Pharmaceuticals Research and Development (R&D) in Bangladesh: ground realities and prospects

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COVER LETTER

This report is part of the broader "Research Collaboration on Technology, Equity, and the Right to Health", between the Global Health Centre (GHC) at the Geneva Graduate Institute in Switzerland, the James P. Grant School of Public Health at BRAC University in Bangladesh, and the Universidad de los Andes (ANDES) in Colombia, supported by the Open Society University Network (OSUN). The larger research collaboration consists of two research projects – one on digital health and human rights, and the other on pharmaceutical research and development (R&D) in the Global South.

As part of the latter research project, three individual research reports present the findings on pharmaceutical R&D in the Global South: one report led by BRAC about pharmaceutical R&D in Bangladesh, another report led by ANDES about pharmaceutical R&D in Colombia, and finally, one report led by the GHC about pharmaceutical R&D in low-and middle-income countries (LMICs).

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ACRONYMS

API	Active Pharmaceutical Ingredients
BAPI	Bangladesh Association of Pharmaceutical Industries
BCSIR	Bangladesh Council of Scientific and Industrial Research
BIRDEM	Bangladesh Institute of Research and Rehabilitation in Diabetes, Endocrine and Metabolic Disorders
BMRC	Bangladesh Medical Research Council
BRAC	Bangladesh Rural Advancement Committee
BRICM	Bangladesh Reference Institute for Chemical Measurements.
BSMMU	Bangabandhu Sheikh Mujib Medical University
BUET	Bangladesh University of Engineering and Technology
BUHS	Bangladesh University of Health Sciences
CBMCB	Context-based multicast content distribution
CHRF	The Child Health Research Foundation
CMCH	Clinical Mental Health Counselor.
CRO	Contract research organization
CRP	Centre for the Rehabilitation of the Paralyzed
CT	Clinical Trials
DGDA	Directorate General of Drug Administration
DMC	Dhaka Medical College
DU	Dhaka University
EC	European Community
EMA	European Medicines Agency
EU	European Union
FDA	Food & Drug Administration
FDAMA	Food and Drug Administration Modernization Act
GDP	Gross Domestic Product
GMP	Good Manufacturing Practice
GPG	Global Public Goods
GPL	General Public License
HEQEP	Higher Education Quality Enhancement Project
ICDDRB	International Centre for Diarrheal Disease Research, Bangladesh
IDB	Investment Decision Board
IDP	International Development Program
IEDCR	Institute of Epidemiology, Disease Control and Research
IP	Intellectual Property
IPR	Intellectual Property Rights
IRB	The Institutional Review Board
KII	Key Informant Interview
LAMB	Lutheran Aid to Medicine in Bangladesh
LMIC	Low Middle-Income Countries
MCHTI	Maternal Child Health Training Institute.
MHRA	Medicines and Healthcare products Regulatory Agency.
MSD	Musculoskeletal Disorders
NBM	New Business Model
NBR	National Board of Revenue

NCE	New Chemical Entity
NIH	National Institutes of Health
NLM	National Library of Medicine
NTD	Neglected Tropical Diseases
PCB	Printed circuit board
PD	Product Development
PI	Project Investigator
SAR	Structure-Activity Relationship
SDC	Swiss Agency for Development and Cooperation
SIDA	Security Identification Display Area
SIU	Special Investigative Unit
TB	Tuberculosis
TGA	The Therapeutic Goods Administration
TRIPS	Trade-Related Aspects of Intellectual Property Rights
UGC	University Grant Commission
UHFPO	Upazila Health and Family Planning Officer
UK FCDO	United Kingdom Foreign, Commonwealth & Development Office
UK MHRA	United Kingdom Medicines and Healthcare products Regulatory Agency.
UN	United Nations
USAID	United Nations Program on HIV and AIDS
USD	United States Dollar
USFDA	United States Food and Drug Administration
VAT	Value-added tax
WHNRC	Western Human Nutrition Research Center
WHO	World Health Organization
WTO	World Trade Organization

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EXECUTIVE SUMMARY

Introduction

The current system of pharmaceutical Research and Development (R&D) produces globally unequal access to medicines, with some innovative needs unmet and high prices built into the system. This has become more visible during the COVID-19 pandemic. Faced with the unprecedented crisis, countries are racing to develop new technologies for medicines (and vaccines). Different approaches to organizing, financing or incentivizing R&D have demonstrated that they can address some of these problems. However, understanding of their potential and challenges is limited, particularly for initiatives in developing countries.

The National Drug Policy 1982 of Bangladesh ensured supply of quality essential drugs at a relatively low price and was instrumental in developing the indigenous pharmaceutical industry in the country. However, the pharmaceutical market in Bangladesh is limited to generic products, arising out of the benefits of the waiver in the Trade-Related Aspects of Intellectual Property Rights (TRIPs), with little indication of activities in the R&D sector. In this multi-country research project (Bangladesh, Colombia and Geneva, Switzerland), we aimed to explore and synthesize the available evidence by mapping technological capabilities in terms of research and development in the pharmaceutical sector in Bangladesh. Through this mapping, we aimed to identify key relevant players from the industry, policymakers, regulatory bodies, academics, donor-partner institutions and civil society groups. Analysis of data was used to assess how well each new business model may (or may not) address weaknesses in the system, and the feasibility of an alternative business model.

Method

To elicit relevant data, we started with a scoping review of peer-reviewed articles (n=21) to visualize the current situation regarding R & D situation in the country. Then, we conducted Key Informant Interviews (n=18) with relevant stakeholders to extract data on the current business model and to assess the feasibility of alternative models. Lastly, to identify the funding flow for overall R&D in the health sector and explore the current status of clinical trials in Bangladesh, the databases World RePORT, G-Finder and ClinicalTrials.gov and International Clinical Trials Platform (ICTRP) have been used. Furthermore, a stakeholder meeting with

participants from the private pharmaceutical companies, research organizations and universities was conducted.

Findings

We identified four main themes from the triangulation of data: current situation of pharmaceutical R&D in Bangladesh, current business model and perspectives regarding possible business model to facilitate R&D, and funding eco-system.

We have found that the current business model of the pharmaceutical industry in Bangladesh mostly focuses on generic formulations, with very little research being conducted by academic institutes, research organizations, and contract research organizations (CROs). The priority of the private industries is to make a profit while providing medicines at an affordable price to the people, if possible. Stakeholders identified a number of challenges such as lack of a policy, lab infrastructure, collaboration, and reluctance of the stakeholders to facilitate R&D in their respective pharma industries. Participants recommended developing infrastructure and skilled manpower along with collaboration among different institutions and improving regulatory approaches. The possible business models proposed supporting research through funding from the government and external sources so that the medication can be a global public good to enable global accessibility at an affordable price. A Few stakeholders were found to be in favor of this new business model, while others thought that this model would slow down research activities because of less competition.

The funding ecosystem has several distinct tracks. While university and research organizations receive funding from the government and other external sources, the industries are self-financing. Data from the World RePORT showed a total amount of USD 333 million received by 67 research organizations in Bangladesh over the past decade. According to the G-Finder database, the amount of total investment in R&D in Bangladesh targeting different neglected diseases during 2007-2020 was 51 million USD in Bangladesh with fluctuations from time to time. These funders included public and philanthropic groups for different projects. Lastly, we found that different national and international organizations (Clinical Research Organizations, universities, and other research organizations) are conducting clinical trials (Phase I to IV) in Bangladesh funded from internal and external sources, mainly on nutritional disorders, diarrheal diseases, pneumonia, cholera, COVID-19 etc. from clinicaltrials.gov registry. Along with that, from the WHO ICTRP (International Clinical Trials Registry Platform) data analyzed

for the distribution of phases and health categories of clinical trials from 1990-2020 showed that most clinical trials are in phases II-IV, and the health category “infectious and parasitic diseases” had the highest number of trials in Bangladesh. The data also showed a higher number of non-commercial sponsors and funders in the country, when compared to commercial counterparts.

Conclusion

The market-oriented pharmaceutical industry of Bangladesh mainly focused on generic production with little to no investment in R&D, thanks to the TRIPS waiver which has allowed Bangladesh pharmaceutical companies to produce generic formulation of medicines patented abroad. Policy, funds (government and external), lack of skilled manpower, and research infrastructure (e.g., labs) are some of the obstacles mentioned by them to engage in more innovative R&D. Urgent attention and investments, both from the government and the industry, will be needed in these areas if Bangladesh wants to overcome the challenges of the post-TRIPS waiver situation.

INTRODUCTION

One of the most crucial factors for economic growth is Research and Development (R&D), as it spurs breakthrough innovations and inventions (Aghion and Howitt, 1996). According to Global Knowledge Index 2021, Bangladesh secured the 120th position among 154 countries, reflecting its poor performance in this sector. This is not surprising, as the country allocates the lowest percentage of GDP in R & D in comparison to technical, vocational education and training, economy, pre-education, enabling empowerment and ICT (The Business Standard, 2021). This is not to say that research culture does not exist in Bangladesh; rather different public and non-state organizations are involved in research and development in sectors such as human health, animal health, biomedical, and genetics and biotechnology, though insufficient. However, research (and subsequent development) is highly concentrated in a few institutions. For example. A search of articles published in Bangladesh between Jan. 2003 to Aug. 2013, showed that six organizations-International Centre for Diarrheal Disease Research, Bangladesh (ICDDR, B), Bangabandhu Sheikh Mujib Medical University (BSMMU), Bangladesh Institute of Research and Rehabilitation in Diabetes, Endocrine and Metabolic Disorders (BIRDEM), BRAC University and University of Dhaka contributed 89% of the publications (Bhuiya et al., 2013)

Research and Development (R & D) in the pharmaceutical sector

New drug development is crucial to improve population health as well as the sustainability and effectiveness of the healthcare system and society at large (Zozaya, Alcalá and Galindo, 2019). The current system of pharmaceutical Research and Development (R&D) produces globally unequal access to medicines, especially in the LMICs, with some innovative needs unmet and high prices built into the system. Faced with the unprecedented crisis like the COVID-19 pandemic, countries are racing to develop new technologies for medicines (and vaccines). Different approaches to organizing, financing or incentivizing R&D have demonstrated that they can address some of these problems.

Thanks to the pioneering National Drug Policy, 1982 of Bangladesh, an indigenous pharmaceutical industry developed in the country, ensuring the supply of quality essential drugs at a relatively low price (Chaudhuri, 2020). It currently exports to 144 countries (including the UK, EU and USA), besides fulfilling 98% of the domestic market. It is the

second-highest contributor to the national exchequer (1.83% to GDP in 2017-'18) after the Readymade Garments industry. Though there are around 150 functional manufacturers (allopathic), the pharmaceutical market in Bangladesh is highly concentrated and 80% of the drugs produced are generic, and 20% are patent drugs (Mitsumori, 2018). Bangladesh's pharmaceutical sector enjoys the benefits of a TRIPs waiver, i.e., exempted from patent protection by the World Trade Organization (WTO) for an extended period until 2033 (Mitsumori, 2018).

This has led to utilize the TRIPS flexibilities to reverse engineer existing products and focus on earning quick money rather than long-term investment in R & D (Ahmed, 2020). A recent study concluded that the pharma investors in Bangladesh perceive R&D cost negatively in their assessment of the firm's financial condition instead of an attempt at innovation (Farin, 2018). The study found that 80% of the sampled firms had below-average levels of innovativeness. Thus, the top 30 indigenous companies have well-equipped product development departments (PD) instead of a full-fledged R&D entity (Ahmed, 2020). As pharmaceutical companies shy away from innovativeness, it will become difficult for them simply to rely on producing generic medicines in the long term.

Justification

Bangladesh's pharmaceutical industry and the government need to proactively prepare for the situation post-TRIPS waiver to combat the impact of fully implementing TRIPS in the production of generic drugs. However, there is little evidence of awareness on this issue in the industry and the government, resulting in little action to prepare the pharmaceutical R&D sector accordingly. To understand the feasibility of applying a New Business Model (NBM), mapping the existing pharmaceutical system and its current business model is imperative. Through this study, we aim to map the current R&D activities and the pharmaceutical industry's business model in Bangladesh, the gaps and challenges it faces vis-à-vis TRIPS exemption expiry in the near future, and the feasibility of developing an alternate, new business model to address these burning issues.

Objectives

General: To map and analyze the rapidly-changing pharmaceutical R&D sectors from a systems perspective and identify the main actors, purposes, funding flows, and outcomes for public health in Bangladesh.

Specific:

1. To map and explore the current situation of pharmaceutical R&D in Bangladesh, including challenges and opportunities
2. To understand how to reform approaches to technological innovation in Bangladesh.
3. To understand the prospect of alternative business models in the pharmaceutical ecosystem in Bangladesh.

Operational definitions

Term	Definition
Business Model	The way R&D is financed (including push funding and pull incentives), organized, facilitated, regulated, and governed.
Global Public Good (GPG)	A GPG is one that is non-excludable and non-rival in consumption globally. "Non-excludable" means that no one can be excluded from consuming the good. "Non-rival" means that consumption of the good by one party does not reduce the amount of good that remains for others to consume. The key idea is that a GPG is freely available to everyone. Examples of important GPGs for health include norms and rules; standards and guidelines; research into the causes and treatment of disease; and comparative evidence and analysis.
Pharmaceutical R&D as GPG	Three criteria- 1. Product must first be generated (for example, the knowledge must be created, and medicine must be invented and demonstrated to be safe and effective); 2. It must be widely available (for instance, physically available in the health systems); and 3. There should be no barrier to access (such as high prices)

Source: (Moon et al., 2022)

Conceptual framework

For the purpose of analyzing the pharmaceutical R&D system in Bangladesh and the prospect of adopting alternative business models in the country, we adopted the conceptual framework of the research project "New Business Models for Governing Innovation and Global Access to Medicines" (NBM), led by our partner institution the Global Health Centre, Geneva Graduate Institute. The project applies a complex adaptive system lens to characterize and analyze the global Pharmaceutical Innovation System (PIS). This approach conceptualizes the PIS as a network of different actors that interact sustainably through time to produce certain outcomes (e.g., the success or failure to develop a new medicine, the degree to which it becomes accessible to people who may need it).

(For detail, please check annex 01)

Methods

Study design and approaches

A cross-sectional study design with a combination of approaches (scoping review, qualitative exploration and database review) was applied for this study.

a) **Scoping review (ScR) for secondary data analysis:** To explore the current situation of Pharmaceutical R&D, a scoping review of available documents was done. We used Google, Google Scholar, PubMed, Scopus and Research4life for searching relevant literature from Bangladesh. Ultimately, 21 articles were included for analysis of which 12 were primary research papers, eight were secondary review papers and one was a national document. Of these, seven are review articles, one secondary qualitative research paper, four qualitative research paper, three quantitative research paper, two mixed method research paper, three thesis paper and one national document. Moreover, 3 of the articles dealt with the research expenditures and pricing of the R&D, 3 articles were about the prospects and growth of pharmaceutical industry in Bangladesh, 4 articles focused on the innovative capacity of pharmaceutical R&D, 6 articles dealt with TRIPS and IPR related implications & challenges, 2 articles related to marketing and management practices, one document on the history of pharmaceutical evolution and one national budget document were included (Figure 1).

