. Of note, the countermeasures approved for Ebola are only for Zaire ebolavirus and do not cover the Sudan strain. MERS, CCHF, RVF, Lassa fever, Nipah and Zika have approved diagnostics, while SARS and Marburg have no approved products.

These numbers represent products approved by stringent regulatory authorities (SRAs), with further analysis to see which of these had also been approved by national regulatory authorities or were pre-qualified by WHO as a proxy for showing which of these are available in Low and Middle Income Countries (LMICs) (see Annex I for more details on methodology). Only COVID-19 and Ebola have products that have been approved by National Regulatory Authorities (NRAs) or obtained WHO PQ. Having approved products on the market and ready to use is the end outcome of the 100DM. However, having an approved product does not equate to real world impact as delivering the product to the people who need it also requires manufacturing, procurement, patient access provision and operational health systems etc. Therefore, this alone is not a sufficient indicator of the health of the pandemic R&D ecosystem. For example, the therapeutics countermeasures approved are monoclonal antibody (mAb) combinations which are not readily accessible in outbreak settings. More on these aspects can be found in the Future Indicator section.

For COVID-19 mAbs, the changing nature of the variants proved challenging. A number of products which were granted early EUAs were subsequently revoked due to reduced specificity against more prevalent variants as the pandemic progressed. This must be considered for other infectious diseases with high replication and genetic diversity, and feed into how we consider the use of mAbs in pandemic response. Developing an initial regimen of therapeutics to minimise mortality and morbidity and support health systems is key, even if in the long term they may become obsolete as a pandemic evolves.

INDICATOR 2.1: Candidates tested in humans

The status of clinical candidates in development is quite different between COVID-19 and all the other priority pathogens.

The COVID-19 clinical candidate pipeline is buoyant with 173 vaccines, 233 therapeutics and 88 late-stage diagnostics. Vaccines and therapeutics are split fairly evenly between Phase I, II and III with roughly a third of candidates at each phase. For diagnostics, around two-thirds are in late development (BB) and the remaining third in early development (AB). This is not the case for any other priority pathogen.

In contrast, the non-COVID clinical pipeline has 92 clinical candidates including 33 vaccines, 12 therapeutics and 53 diagnostics. Countermeasures in all three product categories are being developed for MERS, Ebola, Marburg, Lassa fever and Nipah. Only one non-COVID candidate is in Phase III, the small molecule Remdesivir which is being trialled for Zaire ebolavirus. Ebola is the only pathogen with candidates across different clinical stages but in much smaller numbers. For all other pathogens, most candidates are in Phase I, testing for human safety which can be conducted outside of outbreaks. This isn’t the case for traditional Phase I/III randomised controlled trials which require substantial case numbers to test efficacy. With this limitation, we should think differently about how to demonstrate efficacy and testing outside of outbreaks settings, such as through the use of correlates of protection, Controlled Human Infection Models (CHIMs) and animal models.

INDICATOR 2.2: Platform technologies used in clinical candidates

Investment in platform technologies is another way of contributing to pandemic preparedness, through the development of disease-agnostic methods and tools which can then be quickly pivoted to address a new threat. These platforms contribute to not only accelerating R&D and scale-up but having approved platform technologies will also facilitate the registration of other products which is why it is important to have such technologies for the 100DM. A key example of this have been the platform technologies used to develop COVID-19 vaccines like the ChAdOx platform which has also been used to develop clinical candidates for MERS, CCHF, RVF, Ebola and Zika.

