T20 POLICY BRIEF

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Task Force 01

FIGHTING INEQUALITIES, POVERTY, AND HUNGER

Elevating the Leadership of High TB Burden G20 States in the Development and Delivery of New TB Vaccines

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Abstract

Tuberculosis (TB) is the world's deadliest infectious disease. G20 states must show leadership and mobilise the resources needed to deliver new TB vaccines to meet the 2030 End TB targets. Universally accessible TB vaccines targeting adolescents and adults would prevent disease, combat antimicrobial resistance, sustain pandemic preparedness and response infrastructure, fight health inequalities, and return US$7 for every $1 invested in their delivery over 25 years.

Brazil holds the third of four consecutive high TB burden country (HBC) G20 presidencies, beginning with Indonesia's 2022 call to action on financing the TB response. Multiple late-stage TB vaccine trials are ongoing or planned in these countries, applying decades of experience in HIV vaccine trials with robust community participation. Increased multilateral investments by G20 states can efficiently advance TB vaccine development to fulfil commitments made at the 2023 High-Level Meeting on TB. The leadership and ownership of HBC G20 states are critical as new TB vaccines will save millions of lives while saving costs in almost all HBCs.

This brief, building on the 2023 T20 brief that proposed a TB vaccine investment toolbox for joint action, adaptable to a country's economic and research capacities and disease burden, outlines recommendations for where investments can meaningfully advance TB vaccine development and delivery among HBC G20 states to ensure globally affordable and equitable access. Recommendations concern optimising research and development, country-level investments, harmonising regulatory review, and technology transfer. Opportunities for enhanced multilateral collaboration among HBC G20 states and via existing global initiatives are explained.

Diagnosis of the Issue

Tuberculosis (TB) is the world's deadliest infectious disease. An emblematic disease of poverty, the risk of developing TB is exacerbated by undernutrition, overcrowding, and inadequate water, sanitation and hygiene services. Almost one-quarter of TB cases in high TB burden countries (HBCs) are attributable to undernutrition alone (Bhargava et al. 2022). New TB vaccines that work across all age groups, particularly among adolescents and adults who are most at risk of developing and spreading TB, will be critical to eliminate TB and meet the 2030 End TB targets (WHO 2015).

Universally accessible TB vaccines targeting adolescents and adults would prevent disease, combat antimicrobial resistance (AMR), sustain pandemic preparedness and response (PPR) infrastructure, fight health inequalities, and return US$7 for every $1 invested in their delivery over 25 years (WHO 2022). Further, these vaccines are set to avert up to 76 million cases and save up to 8.5 million lives over 25 years while being cost-saving in almost all HBCs, with returns on investments of up to US$372 billion and generating up to $3 trillion in economic growth globally (Portnoy et al. 2023). This could help reduce wealth inequalities, both within and between countries, that have been exacerbated by the COVID-19 pandemic (World Inequality Database 2022).

The TB vaccine development pipeline is poised for success: several promising candidates are in late-stage efficacy testing, and efforts are ongoing to ensure they will be affordably and equitably accessible once available (TAG 2023a). New TB vaccines are within reach — but only with greatly increased and sustained investments. Governments must fulfil commitments endorsed at the 2023 High-Level Meeting on TB (TBHLM) to invest US$5 billion annually in TB research and development (R&D) by 2027, including

$1.25 billion for vaccines, so that new TB vaccines can be available as early as 2028 (United Nations 2023; Stop TB Partnership 2022). Yet, annual funding for TB vaccines has never exceeded $145 million (TAG 2023b). Governments must accordingly increase public allocations for TB R&D to 0.15% of their total research expenditure to meet their fair share of the $5 billion target (TAG 2023c).