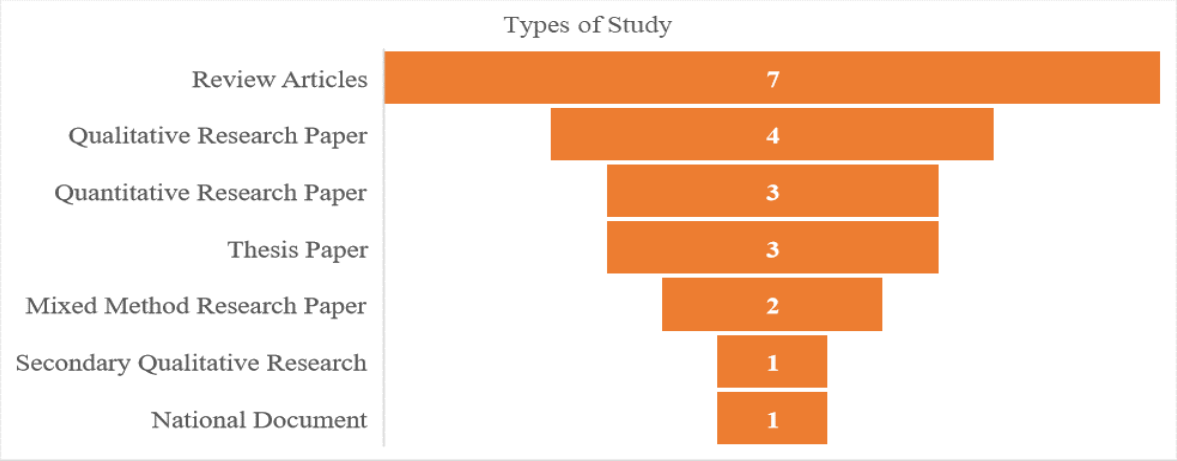

Figure 1: Types of study used for data extraction and analysis

b) **Qualitative Key-Informant Interviews (KIIs) with key stakeholders:** For a comprehensive understanding of the pharmaceutical R&D, their business model, exploring the possibility of adopting alternative business models for their pharmaceutical R&D, KIIs were considered appropriate. 18 KIIs were from different background. The respondents had been categorized into three groups: financers, Implementers, and facilitators. Financiers are authorities of the pharmaceutical companies responsible for deciding on R&D funding strategy, allocation and recipients. We specifically targeted executive directors, managing directors, or general managers since, in the context of our country, they are the ones who decide how much money should be allocated to different departments within the company including R&D. Secondly, the group of people who are actively involved in R&D is known as implementers, and we contacted the head of R&D when looking for implementers. Last but not least, facilitators, including policymakers, intergovernmental organizations, data-sharing platforms, patent pools, product development collaborations, matching initiatives, and analysts, are the ones shaping R&D. We interviewed eight facilitators from various universities and governmental agencies, as well as four financiers and six implementers from well-known pharmaceutical companies (from top 20 companies). All of them are top professionals having more than 15 years of experience

Categories	Key informants participated	Numbers of KIIs
Implementors	Head of Research/ Research Unit Directors, Quality control/ assurance officers	6
Financers	MD/CEO of the pharmaceuticals with R&D or Product Development	4
Facilitators	DGDA, academics/ faculties/researchers (pharmacy & pharmacology) of different universities and research organizations.	8

- For overall R&D in health sector, two types of database analysis have been done.

c) World RePORT and G-Finder: To explore the funding amount in R&D over the years, types of funding organizations, and invested amounts on various diseases that disproportionately affect people in LMICs , World RePORT and G-Finder have been used.

d) ClinicalTrials.gov and ICTRP: To explore clinical trials in Bangladesh (organizations that perform clinical trials, as well as the projects they are working on, their sponsors and collaborators, and the diseases that have been the subject of these trials), the databases ClinicalTrials.gov and ICTRP have been used.

(For detail, please check annex 02).

Thematic findings

The scoping review data and data from qualitative exploration were synthesized and narrative description is made based upon four key themes: I) Current situation of pharmaceutical R&D in Bangladesh; II) Current business model; III) Drug pricing, availability and accessibility; IV) Perspectives of stakeholders on New Business Model. For the themes/sub-themes and relevant codes, please see Table 1.

Table 1: Thematic findings

Themes/sub-themes	codes
1.Current status of R&D in pharmaceutical companies and academic and research institutions	1.1. Purpose
	1.2. Key actors
	1.3. Funding flow
	1.4. Challenges
	1.5. Priority actions
2.Current business model and generic formulation of pharmaceutical companies	-
3.Drug Price and Availability and Accessibility	-
4.The perspective of the stakeholders on alternative business models.	-

I. Current situation of pharmaceutical R&D in Bangladesh

According to one review, Bangladesh's pharmaceutical industry has the greatest rate of R&D-related vulnerability, which leaves 80% of the companies with below-average levels of innovation activities (Ala, 2013). This finding is consistent with our KIIs results, in which each participant affirms that there is not sufficient R&D activity being conducted by the pharmaceutical companies. The development of new chemical entities (NCE) and molecules was commonly referred to as R&D by the stakeholders. They claim that no such work is being carried out by any pharmaceutical company due to a lack of resources such as infra-structure facilities, funding, or manpower. One of the implementers said:

> *"So far, we don't have any innovator product or NCE (New Chemical Entity) molecule that we invented. So, for that invention, actually, the infrastructure and other facilities that are required are not available at this moment in our country. We don't have tissue culture and cell culture facilities, and these are not within their perspective…so NCE, s not right now happening." (KII _Implementer)*

However, findings reveal that a few companies these days have begun emphasizing R&D. In Bangladesh, one organization interviewed is actively researching rare diseases and developing novel molecules. However, they highlighted the complicated procedures of the government, as well as its lack of policy and cooperation.

> *"We work on rare diseases. No one will do it. In meetings, we hear that some companies say that patents will get over so they want to fill the products and sell quickly. And we are thinking here about what will happen after 2026. Now we are doing business, what will happen next? we are working towards sustainable development of Bangladesh." (KII_Implementer)*

Two top companies have revealed that they are patenting one new chemical entity (NCE) outside Bangladesh as there is no policy for patent protection in Bangladesh. One of them has a patent in Europe and another participant claimed to have patents in Australia and Bangalore, India.

> *"So, okay. for example, recently with the Bangalore patent office, we have applied for a patent. Before that we have done a patent with the TGA Australia."*
> *(KII _Implementer)*

Many academic facilitators did, however, revealed that they have been doing a great deal of cutting-edge research in different fields such as phytochemistry, ayurvedic and herbal medicine, neurology and pharmacology, and other areas to develop new drug molecules. The successful research then gets published in high-impact journals, however, due to a lack of industry-pharma collaboration, these are not being scaled up. Nevertheless, one of the successful examples of pharma-academia collaboration is the development of a successful herbal medicine through research carried out by a top university for a top pharmaceutical company, which is currently available on the market, though these events are rare:

> *"We are developing lead molecules and reporting on their activity worldwide and publishing in high-impact journals. I have developed one anti-protozoal drug..... Here in Bangladesh, we have done so many clinical trials under the observations of doctors.." (KII_Facilitator)*

> *"I am working with new drug development. New drug isolation characterization from natural sources, SAR, and biotech assessment plus we are working with different types of nucleosides and nucleotides." (KII_Facilitator)*

The development of a COVID-19 vaccine candidate during the pandemic (Bongovax) by one of the companies in Bangladesh has not been approved yet for a number of factors such as political influence and a lack of policy. This has been cited as one of the most unfortunate events by multiple stakeholders:

> *"Because of political crisis. Every result of Bangovax is okay as I am directly involved with this but because of some political issue, it is not taking place. I cannot tell you everything here about this." (KII_Facilitator)*

Motivation of the pharmaceutical companies, and academic and research institutions

Findings reveal that Bangladesh's pharmaceutical companies are mainly formulation industries. Beside generating substantial revenue, their primary goal is to provide patients with accessible generic medications; these companies do not prioritize local diseases for production of medicines in the country (Chaudhuri, 2020). This was also supported by the KII interviews. In the KIIs, the respondents explicitly delineated the goal of the pharma companies: meeting consumer demand and increasing profits. A few companies also mentioned maintaining quality and achieving public satisfaction as their main priorities. The majority of the companies, however, lacked a vision for research.

> *"They do have an R&D department, but it is not like the real R&D in developed nations. What they do, they study the prevalence of the most occurring disease. In Bangladesh, a study found that 73% of people are suffering from hyperacidity. so we need, esomeprazole, antacid etc..this is how they are prioritizing." (KII_Facilitator)*

Thus, priority is given to the products that produce the highest revenue. As a result, we can say that the pharmaceutical industry is not people-centric but rather business-centric. This is due to the fact that the people suffering from these NTDs are fewer in number and thus do not generate much profit; second, these NTD diseases are not prioritized for research in the most developed countries that our industries follow:

> *"You will see we have 50 kinds of medicines for diabetes, 20 kinds for hypertension, and for TB, only one! No more than five medicines for scabies. Because people who get these diseases are poor, they cannot afford it." (KII_Facilitator)*

In the interviews, the respondents mentioned about their companies actively export pharmaceutical products to other countries. They claimed that the underlying reason for their pharmaceuticals' great demand in other countries is low price. As a consequence, the pharmaceutical companies have to adhere to international regulatory requirements. According to one respondent, this situation is exploited as a tactic for marketing. The company used to brag that the particular company has US FDA approval which accelerates their brand value. Many businesses have obtained US FDA, UK MHRA, and TGA authorization and export medicines to numerous nations.

> *"....We have a separate team for product development of the domestic market as well as for non-regulated markets and the regulated markets of other countries such as the*

European market, UK market as well as Canada, Australia, and some US-based markets. So, we are doing the equivalent product development." (KII_Implementer)

However, there is a positive development that large industries in the country are now producing antiviral, anticancer, and anti-blood flu medications (Gehl Sampath, 2011). Interestingly, all academics have stated that as researchers, conducting research is their primary objective. Many of them claimed that they were not receiving adequate funding despite the fact that they were still conducting research with the assistance of their foreign partners, including foreign governments and institutions. Additionally, several of them used to work on developing new drug molecules and clinical trials. Only one organization reported working towards sustainable R&D, their purpose is the betterment of mankind by prioritizing diseases, especially rare diseases. They are mainly working on biologics, cell therapy, gene therapy, regenerative medicines, diagnostic kits and vaccines.

"We prioritize the disease. Our main purpose is the betterment of mankind. So, we prioritize diseases." (KII_Implementer)

Key Actors for pharmaceutical R&D

Key actors in the government

There are two main governing bodies of Bangladesh's drug and pharmacy sectors, the DGDA & Pharmacy Council of Bangladesh (PCB). DGDA is the governmental regulatory body under the Ministry of Health and Family Welfare and is responsible for all activities related to the import and export of raw materials, packaging materials, Active Pharmaceutical Ingredients etc., along with registration and licensing and pricing of all kinds of drugs (Nadin and Al-Faruk, 2015). According to the respondents, it is the organization that sets regulations for pharmaceutical companies and ensure compliance with Good Manufacturing Practices (GMP). Furthermore, we find from KIIs that testing of drugs is necessary to assess the quality of pre-registration, post-marketed medicines, and the quality of it. There are now two government-run drug testing labs in Bangladesh, one in Chittagong and one in Dhaka. DGDA also appraises new project proposals from all medical systems as one of their major responsibilities.

"Basically, DGDA is referred to as a national regulatory authority who controls the importation, exportation, consumption, and distribution of the medicines" (KII_Facilitator)

Another according to the article, is The Pharmacy Council Bangladesh (PCB), a semi-governmental body established in 1976, is mainly responsible for controlling pharmacy practices. For instance, PCB ensures pharmaceutical businesses adhere to WHO Good Manufacturing Practice (GMP) and pass DGDA inspection (Nadin and Al-Faruk, 2015).

Key actors in pharmaceutical companies

In-house investors: The higher authority within a company is responsible for allocating fund for the R&D activities. They are mainly the owners of the companies. There is no external governmental or non-governmental funding for the R&D activities in the private firms. The respondents confirmed that the funding is not enough to run real-time R&D activities. However, they were unwilling to share the exact amount/percentage of fund allocated for R&D.

> *"Although you all are asking about foreign investments, in this scenario, there is no foreign funding available, and all the funding is covered by the company itself" (KII_Implementer)*

Marketing department: The marketing departments run the market research and select drugs (generic or existing) to work on. According to the opinion of the stakeholders, R&D should start from a disease. But in Bangladesh, the marketing team is responsible for proposing which product to work on based on the market demand. It is done by tools like IMS.

> *"We are following IMS data. Suppose we have a product named "X", It has a 200 crore market. As it is already in the market so ABC company has already launched that product. After launching, they identified that their molecule growth was good. Like every year, they can get a good profit. We are not targeting any disease or therapeutic criteria." KII_Financer*

R&D Department: Based on the market research, the head of R&D starts the pilot batch study (generic formulation). If the pilot batch study passes, the budget is allocated, and further activities are done for launching the drug in the market.

Key actors in research organizations and universities

Apart from the pharmaceutical companies, other institutes promote and conduct R&D, such as the International Centre for Diarrheal Disease Research, Bangladesh (ICDDRB), Bangladesh Medical Research Council (BMRC), Institute of Epidemiology, Disease Control and Research (IEDCR), Institute of Public Health, National Institute of Cancer Research and Hospital,

National Institute of Ophthalmology and Hospital, etc. However, due to lack of funding and of strategic policy direction, and incoherent mandates, the situation led to limited R&D (Chaudhuri, 2020; Shadlen et al., 2011). Along with that, universities produce qualified pharmacists only to be absorbed by the pharmaceutical firms for quality assurance and quality control activities for the production of drugs. Last but not least, PhD holders worked for universities without the resources or financing necessary to encourage an R&D system (Gehl Sampath, 2007).

Funding flow

The findings of qualitative exploration on data regarding funding flow were quite intriguing. It differs significantly from organization to organization. One respondent asserted that, unlike academics, the private pharmaceutical sector receives no funding from external sources.

> *"We get some funding from organizations outside the country, but they are not involved with pharmaceutical company…" KII_Facilitator*

Most Bangladeshi researchers are affiliated with universities and conduct studies/researches utilizing three different sources of funding: government funds, individual funds, and funding from outside. Of these three strategies, most of them rely on foreign funds.

> *"Those who are doing research, how they act! Either they are doing personal investment or other grant support they are getting. Most of the time, they are working with the support of foreign organizations. They are collaborating with foreign universities. This is the context of our research." (KII_Facilitator)*

Many participants have reported getting funds from foreign governments like Italy or Japan.

> *"We have some collaboration like I have with Japan, sometimes we publish some papers. I have got one joint project with my student. The Japanese government provides 75lac Taka (70292.71 USD) and when we were staying over there, we have got a good allowance." (KII_Facilitator)*

Another participant said:

> *"We just get one funding from Italy; they actually even funded for the equipment and chemicals and others for our young researchers." (KII_Facilitator)*

Others claimed to have received support from the Higher Education Quality Enhancement Project in Bangladesh (HEQEP), the National Institutes of Health (NIH), the World Bank, and the Common Wealth. Two participants claimed to have received only US$2000, which is minimal, while one participant claimed to have received US$1 million for just one assignment.

> *"In the last five years, we are getting great support from HEQEP; they have two types of support: one is institutional development and the other is research development…..Sometimes we are getting funds from the World Bank, NIH, or the commonwealth. IDP is also providing us with some support in this sector. But this is a very few amounts. It has been reduced from previous years." (KII_Facilitator)*

Findings reveal that the government-run medical colleges receive funding from the government. A few participants also mentioned receiving funding from the University Grants Commission (UGC), Ministry of Science and Technology, Ministry of Education, and Islamic Development Bank (IDB). However, most of them indicated that the government's support is minimal and that although the funds appear to be substantial, it is distributed across numerous faculties and students. The total amount for one project thus becomes insufficient. However, only selected organizations are compensated well for holding a prominent position.

