INTRODUCTION AND BACKGROUND

The coronavirus disease (COVID-19) pandemic highlighted how public health emergencies can have severe impacts on the overall health security of countries and cause severe social and economic disruptions. Such risks disproportionately affect low- and middle-income countries (LMICs), which face the challenge of inequitable access to medicines and health care, including vaccines. Throughout the COVID-19 pandemic, LMICs including Bangladesh were challenged by delayed access to lifesaving vaccines and other therapeutics, along with frequent supply shortages. Countries, especially those with high pharmaceutical industry potential, currently need to build resilience to health shocks by developing and manufacturing local pharmaceutical products and vaccines. However, not every country can or should invest in domestic manufacturing. It depends on the local industry and regulatory and demand contexts.

Bangladesh has previously demonstrated its capabilities in pharmaceutical product manufacturing by establishing itself as a significant player in the market for generic medicines. However, there is a need to further strengthen domestic manufacturing in the pharma sector by incorporating all parts of the value chain. Research and development (R&D) of drugs and vaccines will be a crucial aspect of enabling self-sufficiency and supply chain security in Bangladesh. Clinical trials are an integral part of R&D of new pharmaceutical products. Regulatory authorities require these when a new drug or vaccine is introduced to establish product safety and efficacy. LMICs including Bangladesh are underrepresented in clinical research owing to the lack of commercial viability and trained researchers, despite the high potential of viability of such efforts in these countries.1

Bangladesh is gearing up to build domestic capabilities for the development and manufacturing of vaccines over the medium to long term. Alongside this, a well-functioning clinical trials ecosystem is required to enable quicker drug development timelines, improve applicability of study results, generate employment, and unlock new foreign investment. This policy brief explores the current landscape of the clinical trials ecosystem in Bangladesh and identifies the systemic regulatory requirements and considerations for strengthening the ecosystem. These recommendations serve as a precursor to setting up end-to-end vaccine and drug development and manufacturing capabilities.

Note: ADB recognizes “Korea” as the Republic of Korea.

Context
Globally, vaccines have played a crucial role in preventing and controlling infectious diseases. The COVID-19 pandemic exposed the vulnerabilities of countries that relied heavily on vaccine imports. During the pandemic, many high-income countries (HICs) stockpiled vaccines (footnote 1), leading to a glaring disparity in vaccine access. Consequently, nonpriority groups in HICs such as younger age cohorts received quicker access to the vaccines than did vulnerable populations in LMICs. Despite the general agreement on a global mission of vaccine equity, rampant vaccine nationalism hampered the access of COVID-19 vaccines by LMICs like Bangladesh, as they relied primarily on bilateral agreements to source vaccines.

Looking to the future, decision-makers in LMICs understand the importance of domestic manufacturing of vaccines and other pharmaceuticals as a part of their overall strategy to ensure health security. As Bangladesh transitions out of Gavi funding by 2029 (footnote 2), it will need to ensure that sustainable mechanisms are put in place for supporting its Expanded Program on Immunization (EPI) and that local development and manufacturing of vaccines can form the base for sustained strengthening of the immunization ecosystem in Bangladesh over the medium to long term. In this regard, Bangladesh’s Prime Minister Sheikh Hasina has stressed the need to bolster domestic production of vaccines and stated government plans to establish an international vaccine institute in collaboration with the Republic of Korea (ROK). Additionally, the health ministry of Bangladesh has formed a committee to examine the feasibility of said institute, which would be led by the director general of the Directorate General of Health Services.

Recently, the Ministry of Health and Family Welfare in Bangladesh carried out a techno-economic feasibility assessment to understand the overall landscape, assess preparedness, identify bottlenecks and risks, and pursue appropriate measures to enable Bangladesh to set up and scale domestic vaccine manufacturing capabilities. The feasibility assessment recommended a phased approach to attain the immediate aim of achieving self-sufficiency by 2027 and the long-term objective of becoming a vaccine exporter by 2030. This will involve strengthening the clinical trials ecosystem and setting up facilities for fill-finish manufacturing initially, followed by full cycle development of targeted vaccines. A well-functioning domestic clinical trials ecosystem is highly important as Bangladesh looks to incorporate upstream value chain elements of the pharmaceutical industry, such as vaccine R&D. Domestically conducted clinical trials can reap several benefits and address local health priorities by contextualizing the results for the local population. Data from locally conducted trials can be leveraged to formulate prevention and treatment strategies for diseases prevalent within the nation. Bangladesh (and a few other LMICs) provides access to a large and diverse patient-population, which could help with generalizability of study findings. Further, a well-equipped clinical system can foster partnerships between local scientists and international researchers. This could lead to increased innovation in terms of development of novel therapies and technologies tailored to the specific needs of the local population. In-country clinical trials could stimulate economic growth by creating new markets and job opportunities. Having a robust clinical trial system in place would also enhance the visibility of Bangladesh as a destination for medical research, which can attract additional investment from pharmaceutical companies and research institutions. Thus, to further Bangladesh’s stated plans on vaccine manufacturing, a well-functioning clinical trials ecosystem is required. This calls for R&D infrastructure that incorporates state-of-the-art data management systems, biorepositories, laboratories, a highly skilled workforce, and other crucial resources.