G20 states, home to half of all people affected by TB, can lead other countries in mobilising the resources needed to develop and deliver new TB vaccines this decade (WHO 2024a). The leadership and ownership of HBC G20 states are critical. Brazil holds the third of four consecutive HBC G20 presidencies, beginning with Indonesia's 2022 call to action on financing the TB response (Indonesia G20 2022), followed by India in 2023, and ending with South Africa in 2025. Brazil and Indonesia chair the WHO TB Vaccine Accelerator Council, and Brazil will host the 7th Global Forum on TB Vaccines in October 2024. Multiple late-stage TB vaccine trials are ongoing or planned in these countries, applying decades of experience in HIV vaccine trials with robust community participation (TAG 2023a).

HBC G20 states bring invaluable expertise in vaccine development and manufacturing and are home to world-renowned biomedical R&D institutes, universities, and manufacturing facilities. The potential public health and socioeconomic impacts of TB vaccine research in HBC G20 states are significant, including strengthening vaccine research, manufacturing, and regulatory infrastructure and expertise and expediting local access to new TB vaccines once available.

Recommendations

This policy brief builds on the 2023 T20 brief that proposed a TB vaccine investment toolbox for joint action, adaptable to a country's economic and research capacities and disease burden (Palmer et al. 2023). We propose that stronger HBC leadership alongside diversified, multilateral financing will cultivate greater country ownership of the resulting vaccines and help ensure globally affordable and equitable access. The G20 is uniquely positioned to lead this effort given the considerable vaccine research, manufacturing, and regulatory expertise and infrastructure of its member states which include HBCs and some of the largest TB R&D funders (Kumraj et al. 2022; Kaddar, Milstien, and Schmitt 2014). The following recommendations focus on enhanced multilateral collaboration and four technical domains: optimised R&D, country-level investment cases, harmonised regulatory review, and technology transfer (Figure 1).

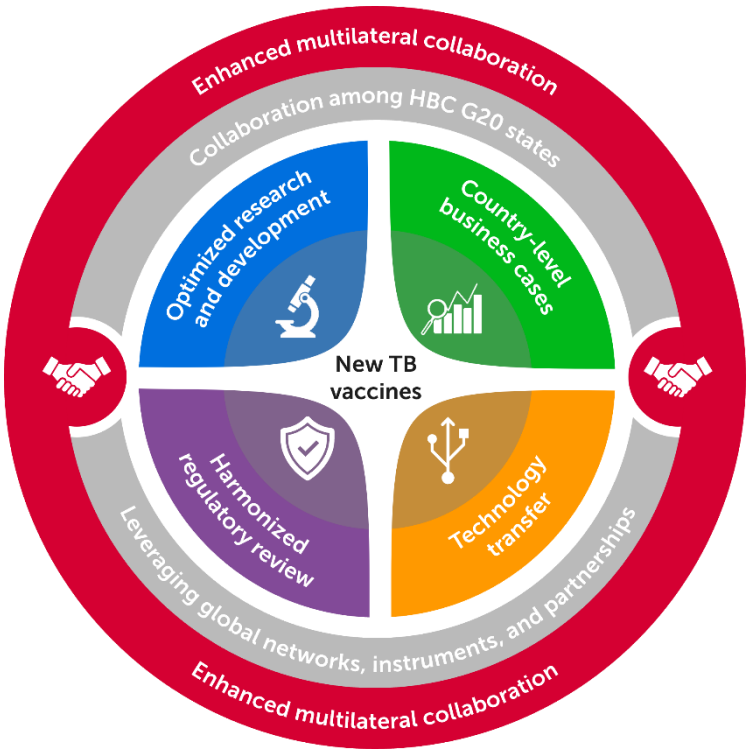

FIGURE 1. Domains for policy impact in TB vaccine development and delivery among HBC G20 states

Enhancing multilateral collaboration in support of a paradigm shift

Collaboration among HBCs

Stronger multilateral collaboration among HBC G20 states can better situate TB vaccine development in local and regional contexts and bolster capacities across the vaccine development and delivery continuum. HBC G20 states can increase their effectiveness by clarifying the requirements for conducting trials in-country, technology transfer, and licensing, and developing fit-for-purpose implementation strategies. Strategic public-private partnerships with research institutions, developers, and manufacturers among HBC G20 states can help HBCs meet local TB vaccine development and delivery needs and strengthen their epidemic and pandemic preparedness and response capabilities (Sell et al. 2021). Existing regional networks, such

as the BRICS TB Research Network, can facilitate collaboration between HBCs and should include Indonesia and the African Union to maximise impact.