> *"The ministry of education is giving good funding. I have got 13lac taka from them once and also 30lac taka for another project. UGC gives some funds to the university. Like UGC provide 20 crore takas to DU as DU is running for almost 100 years, so they wanted to enrich the research. So, they provide research grants." (KII_Facilitator)*

> *"BCSIR researchers are getting 100 crore takas for conducting their research, we are getting nothing compared to them." (KII_Facilitator)*

According to another respondent, the government had recently funded BDT 100 to 300 crore (about 94,000 to 280,000 thousand USD) for health research. He continued by saying that despite receiving this amount of funding from the government, no research was done by the respective stakeholders who were supposed to be actively working on R&D. He ascribed this to the unwillingness of the responsible party:

> *"It's hard to answer. Government had a 100-crore taka budget and recently it got 300 crore taka. So, the government has done a lot, but the responsible person still has a lot to do. Due to this, not a single taka has been spent from the allocated 100 crores. That means they don't have the mindset for research." (KII_Implementer)*

Contrarily, pharmaceutical firms claimed that they rely on their own resources. Interestingly in Bangladesh, there is no direct involvement of the government in R&D financing for the pharmaceutical companies (CHAUDHURI, 2020). One of the respondents mentioned that they had made an investment of about 100 crores in 2022, but he pointed out that this sum was too small in comparison to the R&D investments in the developed countries. Another person who concurs with this stated the following:

> *"I will say, 4% of the total budget is being involved in R&D, whereas abroad they are spending around 20-25% for their R&D. So, with this budget, I have to make up for the local market demands. It will be better if we can increase the allocation." (KII_Implementer)*

Challenges

Many challenges are hindering the path to effective R&D in Bangladesh that came out from our KIIs and scoping review:

- **Market-oriented generic formulation industry**: According to the key informants, the pharmaceutical industry in Bangladesh is based on generic formulation, which generates substantial profits while offering affordable medicine to the general public. Although this contributes significantly to our nation's economy, this business model is unsustainable because the TRIPS waiver will no longer be valid after we graduate from LDC status. Fierce market competition is the primary factor diverting the generic formulation business from advancing innovation. As a result of the enormous profits generated by the generic formulation sector, market competitiveness has increased. This trend was reflected in the findings of the scoping review. These companies invest a substantial number of resources in the promotion of medicines to the physicians. Respondents believed that this money could be invested in R & D. According to the viewpoint of one respondent:

  "So, we need to think ... why do so many companies need to produce the same thing? we need to divide the products among these companies to reduce the competition so that companies can focus less on investing in marketing. Say, for example, 5 companies will produce paracetamol. In that way, they get market protection and improve their product quality." (KII_Facilitator)

- **Lack of infrastructure:** Many of the respondents had significant concerns regarding the absence of necessary infrastructure. In addition to lack of facilities including labs, respondents particularly noted the issue of not having a bioequivalence study and a biotechnology lab, both of which are essential for any R & D operations. Additionally, a small number of pharmaceutical companies have indicated that there are no accredited CROs by foreign regulatory bodies in Bangladesh. Given that they intend to export their products abroad, companies must gain certification from a rigorous regulatory body like the MHRA (UK) or EMA (EU), DGDA certification will not suffice. This is why research is being conducted in conjunction with CROs credited by MHRA (UK) or FDA (US). According to one of the top company's implementers:

  "This infrastructure for clinical studies is not available in Bangladesh. There is no CRO, or Contract Research Organization in Bangladesh to date. No infrastructure is ready for bioequivalence so far." (KII_Implementer)

  Similarly, the review revealed a lack of infrastructure support for conducting the bioequivalence test. Additionally, biotechnological capabilities are limited. This provides a significant obstacle for companies intending to export bio generic products to regulated markets (Chowdhury, 2016). This finding is corroborated by our KII findings as well.

- **Lack of involvement from the government:** There is a consensus among the stakeholders regarding the role of the government in developing a policy environment for the current R&D ecosystem, and government support has been called into question. Neither the government . has funded any pharmaceutical R & D projects in the private pharma sector nor crafted a policy for innovation, especially post-TRIPS waiver. Moreover, they questioned procedures that allow companies to market products if they have FDA or MHRA approval without any prior test in the country. Additionally, one respondent stated that the policy for each step of R&D is lengthy. All of these factors ultimately prevent the responsible person from taking the essential steps for R&D.

  "Our regulatory guideline has a policy which is that there must be a reference product in the USFDA or Europe UK MHRA; we can only get approval then. If we do any innovation which is not approved in USA, UK or MHRA, they will not give us any approval. I recently worked on a product called Astragenthin (which is an antioxidant) in chewable form and applied it to DGDA. but they

did not approve as it was not approved by the UK MHRA. That is why we are discouraged from doing innovative work." (KII_Implementer)

In addition, the government imposes an additional 10% tax on foreign investment. One of the respondents stated:

"Because if you spend in R&D in Bangladesh and someone sends a particular amount of money or foreign investment, the Bangladesh bank will deduct 10% of their income from the investors. If someone spends around 10 lac Bangladesh Bank will deduct 1 lac. If I get an investment of 10 crores, Bangladesh Bank will deduct 1 crore." (KII_Facilitator).

Findings from scoping review revealed that the 1982 and 2008 policies were creating a favorable market for the local firms; nevertheless, they ignored a financial outlay. Therefore, government involvement was hardly seen, such as for assisting export or R&D funding.

- **Lack of collaboration:** In the opinion of many respondents, a collaboration between the pharmaceutical industry and the academia is necessary for innovation to emerge; this is rarely seen in our country. This is a major concern for both the business sector and facilitators. One of the top pharmaceuticals reported to have collaboration with academia but not in Bangladesh:

  "We have done also some collaboration with the academics in universities in India, and so there, we can get the latest inputs and we can co-develop." (KII_Implementer)

  One of the impediments is the disarticulated and weak collaboration among the public sector, industries, and universities to utilize the knowledge of newer products. The universities are producing graduate pharmacists qualified enough to work in quality control, assurance, and production areas only (Chowdhury, 2016).

- **The reluctance of the local industry to invest in R&D:** R&D operations necessitate substantial investments without guaranteeing success. According to stakeholders, this is one of the primary reasons local pharmaceutical companies are unwilling to engage in R & D. In addition, there is no clear government policy or funding, and profit-driven

corporations are unwilling to face the risk of failure. A small number of respondents said that, even if these profits appear to be lucrative, these profits are insufficient to fund R&D.

> *"The second problem is Bangladeshi businessmen do not want to take a risk in their whole portfolio and the policymakers cannot have a system where the risk of a company can be protected." (KII_Facilitator)*

Another respondent stated:

> *"Why Bangladesh is not working on it because it needs a huge investment. if you work on approximately 10 thousand molecules, you are not sure about the success and for this, million dollars need to be spent. So, we do not have the real R&D in Bangladesh but PD departments work on this in Bangladesh." (KII_Implementer)*

Review findings also support the notion that most of the local pharmaceutical companies tended to prioritize short-term revenue gains over long-term investments in R&D. To improve the situation, the government needs to step up and offer funds for conducting some essential research in the pharmaceutical industry (Azam and Richardson, 2012).

Recommendations for priority actions

From the scoping review and qualitative data, the following recommendations emerged:

- **Regulatory approach:** The stakeholders stressed having appropriate policies to support R&D and enhance the regulatory environment. The respondents emphasized the importance of allocating a dedicated budget for research and having appropriate policies for the deduction of company tax and income tax, and also that expenses for R&D activities should be waived. They suggested policy revision and adequate guidelines for policy provisions. According to one of the respondents:

  > *"Our government should have some budget for this. They have different budgets but they need to specify that." (KII_Facilitator)*

  > *"Our government has no plan to revise the policy or work on the existing policies for pharmaceutical research-based activities. This is a very important point." (KII_Facilitator)*

Similar recommendations were in the review findings, which suggested the need to update the country's legislation to maximize the benefit of TRIPS flexibilities in the first place and plan to transfer from an imitative to an innovative strategy (Azam, 2014; Islam, 2011). Implementing insurance policies to encourage researchers to invest in R&D was also suggested by KII respondents.

Some specified recommendations regarding policy included:

- Policy assistance should concentrate on an integrated innovation approach that encourages the development of relevant human skills as well as better coordination between the various parts of the domestic knowledge system, particularly public research and industry;
- Assist in building the local intellectual property office's capabilities so that it can accurately and transparently record information on patent applications and grants (Gehl Sampath, 2007)

- **Infrastructure and skill development:** For many stakeholders, the development of the infrastructure was a prime concern; they recommended to upgrade the laboratory environment, along with the development of science-based labs:

  "Yes, we have to develop an infrastructure to provide a proper environment for the scientist. It would not be like the facility for commercialization...we need to maintain the standard. This is not like what we have.... a demand arises and we fulfil it...it is not like that...it is totally different...it has to be very slowly and scientifically..." (KII_Financer)

This recommendation is similar to the articles reviewed. Bangladesh must consequently concentrate on infrastructure development, including testing of equipment and administrative support. To do this, Bangladesh should bargain with its development partners to secure financial and technical assistance while making the assistance firmly enforceable (Royhan, 2013). It might not be possible right now for the government to establish a large public sector organization for R & D. However, both the government and non-government agencies have a role to play in restructuring the nation's R&D infrastructure. Besides being directly involved in funding pharmaceutical R&D, research activities should be conducted not only in government laboratories but also in

private pharmaceutical companies, academic institutions, and other R&D facilities (CHAUDHURI, 2020). The respondents suggested developing skilled human resources with technical expertise to increase research organizations' and pharmaceutical businesses' ability to conduct R&D, and also suggested technology transfer.

- **Stakeholders' collaboration:** A strong R&D process necessitates cooperation and collaboration among the government and non-government actors, and academic and industry collaboration besides public-private collaboration:

  "So, industry, clinical organizations, and academia need to work together otherwise no innovation is possible in Bangladesh." (KII_Financer)

  A few respondents discussed funding sources from the developed countries as a form of cooperation and also decreasing the dependencies among medical practice, and product commercialization in the pharmaceutical industry as a huge amount of money is allocated for commercialization.

II. Current business model of the pharmaceutical companies in Bangladesh:

The pharmaceutical industry in Bangladesh has a robust formulation sector most pharmaceuticals in Bangladesh produce generic formulations, thanks to the TRIPS waiver, which allows them to replicate the formulation invented by the original company. The product is then developed, produced locally, subjected to quality control inspections, and finally marketed and sold.

"Another thing is that R&D is not like the real one. What we can say is that generic products are being developed here. This is our main focus. The new molecule or dosage form production is not our goal. Rather we are producing the generic form of drugs." (KII_Financier)

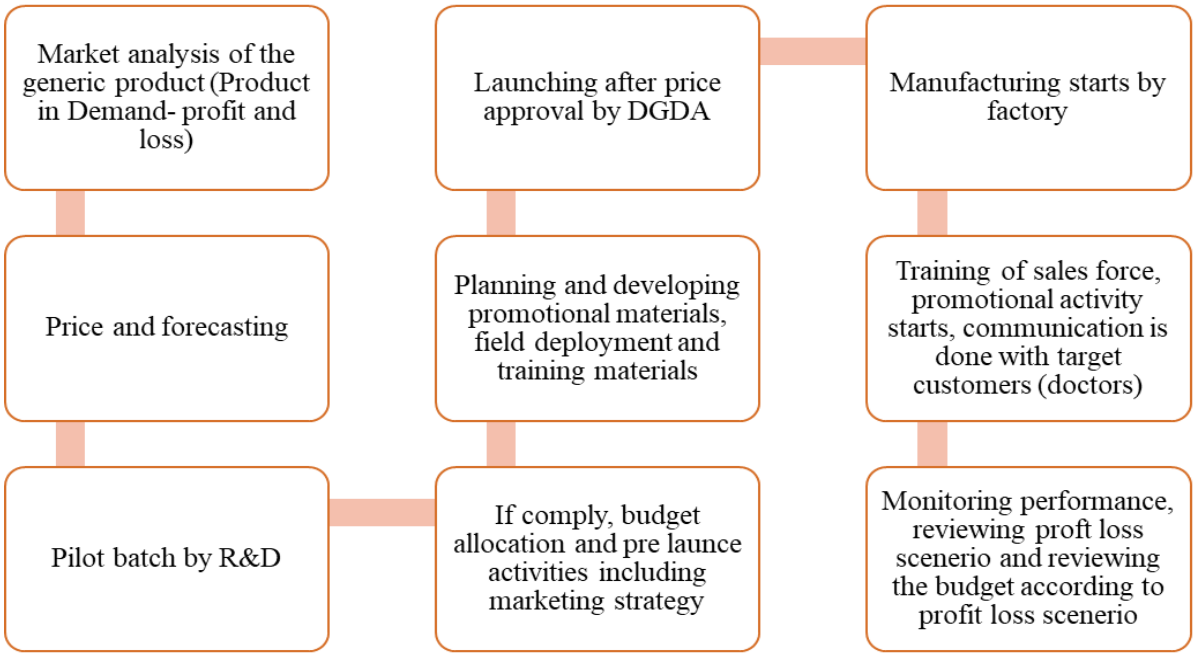

Figure 2: Decision-making flow of the current business model in the pharmaceutical sector of Bangladesh

Figure 2 shows the current business model for the Bangladeshi Pharmaceutical Industry. Based on market research, generic products are selected for production after. a profit and loss analysis. Then the product pricing is done (to be approved by the DGDA), and the forecast is prepared monthly and yearly. Based on these data, R&D department starts producing the pilot batch. After successful pilot, the budget for pre-launch activities will be allocated. After finalizing the procurement planning and promotional items selection, the product will be ready to launch. The persons involved will be well trained before starting the launching activities. After providing training of the salespersons, the salespersons communicate with the target customers and start promotional activities. Lastly, post-launch activities are conducted, like price rechecking, market evaluation, customer satisfaction, and the yearly budget.

Easy accessibility of API leads to the burgeoning generic formulation industry: The key driver of its burgeoning formulation industry is the easy accessibility of API and raw materials from other countries, particularly China and India. In fact, they are the primary suppliers of inexpensive APIs affirmed by reviewed articles (Chaudhuri, 2020). Importing APIs is

considered less expensive than producing them locally. This results in fierce market competition for supplying affordable medications (CHAUDHURI, 2020). Besides, a survey on the R&D investment scale (The year 2000-2007) revealed that reverse engineering is not in practice by pharmaceutical companies either which is necessary for API production (Chowdhury, 2016). Therefore, Bangladesh's pharmaceutical industry manufactures generic formulations only and generates substantial profits. The easy availability of APIs from other countries is also mentioned by one of the stakeholders, adding the intention of increasing API production in the country:

> *"We are also talking about the API to produce as a pharmaceutical product. I would say 90 percent we import from China and India. So, we are trying to just make those also in our country so that at least 50 percent can be made from our own production.… some of the companies are also investing in that area and slowly growing... Beximco has few API production facilities…… we don't have just to be depending on China or India." (KII_Facilitator)*

Exporting medicine as a key part of the current business model: In addition, we learned from the interviews that several businesses actively export their medications to other countries. The respondents claimed that the reason for the drugs' great demand in other nations is their low price. As a result, another important focus for pharmaceutical companies is adhering to international regulatory requirements. According to one respondent, it has evolved into a tactic for marketing, such as mentioning that X company has FDA approval. It accelerates their brand value. Many businesses have obtained US FDA, MHRA, and TGA authorization and export medicines to numerous nations.