CLINICAL TRIALS LANDSCAPE IN BANGLADESH

Clinical Trials Market in Asia and the Pacific
Over the past decade, the global biopharmaceutical industry has been characterized by increased outsourcing of various parts of the value chain, including the clinical phases of R&D. Previously, most such outsourcing was targeted at contract research organizations (CROs) in the United States (US) and Europe. However, multiple factors such as lower operational costs, rapidly increasing capabilities, large potential market sizes,
and availability of treatment-naïve populations,\textsuperscript{10} have spurred rapid growth in the clinical trials market in Asia and the Pacific. Today, the region is an important contributor to the ecosystem, with the total number of trials (including Phase I to Phase IV trials) having risen from 4,562 in 2012 to 7,718 in 2021, a compound annual growth rate of 5.4\% (Figure 1).\textsuperscript{11} As of 2022, Asia and the Pacific had become a nexus for clinical trial activity, accounting for more than 50\% of the clinical trial studies held globally, followed by North America at 27\% and the European Union (EU) at 20\%.\textsuperscript{12} The bulk of trials in the region are conducted in the People’s Republic of China (PRC) (45\%), followed by Japan (21\%), the ROK (13\%), Australia (11\%), and India (10\%); other countries in the region, including Bangladesh, collectively constitute only 10\% of trials (footnote 12). Notably, the relative proportions of the phases of clinical studies have also seen a significant change (Figure 2). Late-stage trials (Phase III and Phase IV) were dominant from 2012 to 2016. Phase I trials have since increased their share of total clinical trials from 14\% in 2012 to 33\% by 2021 (footnote 12). This increasing share of early-stage trials indicates greater levels of innovation within Asia and the Pacific, having developed and tested homegrown novel chemical or biological entities. By comparison, late-stage trials are often conducted to satisfy global regulatory requirements.

\textbf{Figure 1: Total Interventional Clinical Trials Conducted, 2012–2021 (Globally and in Asia and the Pacific)}

\begin{figure}
\centering
\includegraphics[width=\textwidth]{figure1.png}
\caption{Total Interventional Clinical Trials Conducted, 2012–2021 (Globally and in Asia and the Pacific).}
\end{figure}

\textbf{Figure 2: Proportion of Clinical Trials by Each Phase, 2012–2021 (in Asia and the Pacific)}

\begin{figure}
\centering
\includegraphics[width=\textwidth]{figure2.png}
\caption{Proportion of Clinical Trials by Each Phase, 2012–2021 (in Asia and the Pacific).}
\end{figure}

\textsuperscript{10} A person is considered treatment-naïve if they have never undergone treatment for a particular illness. In general, treatment-naïve patients have more options for therapies than treatment-experienced patients as there is no concern regarding drug resistance to one of more classes of drugs, making them suitable for participating in clinical trials.

\textsuperscript{11} A. Siu and A Benson. 2022. APAC as a Clinical Trial Powerhouse. In Vivo.

\textsuperscript{12} Global Data. 2022. Asia Pacific (APAC) Dominance in the Planned Clinical Trials for 2022.
Factors Contributing to the Shift in Clinical Trial Activity to Asia and the Pacific

This gradual but meaningful shift to Asia and the Pacific is attributable to multiple factors. First, challenges in conducting clinical trials in the higher-income US and European economies have meant that there are long delays and high costs associated with clinical research.13 Second, countries in Asia and the Pacific have low existing clinical trial participation rates and can offer large treatment-naïve populations—often with greater willingness to participate in clinical studies as an alternative to high out-of-pocket health care expenditures. Third, as disease patterns in the region are different to those in developed countries, Asia and the Pacific is especially well-suited for clinical studies for a range of therapy areas and indications, including infectious diseases. Fourth, as the economies in the region have grown richer, availability of infrastructure (including health infrastructure) and digital penetration has increased rapidly. Fifth, timelines for recruitment and regulatory approvals in the region can often be shorter, thus improving the overall time to market for pharmaceutical products. Sixth, many countries in the region (including Japan, the ROK, and Australia) offer favorable regulatory regimes with fast-track processes, high levels of data harmonization with international standards, and conducive intellectual property rights environments.

Another factor contributing to the high growth of the clinical trials market in the Asia and Pacific is the presence of CROs. The regional CRO market had an approximate valuation of $7.6 billion as of 2021 and is forecast to hit $11.9 billion by 2025.14 Global CROs such as Covance, Icon, IQVIA, Paraxel, PPD, PRA, etc. have a formidable presence in the region and consistent service offerings throughout multiple locations.

Finally, another attraction to the region is the low cost of conducting the studies. The Asia and Pacific compares favorably to the US and high-income European nations in overall clinical trial costs, making it a desirable location for conducting clinical trials. However, even within the region, the costs vary substantially, with Singapore, Australia, and Japan at the higher end, and the PRC, Malaysia, and India at the lower end.15 Considering that workforce costs form a major share of the overall trial cost (accounting for 30%–35% of total costs), countries like Bangladesh (where person power costs in the pharmaceutical sector are 20%–30% lower than in India) may hold potential to be a hot spot for conducting clinical trials.16

Clinical Trial Activity in Bangladesh

Despite the growth of R&D activities in Asia and the Pacific over the past decade, levels of clinical trial activity in Bangladesh have remained relatively low. On a per capita basis, Bangladesh has conducted fewer trials when compared with both HICs such as the US, the United Kingdom (UK), Australia, Japan, and the ROK and other LMICs of Asia and the Pacific such as Viet Nam, Indonesia, and India (Figure 3). However, Bangladesh has favorable underlying circumstances for clinical trials, such as a large treatment-naïve population, a strong pharmaceutical sector, and low labor costs.17

