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Rapid diagnostic test: a critical need for outbreak preparedness and response for high priority pathogens

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ABSTRACT

Rapid diagnostic tests (RDTs) are critical for preparedness and response against an outbreak or pandemic and have been highlighted in the 100 Days Mission, a global initiative that aims to prepare the world for the next epidemic/pandemic by driving the development of diagnostics, vaccines and therapeutics within 100 days of recognition of a novel Disease X threat.

RDTs play a pivotal role in early case identification, surveillance and case management, and are critical for initiating deployment of vaccine and monoclonal antibodies. Currently available RDTs, however, have limited clinical sensitivity and specificity and inadequate validation. The development, validation and implementation of RDTs require adequate and sustained financing from both public and private sources. While the World Health Assembly recently passed a resolution on diagnostic capacity strengthening that urges individual Member States to commit resources towards this, the resolution is not binding and implementation will likely be impeded by limited financial resources and other competing priorities, particularly in low-income countries. Meanwhile, the diagnostic industry has not sufficiently invested in RDT development for high priority pathogens.

Currently, vaccine development projects are getting the largest funding support among medical countermeasures. Yet vaccines are insufficient tools in isolation, and pandemic preparedness will be incomplete without parallel investment in diagnostics and therapeutics.

The Pandemic Fund, a global financing mechanism recently established for strengthening pandemic prevention, preparedness and response, may be a future avenue for supporting diagnostic development.

In this paper, we discuss why RDTs are critical for preparedness and response. We also discuss RDT investment challenges and reflect on the way forward.

SUMMARY BOX

⇒ Rapid diagnostic tests (RDTs) play a pivotal role in early case identification and management, surveillance and are critical for initiating deployment of vaccine and monoclonal antibodies at the time of an outbreak.
⇒ The performance of RDTs available for high priority pathogens needs improvement and these RDTs must pass through an adequate clinical validation process.
⇒ Despite the critical role of RDTs for preparedness and response against high priority pathogens, investment towards their development has remained minimal.
⇒ Urgent action is needed to devise an innovative mechanism for sourcing immediate and adequate financing for development, validation and for implementation of RDTs in outbreak and epidemic/pandemic situations.

INTRODUCTION

Infectious disease outbreaks are a growing global public health threat.[1] An expanding human population increased zoonotic spillover to humans, and weak health systems are among many factors contributing to the emergence of deadly outbreaks with epidemics and/or pandemic potential. Following the 2014 Ebola outbreak in West Africa, the WHO Research and Development (R&D) Blueprint was created to help guide the development of vaccines, diagnostics and therapeutics for high priority pathogens in an effort to save lives and avert public health emergencies of international concern.[2] This list of high priority diseases is periodically updated through external consultation with global experts. Currently prioritised diseases include COVID-19, Crimean-Congo haemorrhagic fever (CCHF), Ebola virus disease, Marburg virus disease, Lassa fever, Middle East respiratory syndrome coronavirus (MERS-CoV), severe acute respiratory syndrome (SARS), Nipah and henipaviral diseases, Rift Valley fever (RVF), Zika virus

and 'Disease X.[2] Disease X represents the knowledge that a serious international epidemic could be caused by a pathogen currently unknown to cause human disease.

The emergence of SARS-CoV-2 and subsequent development of safe and effective mRNA vaccines in a record 314 days has catalysed a paradigm shift in vaccine and countermeasures development. The world is entering an era of heightened pandemic risk and future threats may already be known to us (eg, a high priority pathogen such as Nipah) or unknown altogether. To prepare for the unknown, and galvanise global political support for the accelerated development of countermeasures, the Coalition of Epidemic Preparedness Innovations (CEPI) and partners have proposed a 100 Days Mission. The bold ambition of the 100 Days Mission is to have accurate and approved rapid point-of-care (POC) diagnostic tests, an initial regimen of therapeutics and authorised vaccines ready to be produced at scale for global deployment within the first 100 days of recognition of a pandemic threat.[3] Instead of focusing on product development for known threats, the 100 Days Mission aims to accelerate development against 'prototype members' or exemplars of each of the 26 virus families known to infect humans while simultaneously building and strengthening global capabilities to accelerate testing, manufacturing, deployment and administration at global scale. The 100 Days Mission has been embraced by the G7, G20 and other governmental, civil society, and industrial stakeholders worldwide.