> *"Now we have USFDA, UK MHRA, Australian TGA, etc. we are exporting 150 countries' medicines."(KII_Facilitator)*

The downside of the current business model: Therefore, the downside of this business model is the insubstantial R&D because of the huge investment in importing 70 to 100% of the machinery, production inputs, and raw materials from India, China, the USA, Italy, Germany, and Spain (Chowdhury, 2016). This might not seem a problem right now as people are getting affordable medicine, however, with the expiration of the TRIPS waiver, they are going to face a serious problem if they are not self-dependent in producing their own APIs and raw materials.

Therefore, these days, very few companies are involved in operationalizing certain steps of API production. They also depend on imported technologies highlighted in one article (Chowdhury, 2016). The manufacturing of APIs is still considered to be a promising area for research, and according to some respondents, a few top companies like Beximco and Square are beginning to take action in this area. Along with these, a few respondents mentioned the production of biosimilar products by one of the top pharmaceutical companies.

> *"We are also talking about the API to produce as the pharmaceutical product…….Beximco has few API production facilities. Maybe a production facility in the square is coming up. I know there is one company in the southern part of the country, Bengal Fine Chemicals, they're also trying. So, this is another area where we can just do the R&D." (KII_Facilitator)*

One article, though, indicates the potential. The local companies are currently concentrating their efforts on developing their reverse engineering capabilities in order to produce APIs. It will be a significant accomplishment and a small step toward more innovative R&D. Additionally, as the importation of API from outside sources accounts for 40–90% of production costs, this enormous sum can be used to fund future R&D (Gehl Sampath, 2011).

III. Drug Pricing, availability and accessibility

The KIIs shed light on how affordable pharmaceuticals are in our nation. Extremely low production cost is the reason. There are a few factors at play there. The affordability of manpower and raw materials is first and foremost. Another respondent cited the absence of costs for toxicity research and preclinical research as the second reason . The fact that they added the bare minimum profit to the product was another explanation offered by a few respondents. These are the justifications claimed for the medications' low cost. Another intriguing finding was that the pricing was determined by the finance team after taking into account the cost of the facility, the cost of the marketing, and the cost of the raw materials. It was then presented to the DGDA for review. The price is examined and approved by DGDA. One of the respondents said:

> *"We have formulations for our product. The formulation is composed of API and excipient. So, there is a cost for it. The costing plus the manpower cost, facility cost and other fixed costs, marketing team cost. All costs are added and the overall cost is added. The costing is added altogether by the finance department. After that minimum profit is added and we submit it to the DGDA." (KII_Implementer)*

As reported by another respondent:

> *"Our medicine is cheap. why our medicines are cheap? because we are not producing any API..Long before 1982, when multinational companies used to steer clear from producing API, since then we had API shortage. But, now, India and China are producing API in bulk amounts, so the price has come down a lot. So, we are not worrying about API. Along with that, the pharmacist/ biochemist/ chemist, whoever is involved, we are providing/ getting a very small salary. Therefore, as the production cost is very low, so you can export at a low price." (KII_ Facilitator)*

Given that it is so inexpensive, the majority of people can afford it. According to one respondent, even though Bangladesh's industry for making generic formulations is diverting innovation, this model nevertheless enables the poor to easily get necessary medications. Additionally, he stated that the medical college gives free medications to underprivileged patients who cannot afford them. Another respondent claimed that they supply their medications to reputable hospitals and government facilities.

> *"Bangladesh Pharmaceuticals is a photocopy industry so to expect innovation from Bangladesh pharmaceuticals is not right. But I am not demeaning. This industry is producing medicines that are treating poor people as people are getting it cheap." (KII_Facilitator)*

The majority of respondents stated that products are made commercially available through distribution channels depending on consumer demand. In addition, the marketing team is engaged in promotional activities. This is how they typically make their items accessible to consumers.

> *"We have a distribution channel. Then we have a marketing channel. marketing team promotes it. it is done as per marketing policy and distribution policy. regional demand. As not all drugs are needed in all regions. If something is needed, it collected within 24 hours. the services are prompt now. the marketing team follow this up." (KII_Financer)*

IV. The perspective of stakeholders on alternative incentives for R&D

One alternative proposal for paying for R&D is to compensate the innovator with funds from external sources in exchange for the knowledge being made available in the public domain as a public good (i.e., not being subject to a patent). We seek the stakeholders' opinions at the KIIs on the potential of this approach in the context of our nation. We were surprised by how widely

different stakeholder opinions are. While some participants believe it is feasible and possible, and that Global Public Goods (GPG) have the potential to increase availability, others believe that if there is no patent policy, researchers will lose interest. They believe that because there won't be any competitiveness, researchers won't work diligently on innovations. One participant suggested that if the innovation is not patentable, there is a possibility of misuse, as it could be marketed by several companies before the product is even fully developed, which will lower the product's quality. Another participant underlines the need for the model to be built around the business context and claims that only vaccination items could be exempt from the patent policy.

> *"There is a chance of getting misused by people. People will take a chance on it and without even developing the product they will market it. As a result, quality will deteriorate. So, we have to stay in between. What you say about patents is in the finished formulation. In our country, there is no patent policy. Everything depends on TRIPS. We are getting a waiver on it." (KII_Implementer)*

Participants also put forth alternate business plans that they believe would work well in the context of our nation. One of the facilitators had an extremely intriguing suggestion. He urged the UN members to step up and invest in research, with the proceeds being shared among the member states.

> *"I would rather try to maintain the United Nations much stronger and let the United Nations invest that amount of money in health research, the total amount of money each and every country is investing, and distribute that money within each and every country. So, each and every country has a vital chance for developing their own product rather than having to look upon another country and waiting for them to give the product like Africa." (KII_Facilitator)*

Another person made the suggestion that wealthy nations may have patents while developing nations should be kept patent-free. In a nutshell, we have noticed participants were split into two groups; one group believes alternative business models are quite possible once our nation begins producing innovative products, while the other group believes it is unlikely and occasionally comes up with a new model considering the country's context.

Findings from the database search

To observe the funding flow for overall R&D in the health sector and to explore the current status of the clinical trials in Bangladesh, G-Finder, World RePORT and ClinicalTrials.gov and ICTRP have been used respectively.

Funding for health-related R&D *(Source: World RePORT and G-Finder)*

One source of information on funding for health R&D is the World RePORT, which since 2012 has collected data from grants for biomedical research from 14 major public and philanthropic funders of health research, all of which are from HICs. The database contained information on 650,875 grants awarded to 23,005 recipient research organizations in 188 countries. For Bangladesh, a total of 894 research projects are included in the database, which were received by 67 research organizations in the country. From the 894 projects, 235 had information about the amount of funding received, which summed up to USD 333.72 million over the past decade. The figure below shows the number of projects received by each of the main recipient organizations. Figure 3 shows number of projects received by the main research organizations in Bangladesh.

Figure 3: Records by research organizations (Source: World RePORT)

Total Investment in R&D stages:

The G-FINDER initiative analysed annual investments in R&D for innovative goods and solutions to address critical global health issues that disproportionately affect people in LMICs. The time frame for analysis was 2007-2020. According to the G-finder results, the overall amount invested in R&D in Bangladesh during the past years fluctuated over time. For investment, the different R&D stages include basic research, unspecified R&D stages,

discovery and preclinical stage, post-registration, clinical and field development, etc. (Table 2). Investments in basic research increased over the years. The investment in basic research was lower in 2007 and increased to almost 6.3 million in 2020. Other research and development stages had a lesser initial investment, but this has slowly increased over time. The total investment in overall R&D was higher in 2020 (7.3 million US$) compared to 3.7 million US$) in 2007.

Table 2: Investment in different R&D stages following 2007-2020 ("Policy Cures Research _ Public Search," n.d.)

Years	Basic research	Cross-cutting or unspecified	Discovery & pre-clinical	Post-registration	Clinical and field development	Total
2020	6.3	0.5	0.4	<0.1	0	7.3
2019	1.3	3.9	0.1	0.4	0	5.7
2018	1.4	3.9	0	0.5	0	5.8
2017	1.5	0	0	1.8	0	3.3
2016	1.6	0	<0.1	1.5	0	3.1
2015	2.6	0	0.1	0	0	2.8
2014	0	0	0.1	0	0	0.1
2013	0	0	0	0.5	0	0.5
2012	0	1.3	0	0	0	1.3
2011	0	1.9	0	0	0	1.9
2010	<0.1	2.0	0.2	0	0.1	2.5
2009	0.1	2.5	0.1	7.2	0	10
2008	<0.1	3.2	0	0	0	3.2
2007	0	3.7	0	0	0	3.7

Funder Categories & Investment (2007-2020)

Different categories of funders provide funds for research and development projects. The funding comes from public sources as well as philanthropic organizations (Fig. 4).

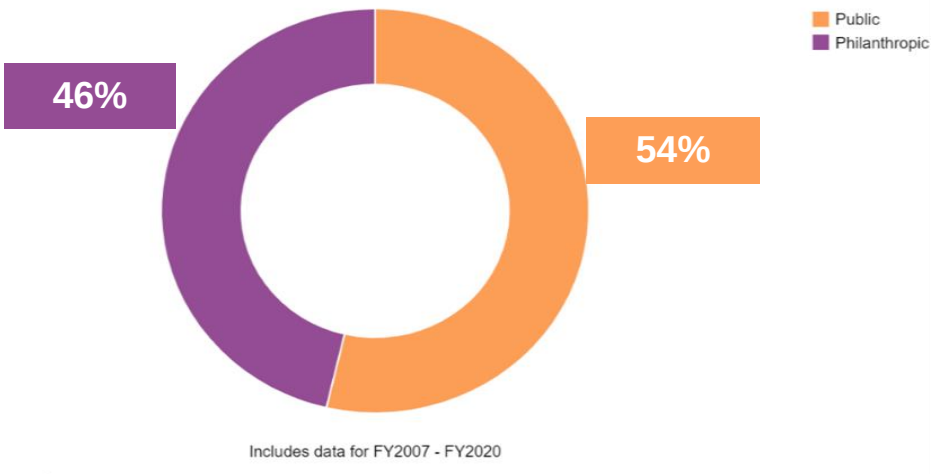

Figure 4: Funder Categories & Investment (2007-2020)

From 2007 to 2020, research and development funding accounted for 46% and 54% from the public sector (including government companies/organizations), and philanthropic organizations (including private companies, NGOs, etc.) respectively.

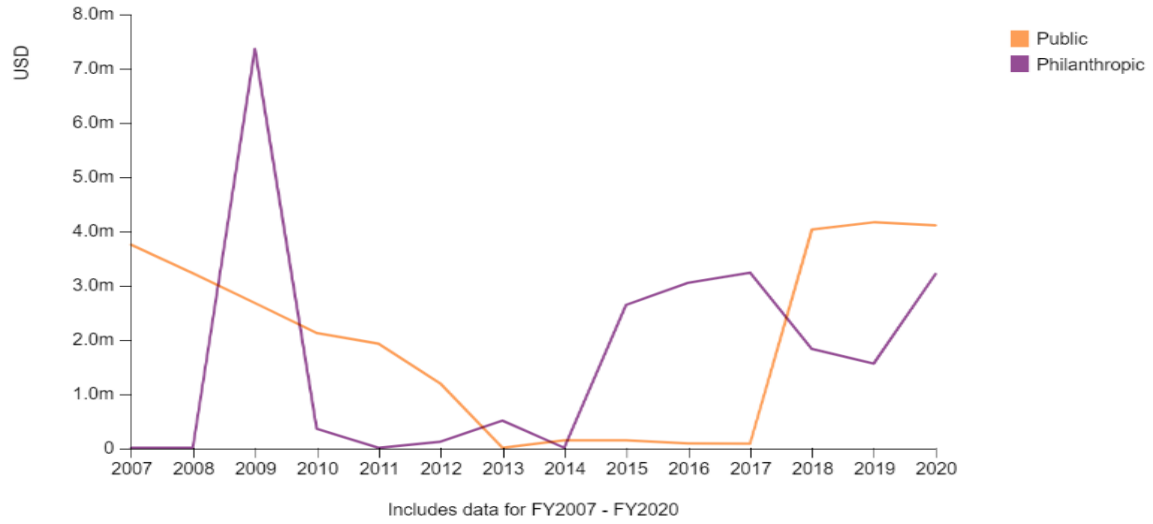

Figure 5: Variation in investment by the funders ("Policy Cures Research _ Public Search," n.d.)

In prior years, the total amount of financing fluctuated by years (Fig. 4). Funding from government organizations was not higher in prior years, but it increased significantly from 2018 until the present. From 2008-2020, funding increased from the private sector, but it gradually dropped. Nevertheless, there has been a recent uptick in investment from the philanthropic sector.

Table 3: Investment following 2007-2020 ("Policy Cures Research _ Public Search,"n.d.)

Funders ↓	**2020**	**2019**	**2018**	**2017**	**2016**	**2015**	**2014**	**2013**	**2012**	**2011**	**2010**	**2009**	**2008**	**2007**
US NIH	3.1	0.1	<0.1	<0.1	<0.1	0	0	0	0	0	0	0	0	0
Gates Foundation	2.5	1.1	1.1	0.8	1.4	2.5	0	0.5	0.1	0	0.1	7.4	0	0
Wellcome	0.6	0.4	0.4	0.8	0.4	0.2	0	0	0	0	0	0	0	0
UK FCDO	0.5	3.9	3.9	0	0	0	0	0	0	0	0	0	0	0
EC	0.4	0.1	0	0	<0.1	0.1	0.1	0	0	0	0	0	0	0
Effecthope	0.1	0.1	<0.1	0.1	0.1	0	0	0	0	0	0	0	0	0

Funders ↓	2020	2019	2018	2017	2016	2015	2014	2013	2012	2011	2010	2009	2008	2007
Global Affairs Canada	<0.1	0	0	0	0	0	0	0	0	<0.1	0.1	0	0	0
Swiss SDC	0	0	0	0	0	0	0	0	0	0	0	0.6	1.1	1.4
Swedish SIDA	0	0	0	0	0	0	0	0	1.2	1.9	1.9	2.0	2.0	2.3
Norwegian SIU	0	0	0	0	0	0	0	0	0	0	<0.1	0.1	<0.1	0
Other	0	0	0.2	1.5	1.1	0	0	0	0	0	0.2	0	0	0
Totals	7.3	5.7	5.8	3.3	3.1	2.8	0.1	0.5	1.3	1.9	2.5	10	3.2	3.7

Table 3 shows funders for conducting research in Bangladesh, a lot of investments are provided by the funders such as US NIH, Gates Foundation, Welcome Trust, UK FCDO, EC, Global Affairs Canada, Swiss SDC, Swedish SIDA, Norwegian SIU, etc. From the World RePORT database, US NIH was the main funder of biomedical research in Bangladesh, followed by the UK Medical Research Council (MRC) and the Bill and Melinda Gates Foundation (BMGF) and Wellcome, as shown in the figure below.