Leveraging global networks, instruments, and partnerships

North-South collaboration must likewise increase, including through bilateral transfer of knowledge, expertise, and technology. HBC G20 states would benefit from providing key leadership in all TB vaccine-related initiatives. The WHO TB Vaccine Accelerator Council includes membership of six HBCs, two major funder countries, and eight global financing and procurement agencies (WHO 2023). While its specific priorities are under development, it is strategically positioned to drive forward innovative and sustainable financing and partnerships to advance TB vaccine development and delivery while bolstering HBC leadership. In the short term, HBC members can demand council members prioritise increased and joint investments to support late-stage candidates through licensure (Palmer et al. 2023). Additionally, frameworks and consortia that have been established to advance TB vaccine development and delivery can be more fully utilised (EDCTP & AIGHD 2021; SMART4TB 2022; WHO 2023), and TB vaccines can be integrated into relevant global health agendas, work plans, and funding calls, including for AMR and PPR, to support other priorities of HBCs.

Optimised research and development

A range of actions can be implemented to optimise R&D processes, including: (1) developer assessment of HBC data requirements to support rapid licensure and scale-up; (2) expanding efficacy testing to new sites to meet these requirements; and (3) developing more sustainable personnel and clinical infrastructure for late-stage clinical trials among

HBCs. Funders can also support discrete, well-defined projects on the development pathway, which may include refined preclinical models and collection of local data on TB incidence to better inform TB vaccine trial site selection and vaccine introduction planning. Other innovative measures can be implemented concurrently, including adaptive trial designs and harmonised clinical trial protocols (EDCTP & AIGHD 2021).

Sustained and transparent engagement of affected populations – including through structured and well-resourced community advisory boards and civil society mechanisms – is essential for the ethical conduct of research and to facilitate uptake of future vaccines by affected communities. Similarly, clinical trial protocols that include all key populations, including people living with HIV and pregnant and lactating women, will generate safety and efficacy data for the use of these vaccines by all people (TAG 2022; SMART4TB 2024).

Country-level investment cases

Global level studies highlight the need to invest in TB vaccines, especially in HBCs (WHO 2022). The lack of in-depth country-specific value proposition analyses is known to limit investments and delay vaccine development (Heaton 2020; Luter et al. 2017). While value propositions for select countries are in development, prioritising this work will ensure all countries have the necessary evidence to support the efficient, timely, sustainable, and fully-resourced procurement and introduction of new TB vaccines. Comprehensive needs assessments conducted alongside the development of country-level investment cases will help determine what investments are needed and how and where they should be applied (Kumraj et al. 2022).

Harmonised regulatory review

G20 states can accelerate vaccine access by supporting harmonised fast-tracked regulatory review at the regional and global levels to help mitigate conflicting regulatory pathways and requirements and avoid duplicative efforts (Dellepiane et al. 2020). This may include mechanisms such as joint dossier review and the WHO Collaborative Registration Procedure, based on principles of cooperation, reliance, harmonisation, and voluntary information sharing (Pagliusi, Che, and Dong 2019). Further, the National Regulatory Authorities of Brazil, India, Indonesia, and South Africa have attained at least an overall Maturity Level 3 as established by the Global Benchmarking Tool and are eligible to undergo performance and compliance evaluation to be designated a WHO-Listed Authority (WHO 2024b). Regional collaborative regulatory and ethical review can strengthen national regulatory capacities and enhance the efficiency and quality of vaccine evaluation across the board, while respecting sovereignty and national decision-making processes (Maïga, Akanmori, and Chocarro 2009). Country-level regulatory and access plans should likewise be developed alongside late-stage development to enable rapid deployment of effective TB vaccines once available.