While the presence of CROs has led to high growth in the clinical trials market across Asia and the Pacific, few such global or regional CROs have established bases in Bangladesh. The CRO market in Bangladesh is largely dominated by local organizations (with 16 national CROs present in the country), which can often have 20%–40% lower operational expenses owing to lower overheads and domestic decision-making structures. Among the global players, only two CROs are present in Bangladesh—Dokumeds and SGS—while others have conducted clinical trials there occasionally in partnership with the local organizations (Figure 4).18 Even of the 16 approved national CROs, few have been operationally active in recent years.19

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18 ICHGP. List of Contract Research Organizations (CRO) in Bangladesh – CRO Database.
19 Insight from stakeholder interview.
As such, there is an identified scope for expanding the CRO presence in Bangladesh, with potential collaborations with other countries in the region being a possibility for the future.20 Further, Bangladesh is not currently a part of large global or regional clinical trial networks such as ATLAS, ARISE, SEAICRN, or EDCTP, even as there are instances of collaborative studies where Bangladesh-based sites have been involved—such as THECA (for Typhoid Conjugate Vaccine) with EDCTP,21 Projahnmo (a groundbreaking partnership with Johns Hopkins University22), and SEPSIS, which was an observational study on severe infection in newborns, conducted with Boston University, McGill University, and University of California San Diego23).

Data from the World Health Organization (WHO) International Clinical Trials Registry Platform (ICTRP) and clinicaltrials.gov shows that the proportion of industry-sponsored trials is relatively low in Bangladesh, suggesting low maturity of the clinical research ecosystem in the private sector (Figure 5).24 Overall, ~12 % of the clinical trials completed in the country were industry-sponsored, compared with most countries both in Asia and the Pacific and globally, which range from 30% to 80%.

Of all 471 clinical trials registered from the year 2000 onward in Bangladesh on which information is available, close to 40% of the studies had the International Centre for Diarrheal Disease Research (icddr,b)25 as a trial site. While icddr,b provides a well-functioning ecosystem for undertaking clinical trials in the country, the lack of availability of alternate sites could mean that conducting clinical trials for therapy areas that are not a focus of icddr,b could be a challenge. Further, a high concentration of clinical trials in limited locations or sites also contributes to lower representation from all parts of the population given the specific focus on certain types of diseases and products. This may be exacerbated by the disproportionate representation of Dhaka-based clinical sites, which account for ~75% of all clinical trial sites in the country.

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20 Insight from stakeholder interview.
21 EDCTP. Publications.
22 JHSPH. Global Collaborations.
23 clinicaltrials.gov. SEPSIS Observational Cohort Study in Young Infants in Bangladesh.
25 icddr,b has demonstrated global experience through collaboration with the National Institutes of Health (NIH) in the US on multiple studies, and has an ongoing 15-year relationship with the Massachusetts General Hospital on a training program in vaccine development and public health.
Figure 6: Interventionsal Clinic Trials by Product Types in Bangladesh, 2000–2022

At icddr,b and other prominent clinical trial sites, such as Dhaka Medical College and Bangabandhu Sheikh Mujib Medical University, vaccines are the most trialed interventional product (Figure 6). In total, ~18% of the trials held in the country since 2000 have been for vaccines, with vaccines for poliomyelitis, cholera, typhoid, dengue, hepatitis B, rotavirus, shigella, and HPV being trialed, among others. Despite the presence of some well-functioning clinical trial sites with demonstrated experience and expertise in conducting clinical trials for priority therapy areas (infectious diseases) and products (vaccines), there is tremendous scope for improving clinical trial activity levels in the country. However, this increase must simultaneously lead to greater representation of all parts of the population. Several underlying challenges related to policies, processes, and infrastructure contribute to the relatively low levels of activity seen in the country. The next section highlights several such challenges, in addition to opportunities for policy and improvement actions derived from expert interviews and global best practices.

GLOBAL BEST PRACTICES AND POLICY OPPORTUNITIES FOR BANGLADESH

A strong domestic clinical trials ecosystem can improve the ability of LMICs including Bangladesh to develop new drugs, vaccines, and therapies. This can improve patient outcomes and advance the domestic pharmaceutical manufacturing agenda through the inclusion of high-value, upstream parts of the pharmaceutical value chain. The outcomes of a robust national clinical trials ecosystem are evident in multiple forms such as

- increased number of domestically developed products trialed and approved by the national regulatory authorities (NRAs);
- greater willingness of international pharmaceutical organizations to conduct multicenter trials in the country;
- faster approval processes; and
- increased confidence of participants and the public in safety, compensation, and ethical policies.

However, to strengthen the overall clinical trials ecosystem at a national level, a systems approach in analyzing the various components that collectively comprise the clinical trials ecosystem is essential. Such components may include processes (such as the application and review processes or data recording and maintenance processes); policies (such as on ethics reviews, compensation, or consent); physical infrastructure (such as trial sites, laboratory equipment); information technology systems (such as those for maintaining clinical trial registries); or intangible human resource elements (such as trained person power to perform key roles as part of clinical trials). Listed in Figure 7 are the six core components of a well-functioning clinical trials ecosystem. Highlighted in this section are the best practices, innovations, and key interventions to address challenges across the clinical trial components, in addition to the opportunity areas for Bangladesh to focus on through policymaking.
Approval Processes

One of the major challenges of conducting clinical trials in LMICs relates to suboptimal regulatory processes\(^{26}\) and administrative challenges to new drugs and associated clinical trials.\(^{27}\) Often, these process challenges result in avoidable delays in the approval process, affecting the overall costs and timelines for conducting clinical trials (Figure 8 illustrates trial approval timelines by economy in 2017).