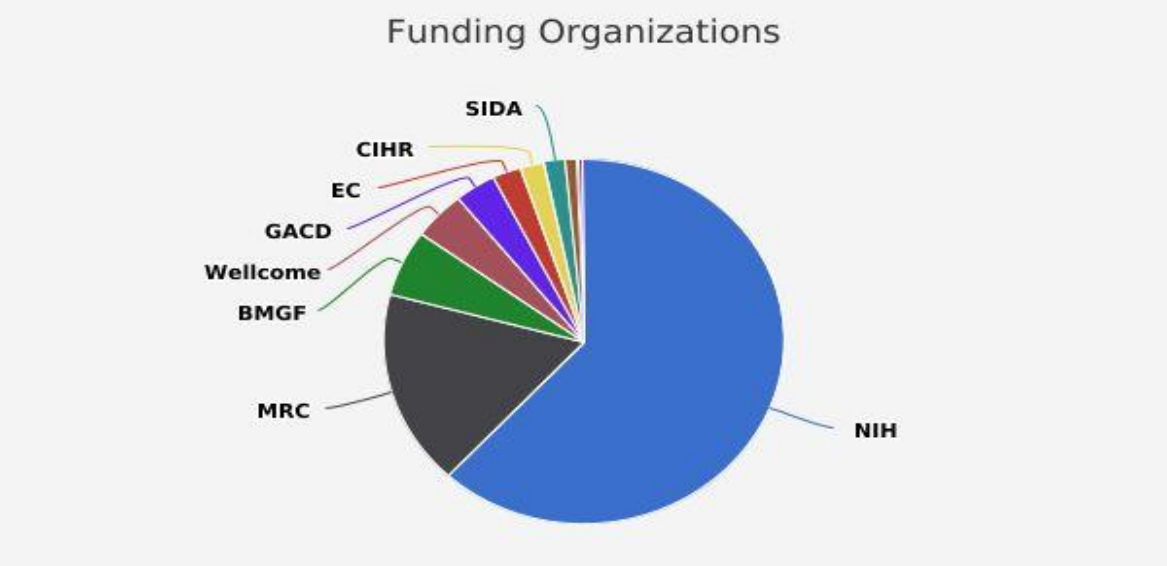

Figure 6: Funding organizations of biomedical R&D in Bangladesh (Source: World RePORT)

Total investment in different diseases

According to the G-finder data, the total investment was US$ 51 million in 2007 to 2020 Most of this fund is spent on diseases such as cholera, diarrheal diseases, sexual &

reproductive health-related diseases, neglected tropical diseases and pneumonia etc. (Table 4).

Table 4: Amount of funding for different diseases mention whether cumulative or in a particular year or years ("Policy Cures Research _ Public Search," n.d.)

Diseases	Millions (USD)
Cholera	16
Multiple Diarrhoeal diseases	9.6
Core funding for an SRH organization	8.3
Core funding for an ND organization	7.5
Fundamental research	3.5
S- Pneumonia	1.5
COVID-19	1.3
Cryptoporidiosis	1.3
Leprosy	0.6
Rotavirus	0.5
Shigella	0.3
Typhoid and paratyphoid fever	0.2
Enteroxigenic E. coli	0.1
Leishmariasis	0.1
Tuberculosis	0.1
N. meningitidis	0.1
Dengue	<0.1
Multiple helminth infections	<0.1
Total	51

Investments in different diseases over the years (2007-2020)

Investment in different diseases varied over the years (Fig. 7). Following the disease occurrence rate, the investment varied over different years. G-finder provides information on the total investments in different diseases from the year 2007 to 2020. In 2020, investments were spent on fundamental research, coronavirus, typhoid and paratyphoid, pneumonia, etc.

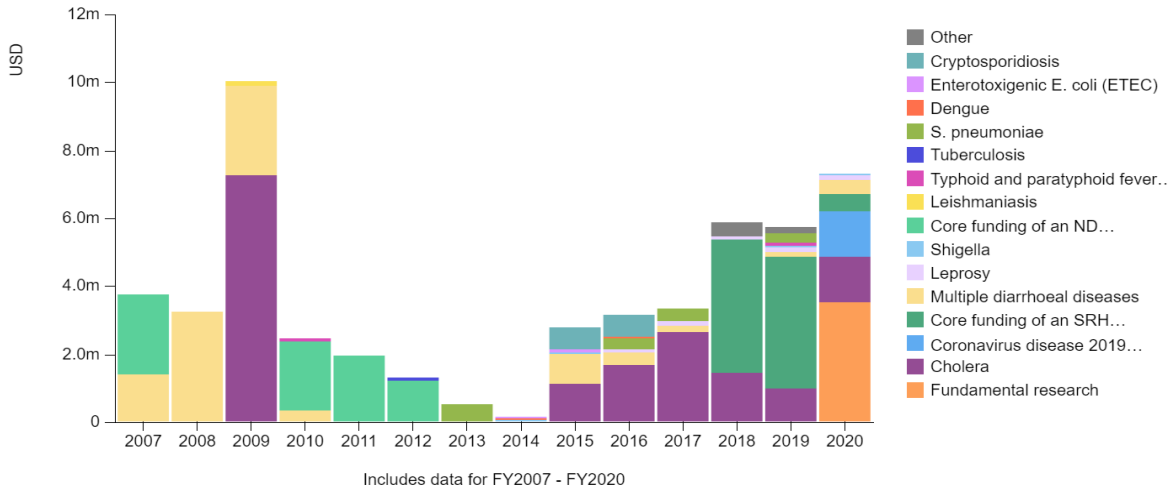

Figure 7: *Investment in different diseases according to 2007-2020 ("Policy Cures Research _ Public Search," n.d.)*

Current Status of Clinical Trials in Bangladesh *(Source: ClinicalTrials.gov &WHO ICTRP)*

A few contract research organisations are running clinical trials in Bangladesh. The top Clinical Research Organisations (CROs), according to KIIs, is the International Centre for Diarrhoeal Disease Research, Bangladesh (ICDDR.B). Additionally, another government organization acting as a CRO is Bangladesh Sheikh Mujib Medical University (BSMMU). Therefore, to support our qualitative data and learn more about clinical trials in Bangladesh, a database analysis from ClinicaTrial.gov was carried out. Information from the ICTRP, created by the WHO in 2005, was used to complement the analysis. A previously cleaned dataset by Merson et al. (Merson et al., 2022) was used to allow for comparability between the three reports of the research collaboration. The dataset was complemented with information about health categories obtained by the Geneva Graduate Institute from the WHO Global Observatory on Health Research and Development. The original ICTRP dataset included 643,414 clinical study registrations and 593,595 after removing duplicate records, for a total of 216 countries. The data is available until December 2020 and includes information about 632 clinical trials conducted in Bangladesh (Merson et al., 2022). Two files with supplementary data used for the analysis of clinical trials are available at: https://zenodo.org/record/7801929 and https://zenodo.org/record/7802113.

ClinicalTrials.gov is a registry providing information on clinical trial databases of different countries worldwide. The data contains details of the project, including current status, PI, location, sponsor, collaborator, condition, and intervention by ClinicalTrials.gov identification number. It is a web-based resource of the U.S. National Library of Medicine (NLM) at the National Institutes of Health (NIH). At the beginning of a study, the information is entered in the website and updated as the study progresses. However, sometimes the information is uploaded after the end of the study. All uploaded information is provided by the sponsors and investigators of the study. The Data have been listed from 50 states of the US and 221 countries of the world. These studies are neither funded by the National Institutes of Health (NIH) nor are they reviewed by the U.S. Food and Drug Administration or other governmental entities (ClinicalTrials.gov, n.d.). As of 7th July 2022, 500 clinical trial data have been uploaded for Bangladesh; these have been analyzed for evaluating the situation of clinical trials in Bangladesh.

Two types of study designs have been seen: interventional studies (n=336), observational studies (n=30), and unspecified studies (134). There are in total 336 interventional studies and these are in different stages of trial. Among 104 interventional studies, 52 are completed, and three are terminated. Besides, there are in total of 30 observational studies in the registry and 13 of them are completed. The details of the clinical trials are shown below in the flowchart:

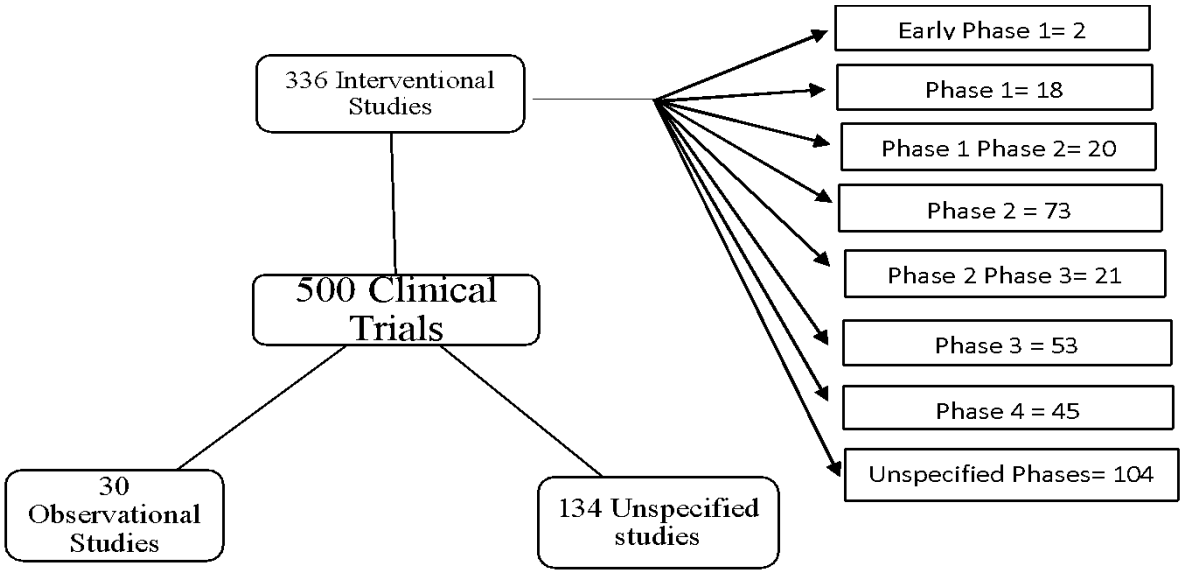

Figure 8: Flow chart of the different studies of clinical trials from ClinicalTrials.gov registry

The data from the ICTRP included information about 632 clinical trials in Bangladesh from the entire period covered (1990-2020). From 2010 to 2020, there was a 347% increase in the total number of trials in Bangladesh, showing growing activity in the country. Looking at the distribution by phase for the entire period, there were more trials in phase 2, phase 3, and phase 4, and only 3.64% of the trials were registered as phase 0 and phase 1 (phase information was available for 58% of the trials). Over time, from 2010 to 2020, the greatest variations were an increase in trials in phase 1/2 (400%) and phase 3 (200%) and a decrease in trials in phase 4 (-75%).

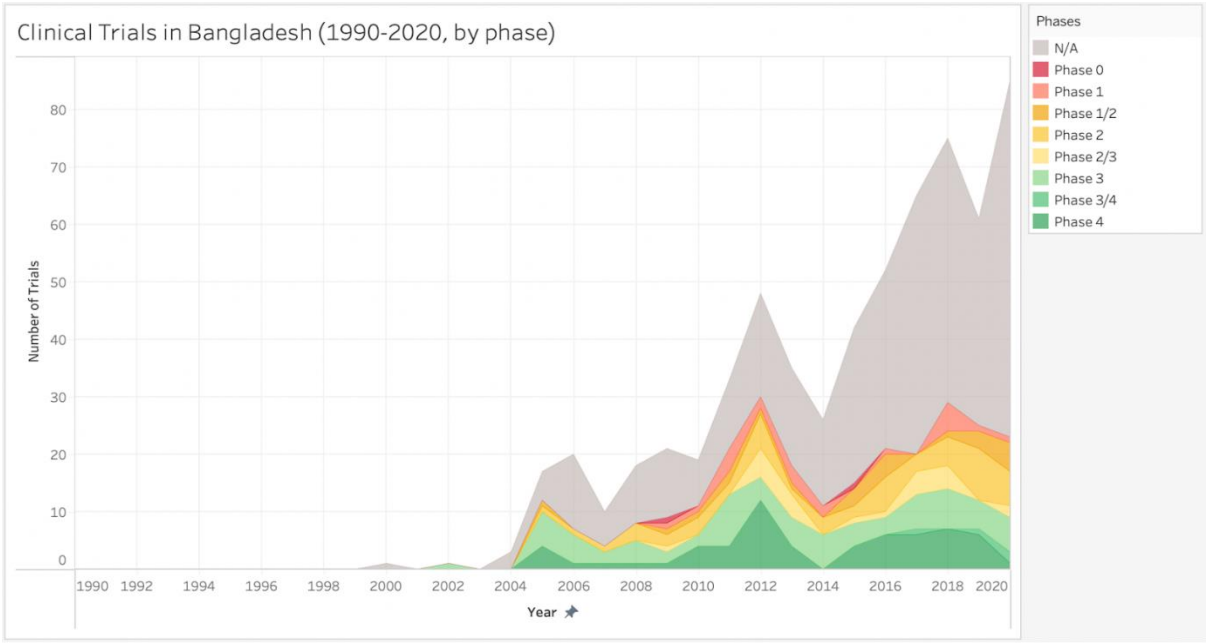

Figure 9: Number of clinical trials in Bangladesh by phase by year (1990-2020)

Organizations working on clinical trials: A brief summary of the number of clinical trials pursued by different national and international institutions is presented below, based on data from clinicaltrials.gov:

Table 5: Number and percentage of clinical trials conducted by National Government Organisation

National Organisation	Organization Type	Name of the Organisation Conducting Clinical Trials	No. of Clinical Trials	Percent
Government	Research Organisation	*Zokiganj Upazila Health Complex*	02	0.4
		BRICM	01	0.2
		BMRC	01	0.2
		Bandarban Sadar Hospital	01	0.2
		Maternal and child health training institute (MCHTI)	01	0.2
		Centre for the Rehabilitation of the Paralysed(CRP)	01	0.2
		Child Health Research Foundation (CHRF)	01	0.2
		Upazila Health and Family Planning Office (UHFPO)	01	0.2
	Universities	*Bangabandhu Sheikh Mujib Medical University (BSMMU)*	91	18.2
		Dhaka Medical College Hospital (DMC)	09	1.8

National Organisation	Organization Type	Name of the Organisation Conducting Clinical Trials	No. of Clinical Trials	Percent
		Dhaka University (DU)	03	0.6
		Chittagong Medical College Hospital (CMCH)	02	0.4
		Bangladesh University of Engineering and Technology (BUET)	01	0.2

Table 6: Number and percentage of clinical trials conducted by National Non-government Organisation

National Organisation	Organisation Type	Name of the Organisation Conducting Clinical Trials	No. of Clinical Trials	Percent
Non-government	Research Organisation	icddr,b	175	35
		BRAC	05	1
		Bangladesh Laser and Cell Surgery Institute and Hospital, Dhaka, Bangladesh	02	0.4
		Bangladesh Reference Institute for Chemical Measurements (BRICM)	01	0.2
		Bangladesh MARIB Bandarban	01	0.2
		BIRDEM General Hospital	01	0.2
		Combined Military Hospital	01	0.2
		UChicago Research Bangladesh	01	0.2
		Stanford University	01	0.2
		Bangladesh Eye Hospital	01	0.2
	Universities	*Bangladesh University of Health Sciences (BUHS)*	01	0.2
		Community Based Medical College Bangladesh (CBMCB)	01	0.2

Table 7: Number and percentage of clinical trials conducted by international organisation in Bangladesh

International Organisation	Name of the Organisation Conducting Clinical Trials in Bangladesh	No. of Clinical Trials	Percent
	University of Virginia	07	1.4
	Columbia University	03	0.6
	Centres for Disease Control and Prevention	03	0.6
	WHNRC	03	0.6
	The Hospital for Sick Children	03	0.6
	University of Saskatchewan	02	0.4
	University of California	02	0.4
	USAIDS	02	0.4
	Brown University	01	0.2
	University of Vermont	01	0.2
	University of Florida, USA	01	0.2
	University of Oklahoma	01	0.2
	University of Calgary	01	0.2
	Texas Tech University	01	0.2

Tables 5-7 show the Number and percentage of clinical trials by the national government organisations, national non-government organisations and international organisations, respectively. Organisations in the non-state sector, such as ICDDR.B, is conducting the highest number of clinical trials (n=175, 35%) followed by Bangabandhu Sheikh Mujib Medical University (BSMMU) (n=91, 18.20%) and Dhaka Medical College (n= 9, 1.8%) clinical trials. The rest of the organisations are conducting 33% of the 500 clinical trials.