To build efficient outbreak preparedness and response capacity, diagnostics must be available to promptly detect cases of an emergent epidemic or pandemic threat. This requires the availability of easy-to-use, highly sensitive, specific and validated rapid diagnostic tests (RDTs). RDTs are simple to operate, quick testing tools that can be used directly at POC level, eliminating the need for advanced laboratory infrastructure or costly equipment. The development, validation and implementation of RDTs require adequate and sustained funding. To date, there has not been adequate investment in the development and validation of RDTs for high priority diseases, likely due to shortage of funds and lack of market incentives. At present, highly sensitive, specific and validated RDTs for high priority pathogens such as Nipah, MERS-CoV and Lassa, do not exist (table 1). In this paper, we discuss RDTs and their role in outbreak preparedness and response for high priority diseases including Disease X. We also discuss RDT investment challenges and provide a recommendation for the way forward.

Table 1 Inhouse and commercially available rapid diagnostic tests for high priority pathogens*

Disease	RDTs at POC level		
	MRDT	RDT (antigen test) (LF)	RDT (antibody test) (LF)
Lassa			
Ebola			
Marburg			
CCHF			
Nipah			
MERS-CoV			
COVID-19			
RVF			
Zika			
CHIK			
Disease X			

RDT availability: green indicates available/validated; yellow indicates not validated/need improvement; orange indicates on development; red indicates not available.
*In the preparation of this table, we reviewed the available literature.[15-24] There is currently no commercially available validated antigen or NAAT-based RDTs for high priority pathogens except for COVID-19.
CCHF, Crimean-Congo haemorrhagic fever; LF, lateral flow; MERS-CoV, Middle East respiratory syndrome coronavirus; MRDT, molecular rapid diagnostic test; NAAT, nucleic acid amplification test; POC, point-of-care; RDT, rapid diagnostic test; RVF, Rift Valley fever.

What are RDTs?

RDTs are medical diagnostic tools intended for use at POC (ie, on doctor's table or at patients' home) or near-POC (ie, peripheral health facility).[4] The three main categories of RDTs for infectious disease diagnosis include: (1) nucleic acid amplification tests used to detect targeted genetic material; (2) antigen tests designed to directly identify specific microbial antigens; and (3) antibody tests intended to detect various antibodies generated by the host's immune response to the pathogen. These tests can be designed for identification of a single or multiple pathogens.

RDTs are particularly useful in low-income countries (LICs) where access to electricity and refrigeration is often limited in rural areas, and highly skilled personnel and robust laboratory infrastructure is often lacking. Patients must often travel (walk) long distances (>10 km) to access appropriate laboratory diagnosis and treatment for their illness, if available. RDTs are critical in LICs as this is where most outbreaks occur. The WHO has set the REASSURED criteria (R: real-time connectivity; E: ease of specimen collection and environmental friendliness; A: affordable; S: sensitive; S: specific; U: user friendly; R: rapid and robust; E: equipment-free; D: deliverable to end users) for the use of RDTs.[5]

The most commonly used RDTs are lateral flow tests (LFTs), due to their ease of use, low cost, robustness and short assay times. During the COVID-19 pandemic LFTs were adopted at an unprecedented scale. LFTs are mostly qualitative or semiquantitative, and thereby suitable for viruses typically presenting high viral loads (and antigen levels). Improvements in sensitivity (S) and specificity (S), sampling (E) and digital connectivity (R) are needed for this platform technology to be applicable across

high priority pathogens for outbreak preparedness and response.[6]

USES OF RDT

Early case detection and management

Early case detection and management is crucial to reduce morbidity and mortality among patients infected with high priority pathogens. Several factors including the non-specific symptoms experienced by patients infected with high priority pathogens,[7] and lack of diagnostic facilities in endemic rural areas contribute to delays in diagnosis and treatment. Patients must travel long distances to referral centres in major towns and cities for confirmatory PCR diagnosis, further increasing the risk of disease progression, death, and exposure to others.[8] Thus, high performing RDTs are needed to identify patients early at a near-POC level to enable health workers to treat or rapidly refer patients to the next level of healthcare for better management.