Although there are differences in platform diversity between diseases and across all three product areas, there is also a distinct lack of therapeutic platform technologies. With the exception of COVID-19 and the filoviruses, no other pathogens have used therapeutic platforms for clinical candidate development. Outside of the infectious disease space, there are interesting and innovative therapeutic platforms being developed including applying AI to determine druggable targets, but why isn’t this more common for epidemic diseases? This is likely due to multiple factors including lower levels of investment, and a lack of coordination and leadership. Despite not have a central champion like CEPI or FIND, there are programs like the National Institute of Allergy and Infectious Diseases (NIAID) Antiviral Discovery platform and the ASAP Discovery consortium working in this space.
R&D ENABLERS

INDICATOR 3.0: Use of animal rule to support licensure

The importance of the “animal rule” for advancing the 100DM hinges on our ability to carry out robust animal model efficacy studies, supported with human safety studies, in the absence of an outbreak to facilitate regulatory approval. The “animal rule” is a term used by US FDA but other regulators have equivalent pathways albeit with different names. This pathway has only been used for Ebola vaccines, by Janssen through the European Medicines Agency (EMA) Extraordinary Circumstances pathway for Mvbola and Zabdeno. The animal rule’s use is not yet routine, but there are also other facets which could enable R&D. For example, having a regulator qualified animal model would give developers more guidance and assurance that regulators would accept the animal study results, which would enable the use of the animal rule and de-risk this approach, enabling approvals outside of outbreaks.

INDICATOR 3.1: Correlates of protection

Few pathogens have established correlates of protection (CoP) to better understand the immunology behind infection and help expedite R&D to achieve the 100DM. A CoP is a reliable, immune marker that can be used as a proxy for vaccine efficacy. CoPs provide robust evidence which support not only the development of vaccines (providing specific targets) but also the regulatory process for vaccines. Currently, only COVID-19 has generally accepted CoPs, as outlined by CEPI. More research and funding are needed in this area as this would enable R&D not just to develop products that are targeting the right parts of the pathogen but also to develop supporting systems like biomarkers, assays and animal models which would enable testing and regulatory review processes. The recent funding call from Wellcome and CEPI is one step to advancing CoPs for pandemic diseases.

INDICATOR 3.2: WHO Target Product Profiles

Up-to-date, normative guidance on how products should be designed are key to inform R&D and deliver appropriate products. The WHO has released several TPPs for the Blueprint Priority Pathogens with more scheduled to be published to fill the current gap left by archived TPPs. Currently there are many vaccine TPPs, with just one diagnostic and one therapeutic TPP – both of which are for COVID-19. The focus on vaccine TPPs reflects the sector’s prioritisation of vaccines as preventive tools against epidemics, however, as COVID-19 has highlighted, therapeutic and diagnostic modalities are also key in the fight against pandemics.

FUTURE INDICATORS

Given limitations on data availability in the epidemic R&D ecosystem (mostly product development) this section covers the desirable indicators which would be helpful to have data on in future Scorecards to assess our readiness to meet the 100DM.

Policy Cures Research has leveraged its “Evidence for Impact” Indicator Framework with 65 indicators which has been developed through a literature review and in collaboration with over 40 experts. The indicators are divided up by area and output/outcome, and can be used as a “menu” to choose relevant indicators to meet different needs. They are applicable across global health and can be tailored to specific contexts. Indicators measuring aspects of clinical trial capacity, regulatory capacity, manufacturing and access were chosen for their pertinence to the 100DM. Additional conversations with the IPPS STEG, identified other areas of interest and importance, such as prototype libraries, which could be incorporated as future indicators. The aim is to have a selection of indicators validated, and modified to ensure 100DM relevance next year, and incorporated into future iterations of this Scorecard.