Sponsors and collaborators*:* According to the information of clinicaltrials.gov registry, many organisations are funding their own research, for example, ICDDR.B, BSMMU, Chittagong Medical College, Dhaka Medical College, BRAC etc. However, different national and international organisations frequently get involved in collaboration and/or sponsorship for conducting clinical trials, e.g., Globe pharmaceuticals Ltd. (n=4), Suzuhiro Kamaboko Co., Ltd., Japan (n=1), University of California, Berkeley (n=6), University of Maryland (n=3),

Harvard University (n=2), Stanford University (n=19), Johns Hopkins Bloomberg School of Public Health (n=32), Sanofi Pasteur (n=4), MSD Wellcome Trust Hilleman Laboratories Pvt. Ltd. Parexel (n=2), Bilthoven Biologicals Serum Institute of India Pvt. Ltd. (n=1), Damien Foundation National TB control Programme Bangladesh Institute of Tropical Medicine, Belgium (n=1), PATH (n=13)etc.

The analysis from the ICTRP database by Merson et al. (2022) contained a categorization of sponsors and funders of clinical trials divided into commercial and non-commercial. “Commercial” were “organizations where evidence of profit-driven corporate mission or company structure was identified", and "non-commercial" were “organizations where evidence of non-profit status was identified, including governments, foundations, academic and research institutions, health care provision facilities, and public health agencies" (Merson et al., 2022). In Bangladesh, almost all trials had information about primary sponsors, 47% had information about secondary sponsors, and 33% about funders. With the available information, non-commercial primary (85%) and secondary sponsors (41%) are prevalent in Bangladesh, and more trials are funded by non-commercial (25%) than by commercial funders (6.5%).

An analysis of the distribution by phase shows that non-commercial actors (primary and secondary sponsors and funders) are predominant in all phases, except for commercial secondary sponsors which are prevalent in phases 1/2 and 3/4. An analysis over time shows that from 2010 to 2020, there was an increase in the share of trials with non-commercial sponsors and funders. Non-commercial funders are the majority in 2020, while there were no trials funded by non-commercial funders in 2010. It is also notable the involvement of commercial secondary sponsors in 2020, while there was none in 2010. An analysis by phase over time revealed that the most significant variation was in phases 1/2 and 3, with greater participation of non-commercial funders and primary sponsors. There was also a significant decrease in the number of trials in phase 4 with commercial primary sponsors and funders.
Combining with the information about health categories, all the actors were primarily involved with research for infectious and parasitic diseases when considering the data for the entire period (2000-2020). From 2010 and 2020, the most notable variation was an increase in the participation of non-commercial primary sponsors in clinical trials for neuropsychiatric conditions (from 0 to 10) and for respiratory infections (from 0 to 25).

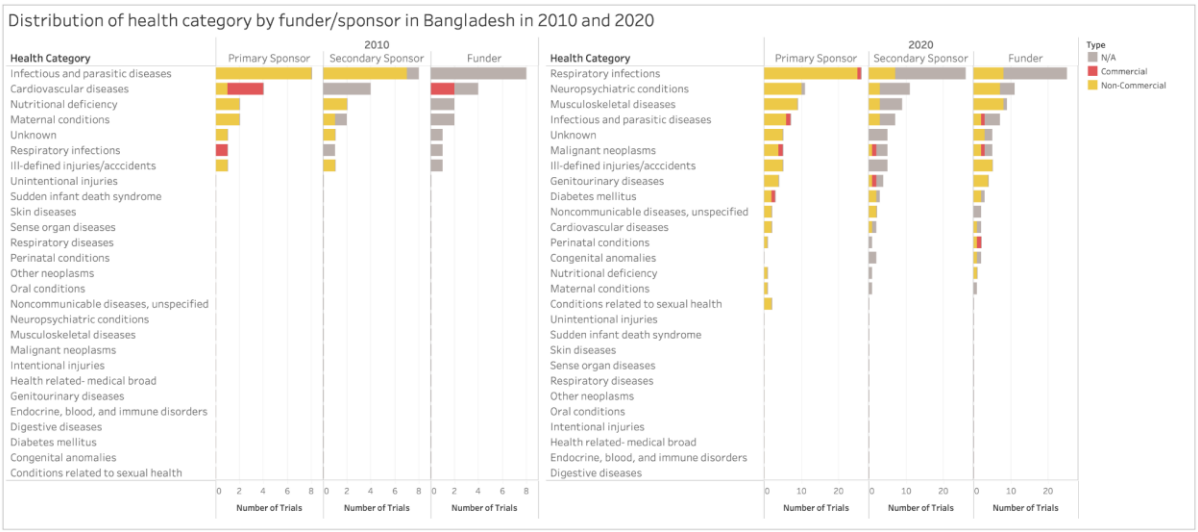

Figure 10: Distribution of health category by funder/sponsor in Bangladesh in 2010 and 2020

Focused Conditions/ Diseases: The ClinicalTrial.gov registry for Bangladesh shows the different number of conditions or diseases (n) that are under clinical trials. Figure 11 shows the percentage of conditions or diseases under clinical trials in Bangladesh. The most focused conditions or diseases for clinical trials in Bangladesh include common nutritional disorders (n=54), COVID-19 (n=31), pneumonia (n=18), haematological conditions(n=10), arthritis (n=9) and other diseases.

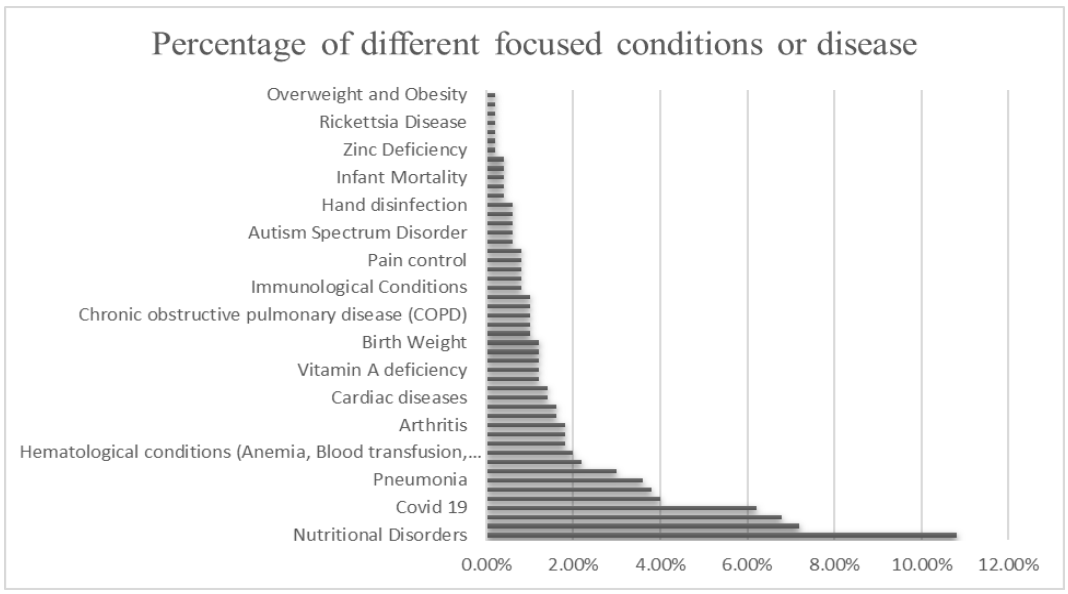

Figure 11: Percentage of conditions or diseases under clinical trials in BD (Time period: 7th July 2022)) (Source: ClinicalTrials.gov)

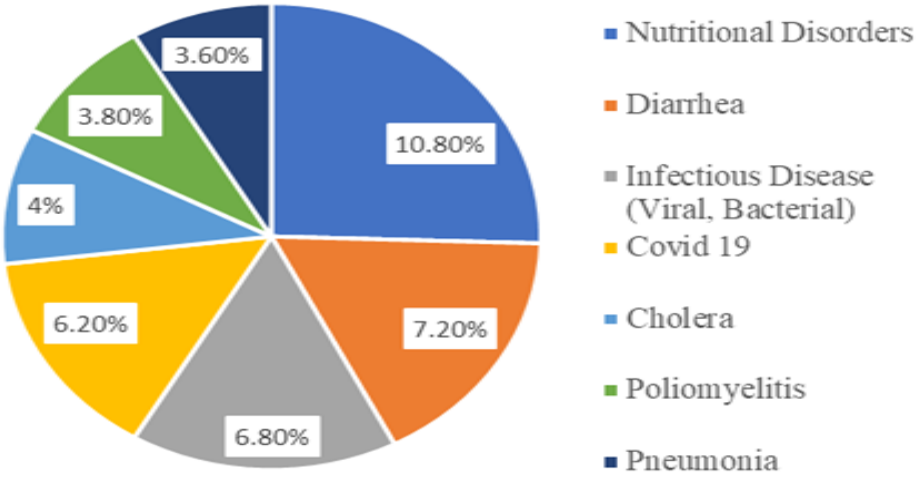

Figure 12: Most frequent conditions or diseases under clinical trials in BD 7th July 2022) (Source: ClinicalTrials.gov)

However, Figure 12 shows that clinical trial studies are mostly focused on nutritional disorders which are 10.80% which is plausible as malnutrition affects more than 50 % of the population in Bangladesh. Moreover, the second most common cause of death in children under five is a diarrheal disease, which is focused at 7.2% in the clinical trial database (Choudhury et al., 2014). Besides, for different viral/bacterial infectious diseases, the percentages are COVID-19 (n=6.8%), cholera (n=6.2%), poliomyelitis (n=4%), and pneumonia (n=3.8%).

Analysing the data from the ICTRP, the health category “infectious and parasitic diseases” (n=173/624) had the highest number of trials in Bangladesh. Comparing the numbers from 2010 and 2020, the highest increases were in the number of trials in “respiratory diseases” (2,600% increase) and “neuropsychiatric conditions” (1,100% increase). Adding the distribution by phase, "infectious and parasitic diseases" was the category with the highest number of trials in all phases. From 2010 to 2020, the most significant variation was an increase in the number of clinical trials for malignant neoplasms in phase 3 (from 0 to 3) and a decrease for cardiovascular diseases in phase 4 (from 3 to 0).

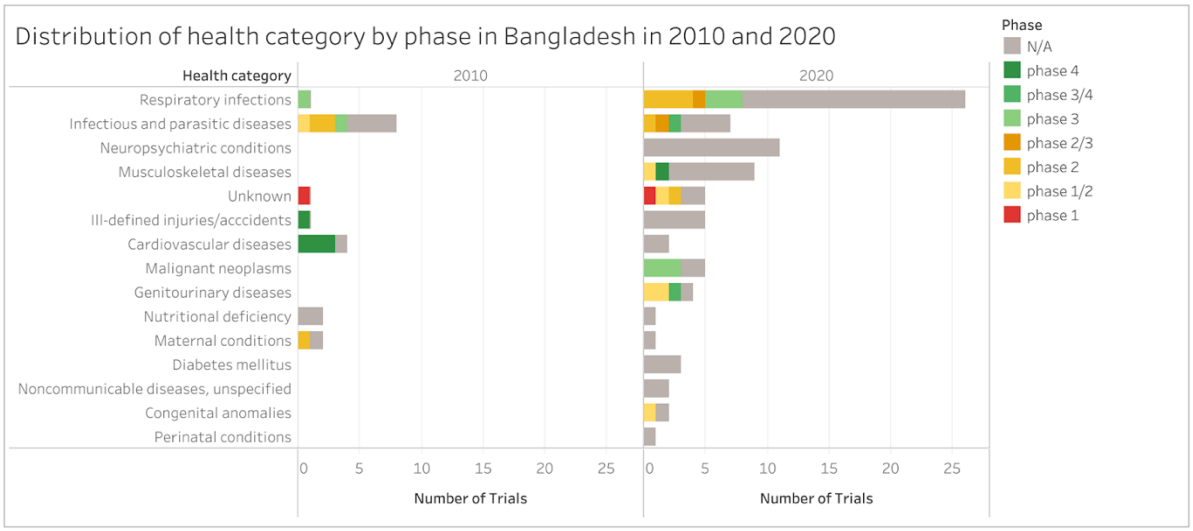

Figure 13: Number of trials by health category and phase in 2010 and 2020

Key findings from stakeholder dissemination

A national dissemination meeting was organized on 6th April 2023 at BRAC Centre Inn, Dhaka to share the study findings. Stakeholders from pharmaceutical industries, academics, and researchers joined the event. Prof. Syed Masud Ahmed, PI brief the study background and objectives, Obaida Karim and Sanjida Ahmed Srishti on behalf of the study team presented the key findings from the scoping review, KIIs, and databases analysis. An open discussion was held following the presentation to gather participants' opinions and insights. The pharma representatives agreed that most of the companies are spending their money on marketing to get "easy money'' and are not ready to take the risk to invest in R&D. They recommended that the government and local pharmaceutical companies should come forward to work in collaboration. Also, to reduce risk and secure the future, regional businesses should work with international R&D firms. They also emphasized that the government should develop legislation requiring local pharmaceutical companies to invest from their profitability in the R&D sector. The academicians and researchers proposed that it would be less risky for pharmaceutical companies to participate in R&D if organizations like the Bill & Melinda Gates Foundation or the NIH could fund the R&D industry. They recommended increased interaction between academics and pharmaceutical companies, wherein the latter may benefit from the academics' expertise on the best ways to conduct molecular research The participants were hopeful about the R&D sector prospers given the proper policy environment, investment, and technical capabilities are addressed. The event ended with thanks note from the study team.

Strength and limitation

As stakeholders from different industries, universities, and research organisations were selected for the study, this sampling method has produced the most diverse and accurate result in assessing the pharmaceutical ecosystem of Bangladesh. Furthermore, the triangulation method has been used, which strengthens the project through the validation of the findings from different sources. However, one of the drawbacks of the study is that the financiers of the pharmaceutical companies were hard to reach. Moreover, few respondents allowed a limited time which made the probing hard to conduct.

Conclusion

The market-oriented pharmaceutical industry mainly focuses on generic production with little to no R&D, which has been credited to the TRIPS agreement waiver allowing for the production of generic versions of medicines patented abroad. Pharmaceutical companies prefer investing their resources in the production and exportation of generics, then investing limited resources in taking the risk to conduct more innovative R&D. Policy, funds, lack of skilled manpower, and research infrastructure are some of the obstacles faced by them. Urgent attention and investments, both from the government and the industry, will be needed in these areas if Bangladesh wants to overcome the challenges of the post-TRIPS waiver scenario.