Contribute to implementation of the 100 Days Mission

A 2021 report on the 100 Days Mission stated that 'Achieving the 100 Days Mission and improving global pandemic preparedness requires, effective surveillance and pathogen analysis so that pandemic threats are identified earlier, and immediate response is initiated. The 100 Days Mission aims to have an accurate and rapid POC test within 100 days of recognition of a new outbreak, epidemic/pandemic threat'.[9] Prompt development of an RDT after full genome sequencing of a new Disease X pathogen would enhance the ability to initiate public health interventions. The interventions may include appropriate case isolation and contact tracing and will help mitigate the spread of disease until vaccines and therapeutics are developed. Thus, prompt development of and access to an appropriate RDT following identification of a pandemic threat will contribute to controlling the infection through non-pharmacological means.

Disease surveillance

Disease surveillance provides timely data for public health planning and rapid response initiation. Despite the importance of these data, there is at present inadequate surveillance for high priority diseases in endemic countries.[8 10 11] Near-POC tests would not only enable patients to be treated and appropriate containment measures implemented, but test results can be reported in real-time to a national surveillance system to enable better understanding of trends in the incidence of infections due to priority pathogens.

Supporting global safety and biosecurity

RDTs for infectious diseases play a pivotal role in bolstering global biosafety and biosecurity. They can serve as a frontline defence against laboratory accidents and potential use of bioweapons. RDTs can create an early warning system in research laboratories and related settings to enable the swift detection and identification of pathogens responsible for disease while also monitoring for potential anomalies. Particularly promising is the convergence of RDTs with wastewater surveillance systems. Wastewater testing is an important tool for understanding disease spread in near real-time and has enabled the design and implementation of tailored public health interventions in the context of emergent pandemic threats (eg, 2022 global monkeypox outbreak), while avoiding the challenges associated with relying on human testing and dissemination of human test results to public health decision-makers.[12]

Genome surveillance

Monitoring the evolution of high priority viruses enables the clinical and transmission relevance of diseases to be defined. Viruses undergo mutations over time that may result in genetic variation in the population of circulating strains. Monitoring mutations is important to identify any mutations that might affect the performance of existing diagnostic assays and to ensure that available vaccines are directed against the most appropriate strain/s and evaluate if a vaccine needs to be altered. RDTs can play a key role in identifying cases and thus expediting sample collection for genome sequencing.

Contribute to case detection and sample collection for research

Contribute to international standards

International standards (IS) for antibodies, antigens and nucleic acids are critical for the development of vaccines, diagnostics and therapeutics. IS have been prepared for several priority pathogens.[13 14] Preferably, IS are produced from convalescent patients of a target disease.[13 14] A near-POC test could play a significant role in increasing the number of active cases detected which would then increase the number of survivors in endemic countries who could be invited to participate in the development of new antibody, antigen or nucleic acids (from active cases) to be used as reference reagents for vaccines, diagnostics and therapeutics development.

Diagnostic assay validation or evaluation

Several diagnostic assays have been developed for high priority diseases; however, none of these have passed through adequate clinical validation.[15–24] The main challenge for validating and evaluating diagnostic assays is shortage of well-characterised patient sera. RDTs help in early case detection and facilitating sample collection for diagnostic assay validation or evaluation.

Support clinical trials

RDTs are important for vaccine clinical trials. RDTs would enable baseline testing, enrolment and participant management. Community health workers can be trained to use RDTs, which are simple and easy to perform, to support testing during participant follow-up. Thus, rapid testing of trial participants through RDTs has the potential to reduce costs by ensuring the right participants are

quickly enrolled into the study, and overall study timelines reduced.