<table>
<thead>
<tr>
<th>AREA</th>
<th>EVOLUTION OF IMPACT INDICATOR (NUMBER AND TITLE)*1</th>
<th>DATA AVAILABILITY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical trials</td>
<td>1.3 Number of clinical trials (active or completed) that include undererved groups</td>
<td>Available but difficult to compare/ aggregate</td>
</tr>
<tr>
<td>Clinical trials</td>
<td>1.4 Number of unique sites where clinical research has taken place</td>
<td>Available</td>
</tr>
<tr>
<td>Clinical trials</td>
<td>4.5 Number of clinical trial site staff trained</td>
<td>Not publicly available</td>
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<tr>
<td>Regulation</td>
<td>5.5 Number of product developers engaging in voluntary sharing Agreements or non-assert declarations that cover at least one LMIC</td>
<td>Partially publicly available</td>
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<tr>
<td>Manufacturing</td>
<td>6.4 Number of employees trained in Good Manufacturing Practice (GMP) that are accepted by recognised national and/or international authorities</td>
<td>Not publicly available</td>
</tr>
<tr>
<td>Manufacturing</td>
<td>3.2 Number of technology transfer agreements/partnerships in place where the product developer transfers knowledge and/or expertise to local manufacturers in LMICs</td>
<td>Partially publicly available</td>
</tr>
<tr>
<td>Access</td>
<td>5.4 Proportion of pipeline candidates with LMIC market access plan in place before starting pivotal trials</td>
<td>Publicly available</td>
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</tbody>
</table>

*1 Indicators in Purple cells are Future Indicators and do not currently exist.
*2 Indicators in green cells are mature and do not require data collection.
*3 Indicators in grey cells have equivalent pathways albeit with different names.
*4 Indicators in yellow cells require data collection.

The aim for future years is that this Scorecard will evolve to incorporate new indicators and data sources. To make that a reality, action is needed now to improve data collection and interoperability to allow for more comprehensive and efficient assessments as well as improved coverage (especially in LMICs). To reach this goal of complete and interoperable data more coordination is needed to ensure the right systems and partnerships are in place to make this a reality.
The first 100DM Scorecard provides an objective assessment of the status of product development for the 100DM. While we recognise that additional indicators and data are needed to provide a more comprehensive assessment of the R&D ecosystem, it does provide valuable insights into key actions that can be taken to support 100DM product development.

A reactive funding pattern that responds to, rather than prepares for outbreaks indicates that we can do more to stay on track. Domination by public funders, particularly the US government, shows there is space for new approaches and funders. More diversity is needed to make the ecosystem more resilient. To further change the reactivity, we must not only change how we fund but also our approach to product development. By focusing on traditional Phase II/III Randomised Controlled Trials (RCTs), we rely on outbreaks to provide sufficient patient numbers needed to answer efficacy questions. However, alternatives are available. In the Scorecard we highlighted the use of the ‘animal rule’ and correlates of protection which are not yet commonplace. Although not in scope for the Scorecard, the FDA’s recent approval\(^{18}\) of the first vaccine for chikungunya shows what is possible. This was approved using correlate of protection data\(^19\) combined with evidence from non-human primate\(^{20}\) studies. Post-marketing surveillance will be required but applying a similar approach to WHO priority pathogens would enable action to be taken outside of epidemics and allow approved products to be available for diseases before the next outbreak.

The Scorecard also shows that funding for “Disease X” [platform technologies] has been increasing, signalling a positive shift to preparedness. There are also steps being taken to establish prototype libraries for vaccines and diagnostics championed by CEPI and FIND. Although none yet exist, next versions of the Scorecard will track their progress.

Vaccines stand out amongst the product areas as being the best resourced, having the largest pipelines with diverse use of platform technologies and the greatest number of WHO TPPs. This reflects the focus of the community on preventative vaccines and the benefit of having leadership from CEPI and GAVI. However, diseases that haven’t had large outbreaks and don’t attract global attention still lag. Diagnostics have the most approved products and larger pipelines reflecting their different development pathway. However, there are fewer diagnostics approved in LMICs, only one WHO TPP and much lower funding. They benefit from having a strong champion in FIND, but others are needed to bolster the space and help tackle challenges with diagnostics that are not only relevant to epidemics but the wider sector. Therapeutics have more volatile funding peaks and troughs, smaller pipelines outside of COVID-19 and Ebola and only one WHO TPP. The use of platform technologies is also lower. This sector lacks a unifying champion to coordinate and guide product development. To effectively respond to future outbreaks, we cannot rely on one modality alone and more coordination across all product categories is needed to ensure we are better prepared.