**Key challenges in Bangladesh.** Approvals for conducting clinical trials in Bangladesh can take up to 5 months on average from the day of submission to the ethics committee. While most countries allow for parallel ethics and regulatory reviews, current policy in Bangladesh prohibits this, adding to the overall approval timelines. Instead, the processes of ethics reviews, regulatory reviews, and import licenses for the drugs and/or vaccines under trial are sequential in nature. Further, ethics approvals are not decentralized to universities or other institutions; instead, all ethics reviews are conducted by the Bangladesh Medical Research Council, which can contribute to the extended timelines. Table 1 highlights other challenges, policy opportunities, and global best practices.

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Table 1: Global Best Practices, Bangladesh Situation, and Policy Opportunities in Approval Processes

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<th>Subcategory</th>
<th>Global Best Practices</th>
<th>Bangladesh Situation and Policy Opportunities</th>
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| Multicenter trials and local representation | [South Africa] Multinational trials held in country are required to have a reasonable proportion of South African researchers on the project team, to include scientists and health care professionals and those from previously disadvantaged communities.¹  
   [Viet Nam] In addition to presenting general research results, a separate analysis is required to determine key safety and efficacy variables on study populations in Asia or Viet Nam using drugs for which racial factors are considered to affect efficiency and safety.  
   [South Africa] With respect to the selection of the clinical trial site, if South Africa is selected, but not the country of origin or other high-income countries, the sponsor must explain the reason(s) why and provide a clear ethical justification.² | There is an opportunity to prioritize participation from national scientists, principal investigators, and health care providers. Such a policy could lead to improved local capabilities over time.  
   While such a guideline is not currently included as a part of the clinical trials policy in Bangladesh, its addition could ensure greater localization and representation of the Bangladeshi population, leading to better patient outcomes.  
   There is an opportunity to include such a requirement and justification, as this could help address concerns about trial safety in local populations. |
| Ethics committees                         | [India] [Viet Nam] [South Africa] Most countries including lower middle-income countries such as India, South Africa, and Viet Nam allow for ethics reviews to be conducted in parallel to regulatory reviews. | Bangladesh’s current policies do not permit conducting ethics and regulatory reviews in parallel, which could contribute to longer timelines for approval processes.  
   There is an opportunity for process expedition by enabling parallel reviews. |
| Clinical review process                   | [India] Clinical trial rules in India provide that any drug discovered in India, or research and development of the drug conducted in India, and that is proposed to be manufactured and marketed in the country, will be approved for clinical trials within 30 working days by the Central Licensing Authority (CLA). Meanwhile, for drugs developed outside the country but marketed in India, a clinical trial schedule of 90 working days is set as the limit for approvals by the CLA. Once communication has been received from the CLA to the applicant, the permission to conduct the clinical trial shall be deemed to have been granted. | Instituting specific timelines for reviews in Bangladesh could help in reducing overall drug approval timelines.  
   There is also an opportunity to prioritize domestic research and development through priority approval processes. |
| Application portal                         | [India] In India, the Central Drugs Standard Control Organization (CDSCO) established SUGAM, an online licensing portal, in March 2016 for importing and registering drugs and medical devices. The online services have been extended to allow pharmaceutical companies to submit clinical trial applications. | An online portal for applying for clinical trials has recently been set up but has limited uptake owing to existing technical issues, necessitating manual submissions.  
   A robust online data system for applications and results submission would lead to reduced review timelines overall and allow for greater transparency. |
| Expedited approvals                        | [United States] The Food and Drug Administration encourages using mechanisms such as pre-investigational new drug application (pre-IND) meetings, Q-submissions, and humanitarian device exemptions to expedite the review of new therapies and devices with potential efficacy and appropriate safety data to enter clinical trials. | In Bangladesh, expedited review may be granted when a valid scientific review committee approves the research proposal as methodologically sound without any intervention and risk of distress or injury, physical or psychological, to participants. However, current guidelines do not provide a standardized provision to expedite the review of new therapies where there is a significant unmet need, which could be crucial during health emergencies and is an opportunity area. |

### Data Transparency

Data transparency is of utmost importance in clinical research as it helps ensure medical decisions are evidence-based. Additionally, clinical data disclosure and transparency are crucial given the legal obligations and compliance factors associated with data disclosure. Poor data quality and data recording practices have been highlighted as barriers to conducting clinical trials in LMICs.28

#### Key challenges in Bangladesh

Presently, while there is an online system for protocol registration in Bangladesh, low uptake levels mean that paper-based submission processes continue in parallel. Further, no notifications on trial approvals are provided through this system, meaning that the sponsors and/or principal investigators track the progress on applications regularly. Another key challenge is that results from previously conducted studies are not made available to sponsors and researchers. Further, a lack of defined templates and formats means that monthly disclosures provided during the trial period are often nonstandardized. A comparison of global practices, Bangladesh’s situation, and policy opportunities in data transparency is provided in Table 2.