Technological transfer and intellectual property rights (IPR)

IPR barriers continue to hamper efficient collaboration and engagement of HBC vaccine developers and manufacturers. An inability to raise external investments and limited access to in-licensing and other partnership opportunities are cited as barriers to novel vaccine development in these countries (Hayman et al., 2021). Prioritising technology transfer and sharing of knowledge and know-how within TB vaccine development will help increase access to high quality products and drive down costs, as

production costs are typically lower in low- and middle-income countries. Further, technology transfer to multiple manufacturers can reduce prices through market competition and may range from one-off transfers of production scale processes to full local production (EDCTP & AIGHD 2021).

Scenario of outcomes

By implementing these policy recommendations, HBC G20 states can elevate their leadership and advance TB vaccine development more efficiently, driving country ownership and priming HBCs for the swift uptake of new TB vaccines once available – ultimately controlling national TB epidemics and helping HBCs address existing and pandemic health threats. Established initiatives, such as the BRICS TB Research Network and the WHO TB Vaccine Accelerator Council, can be leveraged to their fullest potential to support the deliberate redistribution of priority-setting and governance structures to regions with the highest TB burden. Further, these recommendations can facilitate diversified and increased investments among all G20 states across the financial, research, regulatory, manufacturing, and delivery aspects of TB vaccine development toward meeting fair share targets and advancing new TB vaccines to market this decade, while enhancing national, regional, and global health security. There are however a number of key trade-offs in implementing these recommendations. Three examples and measures to mitigate them are presented below.

Competing priorities and budgets

HBC G20 states may face competing demands for limited healthcare and research budgets while competing political and domestic and global health priorities may lead to disparities in investments in TB vaccine development between countries. Conversely, existing funders may reduce investments as new funders enter. As such, there is a risk that increased investments in TB vaccine development could divert resources away from other critical health priorities if increased funding for TB vaccines does not result from larger budgets for health research. It is thus important to determine how different G20

states can most effectively invest in TB vaccines in line with their economic and research capacities to reach funding targets and overcome chronic shortfalls in TB vaccine financing. TB vaccine development should accordingly be positioned as an investment that will yield broad benefits – both by producing an urgently needed tool to end TB and by generating scientific insights that will contribute to progress in other areas of medical science. Investments in TB vaccine development should also be pursued in conjunction with efforts to address other health priorities and strengthen the health system (Hauser and Oliver 2023).

Market constraints

While increased market competition may help reduce prices and expand access, there is the risk that market shares may be insufficient to drive reasonable returns on investment, which may particularly constrain the entrance of smaller manufacturers that lack a large portfolio of vaccines and other products to allow the flexibility of easy diversification (Kaddar, Milstien, and Schmitt 2014). As such, localisation of manufacturing must be informed by accurate demand forecasts and business cases to mitigate market saturation and avoid acquisition of vaccine production facilities by multinational firms and the subsequent loss of regional autonomy in TB vaccine production.

Technological and infrastructural challenges

TB vaccine development remains a technologically complex endeavour. A range of challenges may lead to delays in the development process, including scalability issues, a complex IPR and technology transfer environment, and a lack of efficacy data for all key

populations and geographies. Relatedly, it may take significant time to establish and strengthen the required research, manufacturing, delivery, and regulatory infrastructures. Communication, collaboration, and coordination throughout the product development continuum are critical to ensure contingencies are addressed in a timely and holistic manner to maximise impact on late-stage product development, commercialisation, and access. Provisions should be attached to funding to promote access to the means, methods, and materials for scientific discovery, to the know-how required for manufacturing, and to timely and affordable access to new TB vaccines.

Ensuring accountability

Instituting independent monitoring mechanisms that track the fulfilment of commitments, enforce agreed-upon conditions for affordable and equitable access, and include active participation of community and civil society representatives will promote accountability, effectiveness, and vaccine uptake among vulnerable populations.

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