Deployment of vaccines and monoclonal antibodies

Prior to deployment, vaccines are stockpiled for emmergency use in the event of an outbreak. Stockpiling of vaccines may occur following completion of Phase II trials and Emergency Use Authorisation, and several Phase II/III trials are planned between 2024 and 2026 (CEPI personal communication). RDTs will be essential for deployment of these vaccines by accurately identifying the disease-causing pathogen and outbreak. RDTs could also help inform the deployment of monoclonal antibodies (mAbs) at the time of an outbreak. This is important as mAbs for high priority pathogens such as Nipah and MERS-CoV are in the pipeline.[25–27] Administration of mAbs to Nipah-infected patients and at-risk populations could potentially prevent new infections, treat existing infections and contain an outbreak.[28] Thus, a high-performing and validated RDT is needed for early outbreak identification and to inform the deployment of vaccines and/or mAbs to enable control of the outbreak.

Investment challenges for RDT development

One of the main challenges affecting the development of RDTs for high priority diseases is lack of adequate financing. In general, global funding for diagnostics is limited and recent data suggest that 75% of diagnostics funding was obtained from only six organisations (US National Institutes of Health, Bill & Melinda Gates Foundation, US Department of Defense, US Biomedical Advanced Research and Development Authority, European Commission and Industry).[29] Diagnostics received only 7.2% of the total R&D funding allocated for emerging infectious diseases.[29]

A lack of incentive from the private sector has been a challenge for the development of diagnostic tests. Most high priority pathogens cause localised or pocket outbreaks in endemic countries, and the health policy in endemic countries focuses primarily on preventive healthcare. The delivery of diagnostic assays at the time of an outbreak is a challenge. In such a situation, a highly sensitive, specific and clinically validated test that can be applied with low level of training is of paramount importance. Nonetheless, such a diagnostic test is not practical for routine use owing to the limited market availability following the outbreak. Thus, the private sector is not encouraged to invest in diagnostics for these diseases due to lack of commercial viability.[30]

Another factor which influences funding for RDTs is the small number of cases affected by emerging infectious diseases that are prone to cause epidemics. This results in insufficient availability of clinical samples for use in diagnostic assay validation or evaluation studies. In addition, lack of IS has been challenging to test accuracy evaluation. The availability of adequate and well-characterised samples and IS are needed as part of the regulatory submission and evaluation process for approval.

Poor research and development capacity, particularly in low-income and middle-income countries (LMICs) is a challenge for diagnostic test development.[31 32] For example, Africa bears 25% of the global disease burden and harbours majority of the high priority pathogens: Marburg and Ebola, CCHF, RVF, Lassa fever and others. However, the research output from this continent is estimated to be not more than 2%.[33] Several challenges contribute to the incredibly low research output. These include poor research infrastructure,[29] such as lack of high containment biological laboratories and high-tech laboratory equipment that are required for basic, applied and translational research, lack of well trained and skilled researchers,[34] inadequate career development pathways for scientists, and lack of adequate and sustainable financing for research. These have been contributing to migration of highly skilled biomedical researchers for better salary and benefit to affluent countries.[35 36] Adequate and sustainable financing from donors and local governments in Africa is required to build local research capacity that will be conducive for investment to conduct health research including developing medical countermeasures such as diagnostics.[36]

Another challenge for diagnostics development is limited infrastructure for diagnostic manufacturing particularly in LMICs.[31 32] This directly impacts the development of diagnostic products for the region, as well as the implementation of diagnostics for case detection and expediting the start of appropriate treatment at community level.