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#### Table 2: Global Best Practices, Bangladesh Situation, and Policy Opportunities in Data Transparency

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<th>Global Best Practices</th>
<th>Bangladesh Situation and Policy Opportunities</th>
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| Data protection            | • [Europe—EMA] The European Medicines Agency (EMA) has formulated guidelines on clinical trial information disclosure covering anonymization of patient data, redaction, and patient data privacy. Clinical study reports are redacted before publication to remove personal identifying information with which patients can be re-identified. Redactions were made to protect personal data, for example, redacting case narratives in full in half of all the procedures published, and partially redacted in a further fifth of the procedure.  
  • [United States (US)] US Policy 45 CFR part 46, also known as the Common Rule, requires data anonymization prior to release for further research.  
  • [South Africa] The Protection of Personal Information Act 2013 came into force in South Africa on 1 July 2020. It seeks to strengthen the processing of personal information, including health information. Like the European Union (EU) General Data Protection Regulation (GDPR), it regulates the processing of personal information.                                                                 | While broad level guidance on data protection exists, there is an identified need for a specific policy on data privacy and anonymization requirement on the lines of GDPR to improve data security, privacy, and transparency.  
  Additionally, to assuage concerns related to intellectual property protection, there is an opportunity for Bangladesh to formally define its data protection policies for regulatory data, and ensure underlying mechanisms are put in place to support this. |
| Trial registration         | • [US] As per Health and Human Services (HHS) rules, all clinical trial results should be posted, irrespective of the outcome of the study.  
  • [US] As a result of the Food and Drug Administration Modernization Act of 1997, clinicaltrials.gov was established in 2000. The act required HHS, through the National Institutes of Health, to establish a registry of clinical trials.  
  • [US] The US requires that summary protocol information for an applicable clinical trial (ACT) be submitted to the clinicaltrials.gov public registry not later than 21 days after the first patient is enrolled. Specific updates and amendments must be submitted to the registry within 30 days of the change. Trials must be prospectively registered.  
  • [Europe—EMA] The Clinical Trials Information System is a single-point portal for clinical trial sponsors and other organizations running clinical trials to apply to conduct a trial in the EU Member States and European Economic Area countries and to submit data related to a trial and post-trial results.                                                                 | While Bangladesh has an electronic registry for clinical trials, currently both electronic and paper-based registration processes are being utilized. A robust online data system for applications and results submission could lead to reduced review timelines overall and allow for greater transparency. |
| Results disclosure         | • Globally, most countries follow the 12-month requirement for publishing trial results, which is also the World Health Organization guideline.  
  • [US] The US requires summary trial results for ACTs to be submitted to clinicaltrials.gov a maximum of 12 months after the date of the last visit of the last patient specifically for the purpose of data collection for the primary outcome of the trial.  
  • [Europe—EMA] In Europe, the sponsor submits the results directly to the EudraCT database within 6 months of the conclusion of pediatric trials (and those in an EU paediatric investigation plan with pediatric populations) or 12 months after trial completion for trials without pediatric populations.                                                      | Given the limited uptake of a publicly available electronic registry, results for clinical trials may not be readily accessible. Participating in global clinical registry networks such as International Clinical Trials Registry Platform (ICTRP) could enable wider availability of clinical trial results. This, along with increasing the uptake of electronic systems, is an opportunity area for Bangladesh. |


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Clinical Trial Infrastructure

The clinical trials ecosystem in LMICs faces challenges related to inadequate infrastructure, which includes laboratories, equipment, access to diagnostics, imaging, and pathology services, along with quality assurance, administrative support, and informatics systems. Additionally, this infrastructure encompasses a network of partnerships and global collaborations that incentivize and enable the exchange of ideas, supervision, and mentorship between different places, markets, or people that can facilitate the acquisition of resources and training.

Presently, scarce availability of funds for research in LMICs means that clinical research is often funded by global actors, and such funding is short in term and specific in nature. When these short-term trials conclude, the infrastructure typically disappears, taking with it the data generated from the research and the researchers who secured funding from HICs. For sustained strengthening of the clinical research ecosystem in Bangladesh, it is crucial that investments are channeled toward building and maintaining high-quality research infrastructure, which can act as the base for a robust clinical trial environment. Table 3 highlights policy opportunities for Bangladesh in clinical trial infrastructure, comparing global best practices.

Key challenges in Bangladesh. Challenges in clinical trial infrastructure in Bangladesh relate to both tangible and intangible infrastructure. There are a limited number of clinical trial sites available in the country, most of which are in the Dhaka region. Because of the unavailability of appropriate equipment in public hospitals, most sponsors in CROs prefer to conduct trials in the private sector, even with higher costs. Further, there are no pools or networks of principal investigators for the sponsor to tap into, which delays the recruitment of appropriate clinical trial staff.

Table 3: Global Best Practices, Bangladesh Situation, and Policy Opportunities in Clinical Trial Infrastructure