Throughout the Scorecard, COVID-19 stands out as an outlier. This makes for an interesting reference point, but should it be a benchmark? It is different from the other diseases listed. Causing a global pandemic with impact on every country, garnered international political will and attracted action from industry that other diseases didn’t have. For COVID-19, there is a commercial market driving product development that is missing for the other WHO priority diseases. It’s top-heavy pipeline raises questions on whether the market can absorb all late-stage products. However, further work is needed to determine how to right size our response for all pathogens. This will be a challenge we hope to meet with future Scorecards and contributions from the wider community.


\(^{19}\) https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(23)00641-4/fulltext

The Scorecard and indicators on which this report is based were developed through a collaborative and iterative process spanning September to December 2023. Prior to consultation, Policy Cures Research reviewed data availability and leveraged the “Evidence for Impact” indicator framework21,22, to devise an initial list of indicators. Through consultation with IPPS the indicators and Scorecard visualisation went through three separate consultations on the 27th October (STEG sub-group), 21st November (full STEG) and 26th November (STEG sub-group) with multiple rounds of feedback in between provided through additional meetings or via email. In parallel to these discussions, Policy Cures Research also consulted other stakeholders for data availability including GLOPID-R, READDI, Intrepid Alliance and FIND. Through this process, indicators were refined and prioritized to ensure the Scorecard would deliver a clear and concise picture of the state of readiness to meet the 100 Days Mission.

The scope of the scorecard was set to reflect the current WHO R&D Blueprint priority pathogen list and focuses on the product scope of IPPS and the 100 Days Mission: diagnostics, therapeutics and vaccines.

**WHO R&D BLUEPRINT PRIORITY PATHOGENS**

The WHO established the R&D Blueprint priority pathogen list to highlight which diseases and pathogens should be prioritised for research and development in the context of public health emergencies. The current list includes:

- COVID-19
- Crimean-Congo haemorrhagic fever
- Ebola virus disease and Marburg virus disease
- Lassa fever
- Middle East respiratory syndrome coronavirus (MERS-CoV) and Severe Acute Respiratory Syndrome (SARS-CoV-1)
- Nipah and henipaviral diseases
- Rift Valley fever
- Zika

The Blueprint list of priority diseases also includes a ‘Disease X’, which it defines as ‘the knowledge that a serious international epidemic could be caused by a pathogen currently unknown to cause human disease’. In line with the WHO definition, this report uses the Disease X category to capture cross-cutting platform technologies R&D that is disease-agnostic and therefore applicable to both known threats and unknown diseases.

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**APPROVED PRODUCTS**

We have defined an approved product as:

- a finished pharmaceutical product (FPP), drug, vaccine, biologic, vector control product or diagnostic that has been granted a marketing authorisation (product licence or registration certificate) by a designated medicines regulatory authority, defined as Stringent Regulatory Authorities (SRAs), National Regulatory Authorities (NRAs) of vaccine producing countries of maturity level 3 or above (as define by WHO Listed Authorities framework), or WHO prequalification. The marketing authorisation could be full market authorisation or conditional, such as an emergency use authorisation or approval under the European Medicines Agency’s EUM4All procedure (previously Article 58).23

Product inclusion is based on the molecular entity, using the international non-proprietary name (INN). Except in the case of distinct formulations or routes of administration, we included only one unique INN per indication. Off-label use of marketed products for in-scope indication were not included.

Products that had been approved by National Regulatory Authorities (NRAs) of vaccine producing countries of maturity level 3 or above (as define by WHO Listed Authorities framework) or had received WHO prequalification were included in the Scorecard as being approved in LMICs.

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**CANDIDATES**

We have defined a pipeline candidate as:

- a potential drug (including both repurposed and new molecules), biologic, vaccine, vector control product, diagnostic, or platform technology, currently under investigation for an in-scope disease, that is yet to be approved by a designated medicines regulatory authority (defined above in Approved Products).