A recent consultative meeting organised by Foundation for Innovative New Diagnostics (FIND) and Unitaid, and a survey conducted by PATH[31] involving global health experts and diagnostic manufacturers identified several challenges in the diagnostic value chain that have been negatively affecting manufacturers' interest on diagnostic investment.[31 37] This included lack of financing, lack of skilled manpower, difficult regulatory pathways and policies, 'inefficient purchasing and procurement practices', poor local research and development capacity, limited infrastructure and technology, and lack of support from government.[31 37]

Overall, the lack of funding, low market incentive, poor research and development capacity, limited infrastructure for diagnostic manufacturing in LMICs, difficult regulatory pathways and policies, poor government commitment and lack of adequate samples for validating and evaluating diagnostic tests are the main reasons for poor investment in diagnostics development. Currently, vaccine development projects receive the most funding.[29] Unless all medical countermeasures (vaccines, diagnostics and therapeutics) get sufficient funding for the development and validation of products, outbreak preparedness and response efforts may not be sustainable in containing and controlling a potential epidemic or pandemic arising from existing or future diseases (Disease X).

The economic case for diagnostic investment

The *Lancet* Commission on Diagnostics states that 'diagnosis is the biggest gap in the cascade of care'.[32] Adequate data on 'benefit–cost ratio' of diagnostics for each disease of interest are required to make investment decisions for diagnostics development. However, calculating the 'benefit–cost ratio' of diagnostics is challenging, especially for infectious diseases where preventing transmission is an important benefit which depends on behaviour—nevertheless, the Commission assumed that based on COVID-19 experience, models and scenarios could be developed for each priority pathogen which will likely show a strong economic case for investment in diagnostics.[32] Taking the COVID-19 pandemic as an example, South Korea experienced less economic loss and was successful in initiating economic activities faster compared with other countries in Europe as the country was able to invest in a lot of effort in early case detection and contact tracing activities.[32] Another example is the 2014 Ebola epidemic where the economic loss due to the epidemic in West Africa was estimated at US$53.19 billion.[38] A study showed that if 60% of patients infected with Ebola were rapidly diagnosed, the attack rate could drop from 80% to nearly 0%.[39] This suggests the possibility that the economic loss from Ebola could have been significantly reduced had there been high performing rapid tests for early case detection at the beginning of the epidemic. In general, even though adequate data on 'benefit–cost ratio' is needed to justify diagnostic investment for each high priority pathogen, the case of COVID-19 pandemic and Ebola epidemic provide a good example to understand the significant contribution of early detection in reducing economic loss.

Enabling equitable access to medical countermeasures at the time of epidemics or pandemic

Equitable access to medical counter measures (vaccines, diagnostics and therapeutics) is critical to avert the global impact of an epidemic or pandemic resulting from high priority pathogens. However, enabling equitable access to medical countermeasures has been a challenge. For example, the COVID-19 pandemic has revealed how vaccines and diagnostics were not timely delivered to LMICs. In 2021, more than 3.2 billion diagnostic tests were used worldwide of which only 0.4% were performed in LMICs where three-fourth of the world population lives.[40 41] The shortage in diagnostic test supply happened as there were few diagnostics manufacturers producing the tests. This contributed to unfair competition for limited resources and affected the capacity of LMICs to scale-up testing coverage for their population. In addition, the diagnostic supply chain was complex and inefficient.[41]

At the beginning of the pandemic, LMICs also faced challenges in accessing COVID-19 vaccines because of vaccine nationalism, 'a situation where countries push to get first access to a supply of vaccines and potentially hoard key inputs for vaccine production'. During the first 6 months of the pandemic, several high-income countries had bilateral agreements with the available few manufacturers to secure vaccine supplies for their own people.[42] These deals contributed to limiting COVID-19 vaccines to only be accessible for high-income countries. For instance, by end of third quarter of 2021, a total of 5.82 billion vaccine doses were administered, while in LMICs only 1.9% received at least one dose.[41]

Overall, the inequity resulted in limited and delayed allocation of available diagnostic tests and vaccines to LMICs. There is an urgent need to scale up research and manufacturing facilities in LMICs in preparation for future epidemics and pandemics. This will contribute to enabling equitable access to diagnostics and vaccines to those in need.