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<th>Global Best Practices</th>
<th>Bangladesh Situation and Policy Opportunities</th>
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<td>Clinical trial sites and laboratory infrastructure</td>
<td>• [Republic of Korea] The Korea Drug Development Fund was set up to promote domestic manufacturing and has constructed 15 clinical trial centers since establishment. Between 2007 and 2013, there was a 640% increase in the number of clinical trials that were investigator-initiated. • [United Kingdom (UK)] In the UK, there are 28 clinical research facilities (CRFs) of the National Institute for Health and Care Research (NIHR). These CRFs are purpose-built facilities located within National Health Service hospitals where researchers can conduct early-phase and complex studies. The NIHR has made a £161 million investment in these facilities over a 5-year period, creating dedicated spaces for high-risk experimental medicine studies, including first-in-patient trials and intensive later phase studies. • [India] The National Biopharma Mission (NBM) was set up to help solve difficulties accessing trained and equipped clinical trial sites in India, which was highlighted by biopharma companies. NBM aims to support the establishment of clinical trial networks and strengthen clinical trial capacity in the country.</td>
<td>As per the Bangladesh Health System Review by the World Health Organization (2015), the laboratories require strengthening in the area of quality testing of pre-registration as well as post-market drugs. Prioritizing availability of physical infrastructure including trial sites and laboratory equipment can help improve clinical trial activity in the country going forward. Public hospitals can be specifically prioritized for the development of new clinical trial sites, and additional equipment may be provided to such sites as required. Further, creation of pools of principal investigators under the aegis of the regulatory authority may be explored. Doctors serving in public hospitals can often be more experienced and have a greater patient reach, and thus may be particularly suitable as principal investigators.</td>
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<td>Partnerships</td>
<td>• [India, Japan] The Department of Science and Technology, Ministry of Science &amp; Technology, Government of India, New Delhi and the Japan Society for the Promotion of Science conduct the India–Japan Cooperative Science Programme to promote bilateral scientific collaboration between Indian and Japanese scientists. • [United States (US), Brazil] The US–Brazil Collaborative Biomedical Research Program supports joint research projects, capacity-building, and training programs in various areas of clinical research.</td>
<td>Bangladesh is not a member of any global major clinical trial networks. Limited international collaboration and partnerships may mean that the process of knowledge and expertise transfer in Bangladesh is slower, leading to fewer clinical trials. Going forward, Bangladesh may look to partner with the existing clinical trial networks through its existing clinical trial sites or through development of new sites.</td>
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Table 4: Global Best Practices, Bangladesh Situation, and Policy Opportunities in Human Resources

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| Capacity-building | - **[India]** In India, the government established training institutes to increase the skills of the clinical trial workforce, and hospital departments were provided with additional equipment and funding for staff to perform as clinical trial investigators.  
  - **[Multiple Sub-Saharan African countries]** The African Development AIDS Prevention Trials (ADAPT) capacity program was spearheaded by the Centro de Investigación de Enfermedades Tropicales and funded by the International Development Research Centre through its HIV Prevention Trials Capacity Building Grants program of the Global Health Research Initiative in Canada. The ADAPT program focused on enhancing capacity in HIV trials in 10 Sub-Saharan African countries: Botswana, Lesotho, Malawi, Mozambique, Namibia, South Africa, Swaziland, Tanzania, Zambia, and Zimbabwe. The overarching objective on a global scale was to develop state-of-the-art, autonomous, and sustainable health measurement and planning resources in African countries, facilitating improved implementation and evaluation of HIV and AIDS prevention interventions.  
  - **[Australia]** Through the Clinical Trials Networks initiative, the Government of Australia invested $5 million over 4 years in the Australian Clinical Trials Alliance to build the capacity of clinical trials networks. The purpose of this research funding was to provide better access to and increase recruitment of patients into clinical trials across Australia, better design the quality and efficiency of clinical trials across Australia, and translate research into clinical practice. | While current mechanisms on capacity building of key personnel including principal investigators in oversight of clinical trials in Bangladesh are limited, there is an opportunity for structured official trainings for both the staff conducting clinical trials and regulatory personnel—including awareness-building on the importance of clinical trials. |


**Human Resources**

Evidence from LMICs highlights the lack of trained human resources, expertise, capacity building, and motivation for the conduct of clinical trials as some of the major challenges (footnote 27). It is globally acknowledged that enhancing research capacity and capability in LMICs presents one of the most effective and sustainable method for advancing health and development within these nations. Table 4 provides a comprehensive view of global best practices, and the situation and policy opportunities regarding human resources in Bangladesh.

**Key challenges in Bangladesh.** Presently, there is a need to build capacity on Good Clinical Practice (GCP) guidelines and standards in the clinical trials conduct among researchers. Limited capacity on GCP can often mean that crucial processes related to data recording and patient management are not adequately followed.29 Capacity development of the public and private sector health workforce must also be systematically pursued. Sponsors and CROs also face impediments in recruiting relevant staff from the public sector as there is limited awareness on clinical trials.

**Incentives and Funding**

In addition to ensuring that appropriate infrastructure, resources, and personnel are available, governments across the world have depended on the provision of direct and indirect incentives, benefits, and subsidies to biopharmaceutical organizations and CROs to promote domestic clinical trial activity. LMIC governments, for example, have invested in clinical trial infrastructure to encourage overseas investment that leverages access to their large populations and low-cost base. At the same time, owing to high costs and burdensome regulatory requirements in HICs, the clinical trial services market has been the subject of substantial reform over the past 2 decades. Governments can incentivize clinical trial activity in multiple ways, including through tax incentives in the form of targeted tax credits, direct funding of clinical trial activity through the establishment of R&D funds, or other incentives such as advance market commitments.30

**Key challenges in Bangladesh.** Currently, there are limited direct investments by the government in clinical trial infrastructure, with no monetary or nonmonetary incentives made available to CROs or sponsors.

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29 Insight from stakeholder interview.