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ANNEXURES

Annex 01: Conceptual framework

For the purpose of analyzing the pharmaceutical R&D system in Bangladesh and the prospect of adopting alternative business models in the country, we adopted the conceptual framework of the research project "New Business Models for Governing Innovation and Global Access to Medicines" (NBM), led by our partner institution the Global Health Centre, Geneva Graduate Institute. A central focus of the NBM project is to improve understanding of how alternative models of pharmaceutical innovation that could meet global health needs better may emerge, survive, thrive, and/or decline within a broader ecosystem. To do so, the project applies a complex adaptive system lens to characterize and analyze the global Pharmaceutical Innovation System (PIS). This approach conceptualizes the PIS as a network of different actors that interact in a sustained way through time to produce certain outcomes (e.g., the success or failure to develop a new medicine, the degree to which it becomes accessible to people who may need it). In the PIS, these actors would be the different types of organizations involved in the research and development (R&D) process. The interaction among actors in this system is shaped by a range of factors (e.g., historical, legal, political, social, scientific) operating from local to global levels. These actors are divided into three overarching categories:

- Funders: those providing push or pull funding for R&D
- Implementers: those whose organizations conducting R&D
- Facilitators: those seeking to advance, improve or otherwise shape the R&D process, but not directly conducting or funding R&D

In the PIS, different resources influence the emergence, survival, and/or success of the different actors that exist and how they operate. Those resources comprise financing, knowledge, relationships, and the means to manufacture health technologies.

The PIS is defined not only by its actors and resources but also by the relationships established between and across them. These relationships generate and are governed by different rules and norms (like IPR, regulatory frameworks, or priority-setting processes). For example, the interactions between actors (i.e., universities, companies, and venture capital firms), shape the use of resources like knowledge, financing, and the means to manufacture health technologies.

We applied this conceptual framework to guide our data collection and analysis, analyzing the norms and rules relevant for pharmaceutical R&D in Bangladesh, the main actors involved (i.e., implementers, funders and facilitator), their resources (e.g., financing and knowledge management) and assess the stakeholders' perspective of the feasibility of adopting alternative business models, particularly for generating GPGs.

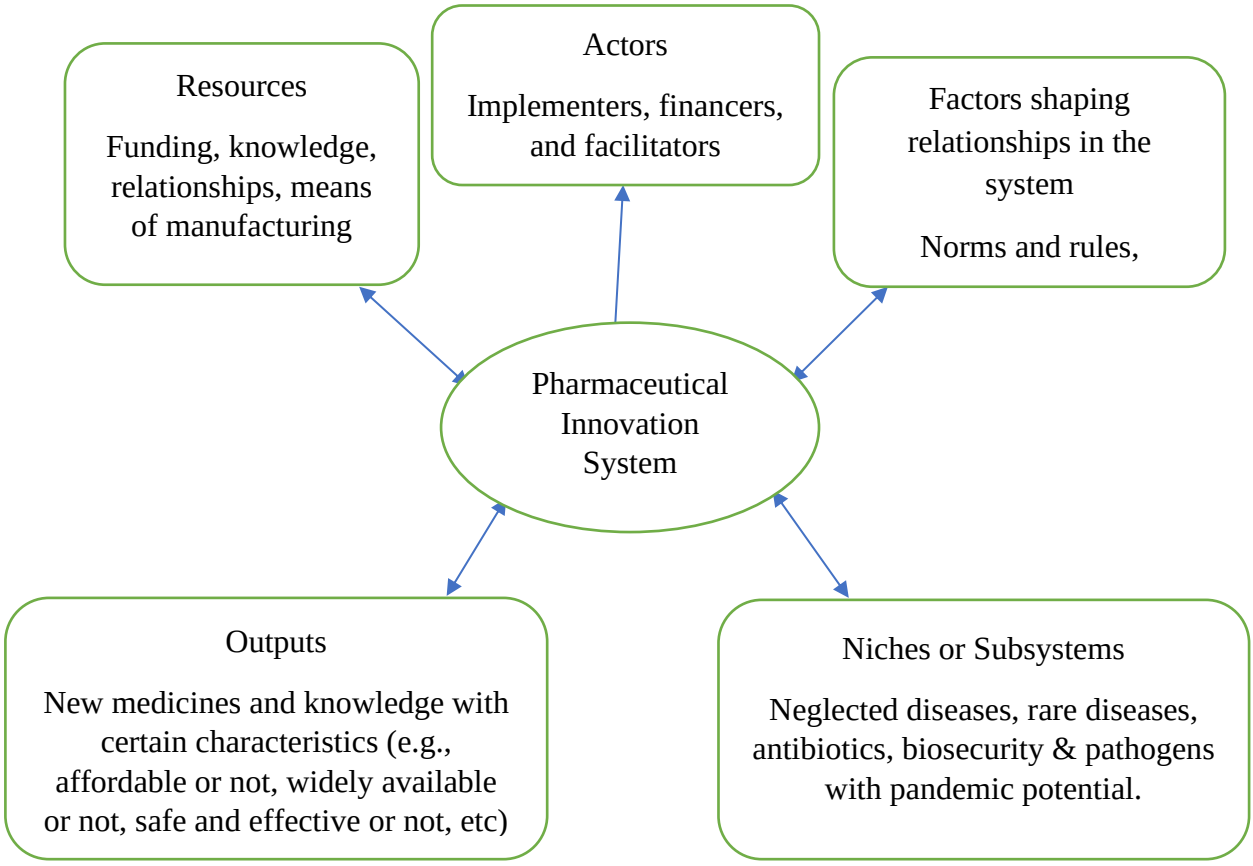

Figure 1: Conceptual framework

Annex 02: Methodology
Study design

A cross-sectional study design with a combination of approaches (Scoping review, qualitative analysis and database review) was applied to conduct the research-

For Pharmaceutical R&D, tri-angulation of scoping review and qualitative analysis has been done.

a) Scoping review (ScR) for secondary data analysis: To explore the current scenario of Pharmaceutical R&D scoping review was done;
b) Qualitative Key-Informant Interviews (KIIs) with key stakeholders: for a comprehensive understanding of the pharmaceutical R&D, their business model,

exploring the possibility of adopting a new business model for their pharmaceutical R&D, KIIs were considered appropriate.

For overall R&D in health sector, two types of database analysis have been done.

a) World RePORT and G-Finder: To explore the funding amount in R&D over the years, types of funding organizations, and invested amounts on various diseases, World RePORT and G-Finder have been used.
b) ClinicalTrials.gov and ICTRP: To explore clinical trials in Bangladesh (organizations that perform clinical trials, as well as the projects they are working on, their sponsors and collaborators, and the diseases that have been the subject of these trials), a ClinicalTrials.gov and ICTRP have been used.

Methodological details

a) Methodology of Scoping Review (ScR):

Approach

A 5-step framework adapted from the framework of Arksey and O'Malley was used for this review: i) identifying the research question; ii) identifying relevant studies; iii) selecting studies, iv) charting the data; and v) collating, summarizing, and reporting the results.

Eligibility criteria

An ScR protocol was developed, which specified the review objectives, inclusion and exclusion criteria and data sources (Table 1).

Table 1: Scoping Review protocol for Inclusion and exclusion criteria's

Search Strategy	Inclusion Criteria	Pharmaceutical innovation and R&D related company and industrial documents in Bangladesh, Pharmaceutical innovation and R&D-related knowledge and practice, Pharmaceutical innovation and R&D-related guidelines and regulatory documents Pharmaceutical innovation and R&D-related policy documents in Bangladesh.
		Both human, and animal and its interconnection with environment-related pharmaceutical innovation and R&D-related plans, strategy, guidelines
		Language: English, Bangla
	Exclusion criteria	All countries other than Bangladesh

	Time frame	Setting the time frame limited potential articles. Moreover, as we have researched from the historical background to the current scenario of pharmaceutical industry of Bangladesh, so no time frame was defined.

Search term and data source

We used four search engines (Google Scholar, PubMed, Scopus, and Research4life) for peer-reviewed publications and Google for grey materials. Besides, we visited the websites of specific organizations and institutions to search for relevant documents and reports. The search terms were fixed, and different search terms were used to find relevant documents (Table 2). Finally, we also hand-searched some relevant journal websites that published articles on the topic to our knowledge, especially within the country (Table 3).

Table 2: Key terms used for searching an electronic database

Pharmaceutical R&D (Combined by 'OR') (a)	**Policy/Plan/Programme (combined by "OR') (b)**	**Geographic location**
"Pharmaceutical Research" OR "Pharmaceutical R&D" OR "Pharmaceutical Research& Development" OR Pharmaceutical Innovation"	"Policy" OR "Plan" OR "Programme" OR "One Health Framework" OR "Governance" OR "Regulatory authority" OR "Guideline" OR "Strategy" OR "Actors" OR "Stakeholders" OR "Goal" OR "Funding" OR "Finance" OR "Incentives" OR "Activities" OR "Outcome" OR "Result" OR "TRIPS" OR "Post TRIPS" OR "IP" OR "Intellectual property	"Bangladesh"
Note: a,b,c groups are combined with Boolean operator 'AND'		

Table 3: Scoping Review protocol for data source

Data source	**Grey literature**	Google
	Published literature	Google Scholar, PubMed, Scopus, Research4life
	Institutional websites	*DGHS*, *DGDA*, *CMSD*, *MoHFW*, *MoFL* *MoA*, *MoEF* , *BLRI*, *WHO*, Private Pharmaceutical Company Websites: *Square* , *Beximco*, *Incepta*, *Nuvista*, *Novonordisk* *etc.*

Screening and selection process

We followed the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) approach to select relevant articles and documents on Bangladesh's current scenario of Pharmaceutical R&D scenario for analysis. A PRISMA Extension for Scoping Reviews (PRISMA-ScR) checklist was filled in to complete this report. Three (3) researchers searched peer-reviewed articles, reviews, commentaries, conference proceedings, and published editorials. After removing duplicate articles, the researchers independently reviewed each abstract and included articles and documents in the analysis. The researchers also incorporated relevant citations from selected articles in the analysis. They critically appraised the selected

articles under the guidance of the principal investigator, as per the PRISMA-ScR (Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews) Checklist (Figure 2).

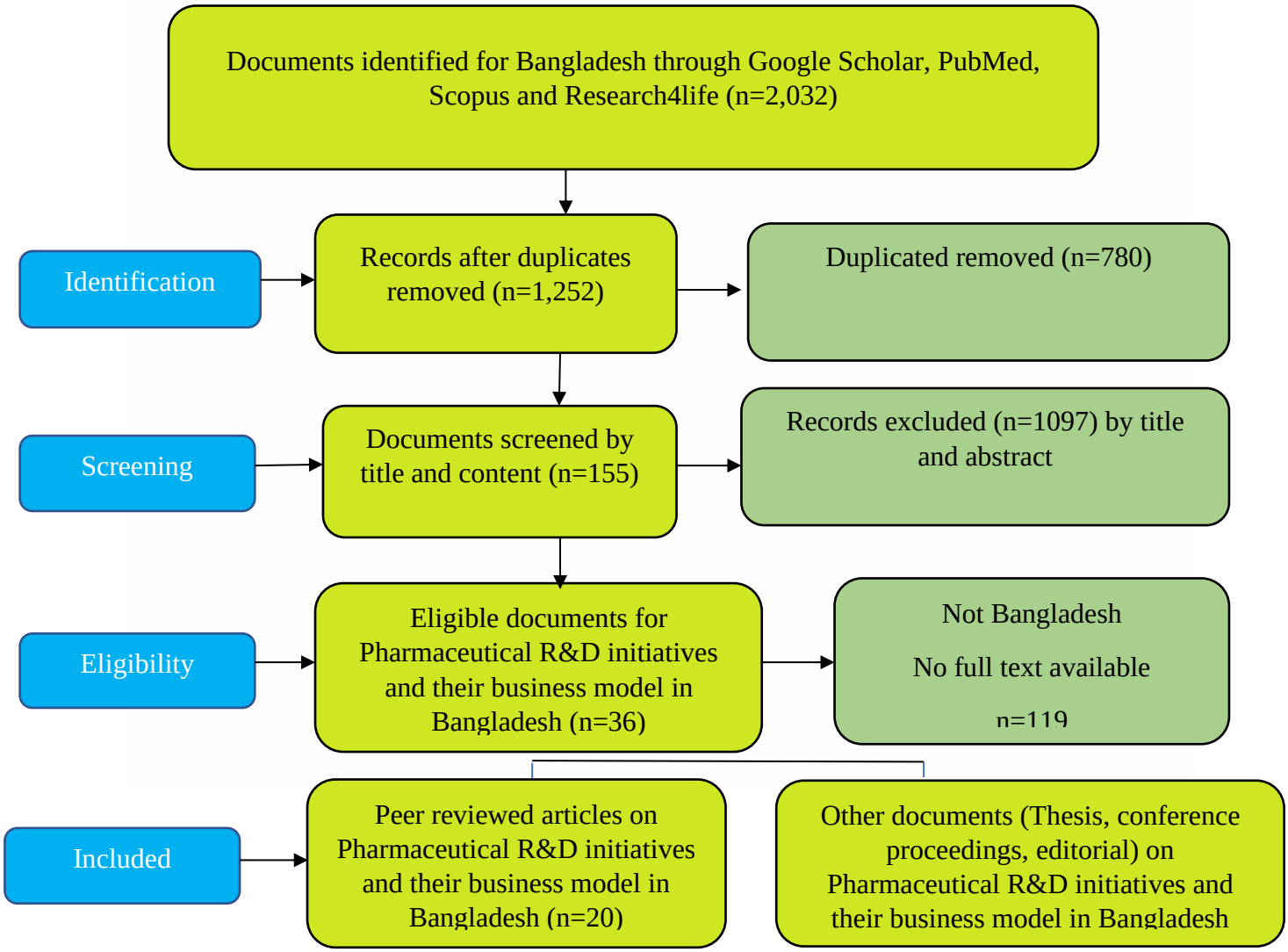

Figure 2: PRISMA diagram for selecting documents on the current scenario of Pharmaceutical R&D in Bangladesh for inclusion in the analysis

Data items and charting process

We used a 'mixed studies review' method for synthesizing evidence from qualitative, quantitative and mixed method studies. A data extraction matrix was used for organizing data and disaggregated into relevant key themes. The data items were the title of the article, author name, type of publication, date & journal, key words, objective, type of study and relevant key themes.

Data analysis

Studies that mainly focused on the current scenario of Pharmaceutical R&D in Bangladesh were included for the analysis. Following the key themes analysis was done (Table 4). Differences in the thematic (or sub-thematic) grouping or interpretation of the evidence in the documents were resolved by discussion among the group and with the PI to reach a consensus, with additional revisions as deemed necessary.

Table 4: Key themes for scoping review analysis

Themes	Current business model and R&D in Pharmaceutical industry Actors and funding Purpose and outcome Innovation in pharmaceutical R&D of Bangladesh Challenge's Priority actions

b) Methodology of Qualitative study (in-depth interviews)

Study population, site and sampling approach

The respondents were categorized into three (3) groups: implementers, financiers and facilitators. The data were collected from different pharmaceutical companies (Top, medium and small companies), academicians and policymakers. For KIIs, we used a combination of purposive and snowball sampling to identify and reach relevant stakeholders. We conducted a total 18 KIIs (Table 5).

Table 5: Study population and sample size

Categories	Definition	Key informants participated	Numbers of KIIs
Implementors	Working in the industry and directly involved in R&D; e.g., senior R&D authorities of pharmaceutical companies/plants	Head of Research/ Research Unit Directors, Quality control/ assurance officers	6
Financers	Authorities of the pharmaceutical companies responsible for deciding on R&D funding strategy, allocation and recipients	MD/CEO of the pharmaceuticals with R&D or PD	4
Facilitators	Policy-makers, Regulatory bodies, pharma sector experts, civil society representatives, academics, research organization representatives.	DGDA, academics/ faculties (pharmacy & pharmacology) of different universities, representatives from CPD and BHW.	8

Study tool-check

The study used a KII guideline that focuses on issues like context and prioritisation of pharmaceutical R&D activities, their business model, resources and sustainability, intellectual property (IP) and data sharing, regulation, affordability and availability, and challenges of pharmaceutical R&D in Bangladesh and recommendations to overcome those. The tool was adopted from the multi-country guideline to Bangladeshi context, and pre-tested to finalize.