THE WORLD HEALTH ASSEMBLY RESOLUTION ON STRENGTHENING DIAGNOSTIC CAPACITY

The World Health Assembly (WHA) recently passed a resolution regarding the need for diagnostic capacity strengthening in all Member States.[43] The resolution includes recommendations for implementation by Member States, including for example 'to consider the establishment of national diagnostics strategies'; 'to extend the scope of packages of essential diagnostic services, and to make essential diagnostics available, accessible and affordable at the primary healthcare'; and 'to commit resources to invest in research and product development and to promote local production capacity for diagnostics, particularly in developing countries'. The WHA resolution is a critical milestone in addressing the current diagnostic gaps for both infectious and non-infectious diseases. Individual Member States are strongly recommended to assess their diagnostic gaps, prioritise their needs and commit local resources to address the identified gaps. However, as this resolution is not binding, and given the resource limitation and other competing priorities particularly in LICs, implementing the WHA resolution in terms of critical diagnostic needs for high priority pathogens may be slow and challenging.

Africa CDC and AUDA-NEPAD initiative on strengthening diagnostic capacity in Africa

With the aim of accelerating access to diagnostics and harmonising regulatory processes for in vitro diagnostics in Africa, the Africa CDC and African Union Development Agency-New Partnership for Africa's Development (AUDA-NEPAD) recently established Diagnostic Advisory Committee (DAC).[44] The Africa Collaborative Initiative to Advance Diagnostics (AFCAD) has been launched following the establishment of DAC. The AFCAD is a timely and important initiative to specifically address hurdles related to enabling equitable access to diagnostics in Africa and contribute to timely detection of outbreaks originating from high priority pathogens. The AFCAD is expected to address several objectives that include promoting local diagnostic manufacturing, establishing

continental biobanking network, facilitating and harmonising regulatory processes and requirements and global market negotiation. As regulatory capacity strengthening is key to enable equitable access in Africa, the African Medicines Agency (AMA) has recently been established, and one of its mandates is to manage regional regulatory harmonisation of medical products including diagnostics.[44]

In general, the establishment of DAC, AFCAD and AMA is an important milestone and may contribute to implementing the WHA resolution on diagnostic capacity strengthening in Africa.

The way forward

Urgent action is required given the need for RDTs for high priority pathogens to achieve the 100 Days Mission. A consultative meeting involving relevant stakeholders could serve as a forum to discuss the financial challenges and consider innovative mechanisms for immediate and sustainable financing for the development, validation and delivery of RDTs for high priority pathogens. These stakeholders could include FIND, WHO, PATH, regulators, academia, product development partners, industry, donors, philanthropists and selected national governments from high-income, middle-income and LICs.

The WHA resolution on diagnostic capacity strengthening provides an important opportunity to support investment for RDT development and implementation for high priority pathogens. To implement the resolution, LICs, need to be supported. This may be achieved by engaging several stakeholders. First, international organisations such as the WHO, FIND, PATH, Unitaid, other donors and product development partners may play a significant role in providing technical support, for example developing national diagnostic strategy and mapping diagnostic needs, facilitating technology transfer, laboratory and research capacity strengthening and financing. The international resolutions including the WHA resolution on diagnostic capacity strengthening, and the international accord for pandemic prevention, preparedness and response (Pandemic Accord)[45] are important documents to encourage donors support to LICs. Second, the Minister of Health (MoH) in LICs need to discuss with their government to increase political commitment in allocating resource to the health sector. The international resolutions may also help MOHs in LICs to better justify their ask for additional resources to their respective government. In addition, various health focused civil society organisations such as medical and public health association in LICs may help develop a well-crafted advocacy strategy to secure parliamentarians' support in bringing the agenda to the government for better resource allocation to the health sector. Increased donors support and national government funding contribute to the implementation of the international resolutions where diagnostic capacity strengthening is a major component.

The private industries should be supported to increase their interest in developing diagnostics for high priority pathogens. In line with this, it is important to implement the recommendations of the recent consultative meeting organised by FIND and Unitaid.[37] The outcome of this meeting provided timely and valuable recommendations on how to incentivise private industry. The recommendations call for 'governments and development partners support in terms of creating regional diagnostic networks, facilitating funding, facilitating pooled procurement of raw materials, providing training, technology transfer and advocating for regionally manufactured products'. In addition, the recommendation calls for 'policy reviews for creating enabling environments for diagnostics industry investment, re-evaluating tariff and non-tariff barriers on raw materials, trade barriers and facilitate regional trade, tax concessions and incentives for potential investors and increasing investment in public utilities and infrastructure'.[37] The meeting has created an opportunity to provide important recommendations that will help address the challenges facing the private industry to develop diagnostics for infectious disease of epidemic or pandemic potential.