Table 5: Global Best Practices, Bangladesh Situation, and Policy Opportunities in Incentives and Funding

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<th>Global Best Practices</th>
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<td><strong>Tax incentives</strong></td>
<td>• [Australia] Australia’s R&amp;D Tax Incentive gave companies with an annual turnover of &lt; $20 million a 43.5% tax credit and companies with revenues of &gt; $20 million a 38.5% credit applied to eligible expenditure. Subsequent estimates suggest that benefits from this policy account for ~10% of overall clinical trial activity in the country.</td>
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<td>• [United States (US)] The Orphan Drug Act (ODA) 1983 provided a 50% tax credit for expenditures incurred in the R&amp;D of a rare-disease drug. Incremental initiatives in the ODA led to a 69% increase in new clinical trials in the US as per studies.</td>
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<td>• [Republic of Korea] The government provided tax deductions for research and development (R&amp;D) costs and established the Global Pharmaceutical Industry Development Fund through the Ministry of Health and Welfare for further incentives. Over 2007–2013, a 50% increase in oncology trials was observed, while investigator-initiated ones increased by 640%.</td>
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<td>• [India] In India, policies allowed for expenditure could be offset against other income for R&amp;D on rare diseases by pre-approved companies.</td>
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<td>• [Australia] In 1985, Australia introduced R&amp;D tax credits of 150% for private sector expenditure, one of the most generous rates in the world. A subsequent review of this tax credit found it had inducement rates of 16.7%. The following year saw a sharp increase (nearly double) in the number of PubMed clinical trial publications.</td>
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<td>• [India] India introduced a 150% R&amp;D Tax Credit that began in 2001/2002 and led to a substantial increase in clinical trials, from 40–50 in 2001 to over 1,850 in 2011.</td>
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<td>• [People’s Republic of China (PRC)] The PRC reduced the corporate tax rate by 15% for eligible companies, leading to substantial growth in the clinical trials industry—from 4 trials registered in 2001 to 497 in 2010.</td>
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<td><strong>Direct funding</strong></td>
<td>• [Australia] The government established a $20 billion Medical Research Future Fund, with the goal of directing $614.2 million over a span of 10 years toward two medical research grants aimed at boosting clinical trial endeavors.</td>
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<td>• [Japan] The government offered financial support for patients through patient cost-sharing. Firm-sponsored new clinical trials increased by 181% when covered by the policy.</td>
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<td>• [Global] GloPID-R brings together and facilitates coordination among major global funding organizations including country members across the globe.</td>
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<td><strong>Other incentives</strong></td>
<td>• [Brazil] The Ministry of Health in Brazil committed to fund vaccines and medicines through a foundation from Phase 1 through to commercialization, with clinical trials occurring within Brazil. The average development cost of clinical trials in Brazil is now around 75%–80% of comparable US clinical trials. There has been strong growth in the number of trials.</td>
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<td>• [India] In India, clinical trials were exempted from sales tax for a specific period. Import duty was lifted on supplies and permission for export of trial specimens was granted at the same time as the protocol was approved.</td>
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</table>

Presently, there are no tax incentives targeted at clinical trial research or contract research organizations (CROs) in place in Bangladesh. There are opportunities to promote participation of global CROs and sponsors in the domestic market through monetary and non-monetary incentives.

No direct funding initiatives for clinical trials are currently in place in Bangladesh, providing an opportunity for government action.

No other monetary incentives for clinical trials are currently in place in Bangladesh.

## Table 6: Global Best Practices, Bangladesh Situation, and Policy Opportunities in Patient Rights and Awareness

<table>
<thead>
<tr>
<th>Subcategory</th>
<th>Global Best Practices</th>
<th>Bangladesh Situation and Policy Opportunities</th>
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<tbody>
<tr>
<td>Compensation</td>
<td>• [India] In India, the revised clinical trials guidelines of the Central Drugs Standard Control Organization require compensation to be paid only to the point that the drug resulted in an adverse reaction in a patient participating in the trial. This is a significant change from the earlier regulation, stating that compensation had to be paid irrespective of whether the drug caused the serious adverse event or not.</td>
<td>While broad guidelines on compensation for patients in case of trial-related injuries are present as a part of the Bangladesh Good Clinical Practices, specific guidelines on compensation calculation mechanisms may be required. Such calculation mechanisms can help preemptively address the concerns of potential trial participants, which may currently be impeding participant recruitment efforts.</td>
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<td>• [India] In India, compensation for injury is ultimately determined by the Drug Controller General of India based on recommendations from an expert committee, as opposed to an ethics committee. This compensation must be paid within 30 days of the order.</td>
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<td>• [United States (US)] In the US, the Orphan Drug Act (ODA) extended public health insurance (Medicare) to encompass expenses of trials for patient participants. It is observed a significant increase in new clinical trials for rare disorder drugs in the 3 years immediately following the passage of the ODA, although this reflected the cumulative impact of ODA interventions.</td>
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<td>Insurance</td>
<td>• [South Africa] In South Africa, all clinical trial sponsors and investigators are mandated to obtain adequate insurance and indemnity to cover any liability claims during the conduct of a clinical trial, in accordance with responsibilities described in South Africa’s Good Clinical Practices guidelines. These state that the sponsor should provide written assurances to the investigator that they will agree to pay compensation to participants and/or their legal heirs in the event of trial-related injuries or death. The investigator, in turn, communicates this information to the relevant ethics committee.</td>
<td>As current policy does not mandatorily require insurance for clinical trial participants, there is an opportunity to include the same and remove potential hindrances to the recruitment of participants and provide an improvement opportunity.</td>
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<td>• [Viet Nam] Viet Nam guidelines require that, among essential documents, the principal investigator, institution, and sponsor must obtain an insurance contract before conducting a clinical trial. The purpose of the insurance contract is to guarantee that research participants will be compensated in the event of a trial-related injury.</td>
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Participant Rights and Awareness

Last, ensuring the right policies on informed consent, fair compensation for injuries resulting from clinical trials, and insurance for trial participants is crucial for building a robust clinical trials ecosystem.