For a pipeline candidate to be included, it must:

- be currently under investigation for a disease or indication in the G-FINDER scope for neglected or emerging infectious diseases (EIDs match that of the WHO R&D Blueprint priority pathogen list with some additions);
- have a development status that can be independently verified; and
- be unique (one count per indication) or innovative (new chemical class, new target, new mode of action). Repurposed drugs are included only if research involves a new indication.
EXCEPTIONS AND LIMITATIONS

The data used in the Scorecard was limited to that which is publicly available and relied on leveraging data collected for other purposes. There were some initial data gaps and attempts were made to fill these using different data sources. However, these used different data collection methodology. Specifically:

- **COVID-19 diagnostic data**: definitions of development stage and technology type were consistently applied, however the methodology for data collection differed.

- **BIO COVID-19 therapeutics tracker data**: the same principles were used to categorise therapeutic candidates, however, comprehensive independent validation of all therapeutics was not undertaken given project time constraints. This could have led to an overestimation of candidates.

DATA SOURCES

The scorecard and accompanying report draw from a number of different data sources to present, where possible, the most up to date picture of the epidemic R&D ecosystem. A complete list of the indicators used in the scorecard with their definition and data source are listed in Table 2.

### TABLE 2

<table>
<thead>
<tr>
<th>INDICATOR</th>
<th>CATEGORY</th>
<th>DEFINITION</th>
<th>SOURCE</th>
</tr>
</thead>
<tbody>
<tr>
<td>R&amp;D funding for diagnostics, therapeutics and vaccines (DTVs)</td>
<td>Now</td>
<td>This indicator shows the total R&amp;D funding invested by disease between 2019 and 2022 broken down by donor.</td>
<td>G-FINDER R&amp;D funding data²</td>
</tr>
<tr>
<td>Approved products</td>
<td>Now</td>
<td>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. 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.</td>
<td>Policy Cures Research’s updated infectious disease R&amp;D tracker data¹, and additional data sources for COVID-19, including data from FIND on diagnostics</td>
</tr>
<tr>
<td>Clinical candidates tested in humans</td>
<td>Future Readiness</td>
<td>This indicator shows the number of candidates for each disease that are being tested in humans. These are broken down by R&amp;D stage and include Phase II/III for vaccines and therapeutics and late-stage development for diagnostics. Candidates were defined as potential drugs, vaccines, vectors, control products, diagnostics, or platform technologies, currently under investigation that had yet to be approved by a medicines regulatory authority.</td>
<td>Policy Cures Research’s updated infectious disease R&amp;D tracker data¹, and additional data sources for COVID-19, including data from FIND on diagnostics</td>
</tr>
<tr>
<td>Platform technologies</td>
<td>Future Readiness</td>
<td>This indicator shows if platform technologies are being used to develop clinical candidates. The outer section shows where multiple technologies (i.e., &gt;3) are being applied to the pipeline. The platform technology category includes vaccine, drug, and biologics platforms; adjuvants and immunomodulators; and general diagnostic platforms.</td>
<td>Policy Cures Research’s updated infectious disease R&amp;D tracker data¹, and additional data sources for COVID-19, including data from FIND on diagnostics</td>
</tr>
<tr>
<td>Use of animal rule to support licensure</td>
<td>R&amp;D enablers</td>
<td>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.</td>
<td>US FDA⁴ and EMA³</td>
</tr>
<tr>
<td>Generally accepted correlates of protection</td>
<td>R&amp;D enablers</td>
<td>This indicator shows where there are generally accepted correlates of protection as defined by CEPI⁸⁻¹⁰.</td>
<td>CEPI⁸⁻¹⁰</td>
</tr>
<tr>
<td>WHO Target Product Profiles (TPPs)</td>
<td>R&amp;D enablers</td>
<td>This indicator shows which diseases have active WHO Target Product Profiles for vaccines, diagnostics and therapeutics.</td>
<td>Policy Cures Research’s updated infectious disease R&amp;D tracker data¹, and additional data sources for COVID-19, including data from FIND on diagnostics</td>
</tr>
<tr>
<td>R&amp;D funding for platform technologies</td>
<td>Disease X</td>
<td>This indicator shows total R&amp;D funding invested into platform technologies between 2019 and 2022 broken down by donor. 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&amp;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.</td>
<td>G-FINDER R&amp;D funding data¹</td>
</tr>
</tbody>
</table>
G-FINDER FUNDING DATA SCOPE