Similarly, it is useful to implement the recommendations of the outcome of the survey conducted by PATH in collaboration with Accenture.[31] The assessment focused on four areas in the value chain: research and development, manufacturing, procurement and distribution and service delivery. This approach helped to identify important challenges in the value chain impacting diagnostics availability and access to LMICs. Several recommendations have been provided to address the challenges. Among others, the need for 'end-to-end investments to strengthen local manufacturing capacities, demand-planning, workforces, quality assurance and partnerships' have been highlighted. It also recommended the need for a strong and sustainable collaboration among the stakeholders and players within the diagnostics ecosystem.[31]

Overall, it is important that individual countries, and other relevant stakeholders in the diagnostic ecosystem consider providing support for the implementation of the above recommendations documented by FIND and PATH so that the private industry is incentivised to contribute its share towards realising the WHA resolution for diagnostic capacity strengthening in LICs, in particular.

Adequate and well-characterised samples are crucial for validating and evaluating diagnostic tests. Supporting biobanking initiatives in all countries is imperative to realise proper collection, archiving and management of biological samples for use in diagnostics and other countermeasures development research. This will have its contribution in facilitating the availability of samples for use by private industry.

New and evolving financing mechanisms, such as the recently established Pandemic Fund (PF), created for pandemic prevention, preparedness and response

(PPR) in September 2022,[46] may be a potential source of funding for diagnostic preparedness. The PF is primarily dedicated to longer-term financing to strengthen PPR capabilities in LMICs. The first round of funding was recently allocated to projects focused on infectious diseases surveillance, laboratory capacity strengthening and human resource capacity building. Disease surveillance without access to appropriate diagnostics at a POC level will lead to suboptimal outbreak responses in LMICs. This is also a critical gap affecting implementation of the 100 Days Mission. Allocation of funding to diagnostics R&D, particularly for development of RDTs for high priority pathogens, is imperative for the ecosystem.

CONCLUSION

RDTs are critical for an expedited response to an impending outbreak, epidemic or pandemic originating from high priority pathogens. RDTs play a significant role in early case detection, referral and management thereby contributing to achieve the 100 Days Mission. RDTs are useful for informing vaccine and mAb deployment at the time of an outbreak and important for disease and genomic surveillance. Currently, there are not highly sensitive, specific and validated RDTs for high priority pathogens.

The private industry plays key role for development and manufacturing of RDTs. A number of challenges within the value chain are contributing to low market incentive for diagnostic investment for high priority pathogens. Various actions are needed to increase the private industry involvement in RDT development. These may encompass diagnostic research infrastructure strengthening, regulatory framework strengthening, developing favourable policy for creating conducive environments for diagnostics investment and strengthening biobanking initiatives in all regions. In addition, scaling up manufacturing facilities will contribute to enabling equitable access to diagnostics at the time of an epidemic or pandemic, in particular for LMICs.

The development, validation and implementation of RDTs require adequate and sustained financing. There is no sufficient commercial incentive for the diagnostic industry to develop RDTs for high priority pathogens. The WHA resolution regarding the need for diagnostic capacity strengthening in all Member States is a critical milestone to address the current diagnostic gaps. However, as the resolution is not binding, and given the resource limitation and other competing priorities particularly in LICs, implementing the WHA resolution for high priority pathogens may be challenging. Therefore, urgent action is needed to devise an innovative mechanism for sourcing immediate and adequate financing for development, validation and for implementation of RDTs in outbreak, epidemic/pandemic situations. In addition, engaging the PF Board is imperative to secure R&D funding particularly for RDT for priority pathogens.

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