Key challenges in Bangladesh. Based on the current guidelines in Bangladesh, overall compensation to clinical trial participants is limited, and does not take into account the various opportunity costs incurred by participants. Further, there are limited guidelines on compensation for injuries or ill-health incurred as a consequence of participation in the trial.

POLICY CONSIDERATIONS AND RECOMMENDATIONS

As Bangladesh seeks to create a well-functioning domestic vaccine manufacturing sector, ensuring that the high value-generating upstream operations such as R&D are performed within the country will become increasingly important. While Bangladesh has progressed in building the appropriate policies for improving the clinical trial activity domestically, it still lags both HICs and LMICs on a per capita level. There is a need to develop a more robust clinical trials ecosystem that has minimal process redundancies; incorporates the latest innovations including those based on digital technologies; and relies on secure, high-quality, and accurate data made available to the research community widely and transparently. Further, such a system must also incentivize participation of both international and local pharmaceuticals and CROs, while investing in the necessary clinical trial infrastructure—both tangible and intangible. Finally, to ensure robust participation and public trust in the system, policies related to participant rights—including compensation, insurance, and informed consent—must also be revised. Such a program for strengthening the ecosystem requires additional policy efforts, including the following:

Key Policy Development Opportunities for Bangladesh

1. Strengthen the regulatory framework and optimize clinical trial processes. The regulatory framework for domestic clinical trials must take cognizance of the impediments currently faced by the system—including those related to limited representation of the Bangladesh population in clinical trials globally, lack of streamlined processes for applications and review processes, and lack of incentives for domestic companies leading to dependence on international organizations. Bangladesh’s current policies do not allow for ethics and regulatory reviews to happen in parallel, which adds to the overall timelines of product approvals and presents a key opportunity for mobilization from a policy perspective. Further, setting specific deadlines for approving clinical trial applications, including through single window clearance mechanisms and digital portals for
submissions, could help in expediting the overall processes. To incentivize clinical trial activity by domestic organizations, prioritized application processing could also be offered.

To address the challenges of representation, Bangladesh could mandate a separate analysis of research results specific to its population, similar to that in Viet Nam. Like South Africa, Bangladesh could require local representation in leading the clinical trials held in country, such as for key personnel like principal investigators.

2. Build clinical trial infrastructure and capacity of clinical trial personnel. The government can support efforts to promote clinical trial activity in Bangladesh by investing in the underlying tangible and intangible infrastructure that is utilized as part of clinical trials. For physical infrastructure, this may include channeling greater funding toward setting up of clinical trial sites and new laboratories or equipping existing ones. Additionally, the government can help improve the infrastructure through investments in capacity building of clinical trial personnel. This can include investigator training through standardized core content and availability of continuing medical education, and centralized certification processes for clinical investigators. Investments in information technology solutions for matching investigators to sponsors may also be developed.

On the partnerships front, governments elsewhere have played a substantial role through setting up international collaboration networks for researchers. Other examples of international partnerships include those for capacity-building of research staff in LMICs through trainings and joint research projects with international staff from other countries. Bangladesh may also choose to intervene in this way to build the necessary infrastructure for a robust clinical trials ecosystem.

3. Prioritize data transparency, availability, and privacy. Clinical trial data transparency is of the utmost importance to policymakers, public health bodies, the research community, health care professionals, and patients. Bangladesh should prioritize the implementation and increased uptake of the electronic clinical registry. Such a registry should be made publicly available, capture data on all ongoing clinical trials, and be accurate and up to date with respect to the status of all trials. Further, policies that necessitate the publishing of CSRs and making them available within a specific amount of time will also help in improving overall data transparency. Further, the regulatory authority, the Directorate General of Drug Administration, could choose to set, and regularly report against, public targets for achieving progressively more ambitious reporting rates on both trial status and CSRs over time, with 100% compliance by all trials as the ultimate target and limited to no exceptions (which are granted only in exceptional cases). To assuage the concerns of data privacy among potential clinical trial participants, specific guidance and mechanisms for data storage, anonymization, and protection should be created. Last, making the latest surveillance data available to clinical trial practitioners could allow for faster identification and recruitment of participants.

4. Offer incentives to promote investments by the private sector. Many countries have realized substantial increases in clinical trial activity by offering monetary incentives in the form of tax subsidies and direct funding. Tax incentives in the form of credits and exemptions can help facilitate a private sector response but generally act as a nonspecific tool to promote such activity. This is because clinical trials account for only a limited proportion of spending for R&D-focused organizations. On the other hand, interventions that directly fund specific trials or address specific deficiencies are generally delivered through state-funded organizations or collaborative partnerships. Bangladesh can develop such instruments to offer broad or specific incentives to both domestic and international organizations, in combination with other policy reforms to improve regulatory and approval processes. However, it will be crucial to monitor and assess the effectiveness of such interventions as the cumulative fiscal burden may be substantial.

Thus, over the short to medium term, several high-impact actions can be undertaken to improve clinical trial activity in Bangladesh by reducing the regulatory burden and optimizing clinical trial processes. Other key initiatives, such as participating in international clinical trial networks or laying the foundations for new ones through the establishment of new sites and a principal investigator pool, can have a rapid impact on the ecosystem as well. Over the medium to long term, initiatives aimed at infrastructure, strengthening such as expansion of electronic data systems and financial incentives, can help in improving clinical trial activity in the country.

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