G-FINDER R&D funding data has evolved and expanded to mirror the WHO list. Following the start of the Ebola epidemic in 2014, the G-FINDER survey included R&D spending on Ebola virus disease. The following year, following the establishment of the WHO R&D Blueprint list, the survey was expanded to include five additional diseases: Marburg, Crimean Congo Haemorrhagic Fever (CCHF), Rift Valley Fever (RVF), Lassa fever and Zika. In 2016, R&D spending on coronaviral diseases (including MERS and SARS-CoV-1), and henipaviral diseases (including Nipah) was added to the survey along with ‘Disease X’ funding and core funding for multi-EID organisations. The last update to the WHO R&D Blueprint diseases was in 2020, with the addition of COVID-19. For full details of the G-FINDER scope please refer to the Policy Cures Research website.24

PRODUCT DATA

The data for approved products and pipeline candidates was predominately sourced from the Policy Cures Research Infectious Disease R&D Tracker which was last updated in October 2023. The scope mirrors that of G-FINDER and includes all WHO R&D blueprint pathogens. More information on the scope and methodology used for the curation of this data can be found on our website25.

24 www.policycuresresearch.org/g-finder/
25 www.policycuresresearch.org/pipeline-database/
ANNEXE II - EVIDENCE FOR IMPACT INDICATORS

TRIALS

Number of clinical trials (active or completed) that include underrepresented groups

The inclusion of underserved groups in clinical trials is crucial for ensuring that results are generalisable, and for enhancing our understanding of how medical interventions affect different subpopulations. This is foundational in ensuring equitable access, which is a critical component of the 100DM.

Information on the inclusion of underserved groups in individual clinical trials may be found in clinical trial registries and results databases, as well as published results of completed trials. However, the definition of who is underserved is often context and study specific and the data may be difficult to aggregate.

Number of unique sites where clinical research has taken place

This gives us an indication of the volume and geographic breadth of trial sites. Expanding the number of clinical trial sites and locations widens the potential pool of eligible participants and widens the economic and societal settings that the product is researched within, which similar to the indicator above, helps to ensure that study results are broadly applicable. Furthermore, improvements to trial efficiency and shorter timelines may be seen with a higher number of unique sites, as multiple locations enable parallel enrolment and data collection. This is imperative for the speed required in the 100DM.

Data on study locations are readily available via online registries of clinical trials and results databases. However, trials may be registered before a clinical trial location has been chosen, and so there may be a delay to when this information is available.

Number of clinical trial site staff trained

This indicator measures the number of clinical trial site staff that are trained, at a determined point in time, on the relevant clinical trial protocol, related documents and study product(s) required to fulfil their delegated duties and functions for the clinical trial(s) they are working on. Well-trained staff uphold ethical standards, ensure participant safety, and enhance data accuracy. This ensures high-quality, efficient trials, which is important for the rigorous and efficient testing of DTVs.

Organisations should already be collecting data on how many staff have been trained on clinical trial protocols and related documents and products as part of clinical trial monitoring. However, this data may not be publicly available.

Regulation

Number of product developers engaging in voluntary licensing agreements or non-assert declarations that cover at least one LMIC

The IFPMA26 defines a voluntary licence as ‘a voluntary authorisation given by the patent holder to a generic manufacturer, allowing it to develop and manufacture generic versions of patented medicines’. The IFPMA2 also defines Non-Assert Declarations (NAD) as an instance ‘where a rights holder commits not to enforce certain patents in a defined group of countries allowing a generic version of a patented protected article to be produced in a resource-limited setting’.

Measuring the number of product developers engaging in voluntary licensing agreements or non-assert declarations for LMICs is crucial for promoting global access to products, which is key to the 100DM. The Medicines Patent Pool (MPP) database27 tracks voluntary licences negotiated through MPP (note though that voluntary licences can be and are also negotiated outside of the MPP), and the Access to Medicine Index28 published biannually by the Access to Medicine Foundation includes data on voluntary licences (both MPP and private) and on NADs.

Manufacturing

Number of employees trained in Good Manufacturing Practice that are accepted by recognised national and/or international authorities

Good Manufacturing Practice (GMP, also referred to as ‘cGMP’ or ‘current Good Manufacturing Practice’) is the aspect of quality assurance that ensures that medicinal products are consistently produced and controlled to the quality standards appropriate to their intended use and as required by the product specification. The number of employees trained in GMP is an important indicator to assess capacity levels for manufacturing goods to a high standard.

The number of employees trained in GMP is an important indicator to assess capacity levels for manufacturing goods to a high standard. Data on GMP completion might not be currently collected but it is important information to collect in both the current and future global health context.

Number of technology transfer agreements/partnerships in place where the product developer transfers knowledge and/or expertise to local manufacturers in LMICs

This indicator is important as technology transfer, especially from High Income Country (HIC) actors to LMIC actors, bridges R&D gaps, increases the availability of vaccines and medicines, and can stimulate investment in R&D and associated infrastructure. This is important in ensuring R&D and manufacturing capacity, as well as equitable access.

By assessing the number of technology transfer agreements with manufacturers in LMICs, we can get a better indication of the volume of technology transfer from product developers (often from HICs) to manufacturers in LMICs. This data on agreements and partnerships is available from product developers, although may need some further analysis along lines of geography and income status to better understand the strength of partnerships with, within and among LMICs.

26. Investing in Global Health R&D: An Impact Assessment Framework” produced by Policy Cures Research. A full list of indicators and their definitions can be found here. From this list, the following indicators could be incorporated in future versions of the 100 Days Mission Scorecard to make it more reflective of the wider epidemic R&D ecosystem.

27. From this perspective, the IFPMA defines a voluntary licence as ‘a voluntary authorisation given by the patent holder to a generic manufacturer, allowing it to develop and manufacture generic versions of patented medicines’. The IFPMA also defines Non-Assert Declarations (NAD) as an instance ‘where a rights holder commits not to enforce certain patents in a defined group of countries allowing a generic version of a patented protected article to be produced in a resource-limited setting’.


29. IFPMA also defines Non-Assert Declarations (NAD) as an instance ‘where a rights holder commits not to enforce certain patents in a defined group of countries allowing a generic version of a patented protected article to be produced in a resource-limited setting’.


31. The Medicines Patent Pool (MPP) database provides a searchable database of voluntary licences and non-assert declarations for LMICs. The database includes data on voluntary licences (both MPP and private) and on NADs.
Proportion of pipeline candidates with LMIC market access plan in place before starting pivotal trials

An access plan is defined as 'plans to ensure that public health needs are taken into consideration during R&D. These plans facilitate availability, accessibility and affordability for patients in countries (for example, registration commitments, equitable pricing strategies, sufficient supply commitments, non-exclusive in specified territories, waiving patent rights, royalty-free provisions and applying for WHO pre-qualification)'.

Data is available from Policy Cures Research on pipeline candidates while the Access to Medicine Foundation has data on access plans for 20 pharmaceutical companies including a breakdown per company and their associated late-stage R&D projects and number of access plans including LMICs. Data outside of the 20 companies covered by the Access to Medicine Index would need to be sourced manually.

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1. www.gfinderdata.policycuresresearch.org
2. www.accesstomedicinefoundation.org/resource/2022-access-to-medicine-index
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