Data collection process

Based on document review, previous study experience, and network in pharmaceutical sectors, we prepared a tentative list to map and identify organizations and actors relevant to pharmaceutical R&D and relevant business models in Bangladesh. These included pharmaceutical R&D-related financial decision-makers, pharmaceutical R&D personnel, regulatory authorities, representative of the Directorate General of Drug Administration (DGDA), academics, researchers, and personnel from civil society organizations and development partners. Using the list, we contacted to approach the KIIs to participate in our study via an initial email invitation. In the email invitation, we shared the project background, aim, and objective, requesting their participation to have their valuable knowledge and insights on the study matter. Up to three follow-up emails were sent to non-respondents, after which point non-respondents are contacted by other means such as telephone calls or face-to-face meetings. Apart from this, the KII guideline had a brief section to map further and identify important actors who would also be approached to participate in the study. We stopped when

saturation was reached as no new names are generated. In addition, demographic data and relevant individual attributes, including the organization the actor is from and the number of years of experience in the specific organization/field were being collected. 18 actors had been selected from the mapping exercise to participate in the KII. KIIs were conducted face-to-face at a time and place convenient for the respondents. Given the COVID-19 situation, if a face-to-face interview was not possible, the researchers conducted the interviews over zoom calls as convenient. During the online interview, e-signature was taken from the respondents. The sessions were audio-recorded with the respondent's consent and anticipated to take one hour to 90 minutes. In case of non-consent, notes were taken during the interview. All respondents were de-identified to maintain confidentiality. A research team comprised of four (4) members (a mix of physicians and pharmacists) carried out the interviews. They were trained to conduct the interviews and will be familiarized with key pharmaceutical terms. A summary note of each interview was prepared within 24 hours of each interview prior to the full transcription and translation of the KII. All these documents were stored in and shared by Google drive

Data management and analysis

We have used the summary notes for the initial analysis of the draft report using the KII guideline themes. For full analysis, audio recordings of all the KIIs are transcribed verbatim. If the KII was conducted in Bengali, it was translated and transcribed into English. All interviews were coded through an inductive approach with thematic analysis; a coding manual was developed for this purpose with the support of partners. For data visualization, a data matrix was created. Data collection ceased when theme saturation was reached, and new data collected does not shed further light on the themes identified from the analysis.

Triangulation of data from scoping review and KII were done to find out the most common themes for necessary actions by the stakeholders in policy and practice. Data were collected from the respondents maintaining the following domains to capture their business model according to the multi-country guideline:

1.Context and prioritization of R&D activities

2.Business model

3. Financing, Sustainability and Incentives

4. IP and Data

5.Regulation

6. Pricing and Availability

7. Prospects and challenges
8. Recommendations

The following key findings/ themes and sub-themes emerged from the analysis of the scoping review and KIIs:

Theme cluster	**Sub-Themes**
1.Current status of R&D in pharmaceutical companies and academic and research institutions	1.1. Purpose
	1.2. Key actors
	1.3. Funding flow
	1.4. Challenges
	1.5. Priority actions
2.Current business model and generic formulation of pharmaceutical companies	-
3.Drug Price and Availability and Accessibility	-
4.The perspective of the stakeholders on the New Business Model (NBM)	-

Experience with field implementation:

Data was collected from January 2022 to June 2022. Due to the wave of the Omicron variant of COVID-19, data collection was hampered for some time during this time. The actors from the pharmaceutical industries are too occupied with their professional activities; hence the study team had difficulties making appointments with them. Furthermore, it was tough to reach the financier of the pharmaceutical industry. Because of their unavailability, it was hard to conduct the whole activities with the financier. Additionally, the maximum R&D department in Bangladesh usually deals with product development, so it was tough to find out the real R&D activities and conduct the KII Session with the actors. Moreover, for the KIIs on the outskirts of Dhaka, the terrible road traffic situation was too time-consuming.

Ethical Considerations:

Institutional Review Board (IRB) of James P. Grant School of Public Health, BRAC University, gave ethical clearance to conduct the study (IRB Reference Number-IRB-21 December'21-048). The respondents were informed about the project background, objective, risk and benefits of participation including their full authority to withdraw from the interview

whenever they wanted or wished to. Thus, informed voluntary written consent was obtained before their participation. Respondents' anonymity and confidentiality were ensured by restricting access to data, recordings and transcripts and assigning unique identification numbers.

c) Methodology of databases review (World RePORT and G-finder)

In order to track yearly R&D spending on novel products and solutions the G-Finder project (https://gfinderdata.policycuresresearch.org/) is used. This includes information on funding provided for fundamental research as well as on novel medicines, vaccines, diagnostics, and other tools for addressing global health needs, particularly for neglected diseases, emerging infectious diseases and sexual and reproductive health. The total amount of investment over the previous years is analyzed following the resource. The World RePORT is a open database maitened by the US NIH gathering data from grants for biomedical research from 14 major public and philanthropic funders of health research (https://worldreport.nih.gov).

d) Methodology of databases review (ClinicalTrials.gov and ICTRP)

For mapping the current scenario of clinical trials in Bangladesh, the Clinicaltrials.gov registry platform is used (https://clinicaltrials.gov/). It is a web-based resource of the U.S. National Library of Medicine (NLM) at the National Institutes of Health (NIH) which provides information regarding the current status, PI, location, sponsor, collaborator, condition, and intervention of different projects on clinical trials. As of 7th July 2022, a total of 500 clinical trial data were uploaded for Bangladesh. Therefore, the data analysis is done for 500 clinical trials to evaluate the situation of clinical trials in Bangladesh. Aditional information for clinical trials analysis was obtained from the WHO International Clinical Trial Registry Platform (ICTRP), using a dataset created by the Global Health Centre, Geneva Graduate Institute combining information from Merson et. al. (2022) and the WHO Global Observatory on Health Research and Development. The dataset and analysis are available as supplementary data at https://zenodo.org/record/7801929 and https://zenodo.org/record/7802113.

Annex 03: Guiding Tool for KII

A. Target KI: "Implementers."

Definition: those whose organisations are conducting R&D (e.g., private firms, non-profit organisations, academic and public labs)

Block 1 – Concept, Context and Prioritisation of the R&D activities

1a Please tell us about your organization- the mission, vision etc. (Probe: when established, type- small/medium/large enterprise/ national/international/multinational/private/public/research organsiaiton/ academic/other types- specify)

1b What is your role within the organization? (Probe: designation/position, prime role and responsibilities, link to R&D)

1c In your opinion, what is pharmaceutical R&D, what type of activities it usually includes? Usually how R&D priorities are set? (Probe: innovation, use of technology, priority issues- access, quality, price etc.)

1d What are the R&D activities in your company? If yes, what are the priorities? (Probe: Nature of innovations, innovation capacity, use of technology, the extent of industry awareness, what are the researches currently going on?) If no, are you planning to work on it?

1e What unmet needs or gaps in the health technology R&D system is your organisation trying to cover? (Probe: Focus, therapeutic areas, process, steps, types)

1f What do you think what are the strategic difference between your company and other local companies or MNCs (Multinational Companies) which have some level of R&D activities? (Probe: product and process innovations, use and transfer of technology).

1g Given your experience, what is your opinion of pharmaceutical R&D in Bangladesh? (Probe: History of initiation, current status, current focus, current capacity, any major outcomes for public health etc.)

Block 2. Business model (Current and new business model)

2a In your opinion who are the prime actors and How are the different actors or stakeholders (e.g. academics, DGDA, Industry, etc.) of our pharmaceutical system interacting? How does it impact Bangladesh's pharmaceutical R&D activities and output? (Probe: Role. Partnership, Corporate social responsibility)

2b In your opinion, what are the current business models (the way R&D is financed- including push funding and pull incentives, organized, facilitated, regulated and governed) that our pharmaceutical industry is following? How the business models are linked to the concept of medicine as a 'Global public good'? (Probe: categories and examples of GPG, out-puts descriptions (vertically integrated/multi-player models), Disease, technology and drug specific R&D etc.)

2c How do you think the existing business model is impacting on Pharmaceutical R&D in Bangladesh? How well does the current business model delivers GPG (Global Public Good)? (Probe: Affordability and accessibility, Output, cost, risks of current mdoels)

2d In your opinion, what might be some alternative approaches/new business model to promote medicine as GPG. What is your thought on that if you are working on innovative medicines or planning to work on it? (Probe: Making medicine affordable and accessible to all, COVID-19 medicine).

2e In your opinion, what should be the new business models focusing on and what shortcomings are needed to be addressed in this regard? (Probe: Focus- Neglected disease, rare disease, biosecurity, antibiotics; Shortcomings- lack of invention, lack of affordability and availability; innovation capacity, industry awareness, use and transfer of technology etc.)

2f Is there any other organization like DGDA which is looking after R&D? (Probe: DGHS/ biotechnology/ ministry)

2g What are the pre-clinical and clinical research organization in Bangladesh?

2h Do you have any partner outside Bangladesh to run R&D?

Block 3. Financing, Sustainability and Incentives

3a What is your organisation's financing strategy? What are the main challenges you face in sustaining the organisation R&D activities financially? (Probe: Govt role/ fund in R&D? Allocation for research?)

3b What other incentives/resources are essential for your organisation, whether financial or non-financial?

3c Is the finance from the current investments enough for R&D activities? If not, how do your organisation manage? (Probe: Source and type of fund, R&D expenditure and firm performance)

3d Is the Government funding the labs for pre-clinical studies?

Block 4 – Intellectual Property (IP) & Data

4a What is your approach to IP management (e.g., patenting, in- or out-licensing, geographical coverage, enforcement), and what role (if any) do your financing sources play in shaping this approach?

4b How is the TRIPS agreement impacting our pharmaceutical industry and its R&D? (Probe- Extension, obligation, opportunities, challenges, TRIPS waiver longevity, what will happen after that? What are the pharmaceuticals and Government doing towards that issue?)

Block 5- Regulation:

5a What are some of the prime R&D regulation in the country? How does the regulation from the authorities impact pharmaceutical R&D in Bangladesh? (Probe: Policy attention, Norms, rules, policies, guidelines, institutional frameworks for promoting innovative capacity and competitiveness, Tax, fee and incentives that are needed to run the R&D activities? Is it a difficult for the industry, Renewal policy?)

5b What are the steps to apply for R&D?

Block 6 - Pricing and Availability

6a What factors does your organisation consider to decide on the price of the existing products and innovative products if any (e.g., at which stage of development is pricing considered? How does the approach to financing affect the approach to pricing, if at all?)

6b How does your organisation decide on where and when it will make products available (e.g., registration, volumes, supply agreements)?

Block 7 – Prospect and challenges

7a In your opinion, what are the prospects and challenges faced by pharmaceutical industries for R&D activities in Bangladesh?

7b To promote R&D what is done by DGDA, or other ministry, or organization?

(Probe- Prospects and facilitating factors- Investments, Incentives- financial and other, push and pull incentives, data-sharing platforms, patent pools, intellectual property, product development partnerships, matchmaking efforts, and analysts)

Probe- Challenges- risks, lack of skill human resource and scientific physical infrastructure, lack of biotechnical capabilities, more investment in promotion, market commitment, technology transfer, ability to conduct clinical trials, approaches for antibiotics)

Block 8 -- Recommendations

8a What else is essential for the research team to understand your organisation's business model (i.e., any key topic we have not discussed yet)?

8b Any specific recommendation for pharmaceutical R&D in Bangladesh?

8c Who else would you recommend we try to speak with within or outside your organisation?

a. Guiding tool for KII Financer

B. Target KI: "Financers."

Definition: those who provide push or pull funding for R&D (e.g., government funders, firms, investors, foundations)

Block 1 - Context and Prioritisation of R&D activities

1a What is your role within the organization? (Probe: designation/position, prime role and responsibilities, link to R&D)

1b In your opinion, what is pharmaceutical R&D, what type of activities it usually includes? Usually how R&D priorities are set? (Probe: innovation, use of technology, priority issues-access, quality, price etc.)

1c What are the R&D activities in your company? If yes, what are the priorities? (Probe: Nature of innovations, innovation capacity, use of technology, the extent of industry awareness, what are the researches currently going on?) If no, are you planning to work on it?

1d What unmet needs or gaps in the health technology R&D system is your organisation trying to cover? (Probe: Focus, therapeutic areas, process, steps, types)

1e What do you think what are the strategic difference between your company and other local companies or MNCs (Multinational Companies) which have some level of R&D activities? (Probe: product and process innovations, use and transfer of technology).

1f Given your experience, what is your opinion of pharmaceutical R&D in Bangladesh? (Probe: History of initiation, current status, current focus, current capacity, any major outcomes for public health etc.)

Block 2- Business model

2a In your opinion who are the prime actors and how are the different actors or stakeholders (e.g. academics, DGDA, Industry, etc.) of our pharmaceutical system interacting? How does it impact Bangladesh's pharmaceutical R&D activities and output? (Probe: Role. Partnership, Corporate social responsibility)

2b In your opinion, what are the current business models (the way R&D is financed- including push funding and pull incentives, organized, facilitated, regulated and governed) that our pharmaceutical industry is following? How the business models are linked to the concept of medicine as a 'Global public good'? (Probe: categories and examples of GPG, out-puts descriptions (vertically integrated/multi-player models), Disease, technology and drug specific R&D etc.)

2c How do you think the existing business model is impacting on Pharmaceutical R&D in Bangladesh? How well does the current business model delivers GPG (Global Public Good)? (Probe: Affordability and accessibility, Output, cost, risks of current mdoels)

2d In your opinion, what might be some alternative approaches/new business model to promote medicine as GPG. What is your thought on that if you are working on innovative medicines or planning to work on it? (Probe: Making medicine affordable and accessible to all, COVID-19 medicine).

2e In your opinion, what should be the new business models focusing on and what shortcomings are needed to be addressed in this regard? (Probe: Focus- Neglected disease, rare disease, biosecurity, antibiotics; Shortcomings- lack of invention, lack of affordability and availability; innovation capacity, industry awareness, use and transfer of technology etc.)

2f Is there any other organization like DGDA which is looking after R&D? (Probe: DGHS/ BIOTECHLOGY/ ministry)

2g What are the pre-clinical and clinical research organization in Bangladesh?

2h Do you have any partner outside Bangladesh to run R&D?

Block 3 - Financing, Sustainability and Incentives

3a What is your organisation's financing strategy? What are the main challenges you face in sustaining the organisation R&D activities financially? (Probe: Govt role/ fund in r&d? Allocation for research?)

3b What other incentives/resources are essential for your organisation, whether financial or non-financial?

3c Is the finance from the current investments enough for R&D activities? If not, how do your organisation manage?

3d In your opinion, what role does the healthcare budget play on your organisation's R&D? How does it affect the R&D outcome of your organisation?

Block 4 – IP and Data

4a What is your organisation's approach to information- and data-sharing, whether internally or externally, among recipients of your funding? (e.g., funding allocation, contracts, data, clinical trial results, IP management, and publication)?

4b How is the TRIPS agreement impacting our pharmaceutical industry and its R&D? (Probe- Extension, obligation, opportunities, challenges, TRIPS waiver longevity, what will happen after that? What are the pharmaceuticals and Government doing towards that issue?)

Block 5- Regulation

5a What are some of the prime R&D regulation in the country? How does the regulation from the authorities impact pharmaceutical R&D in Bangladesh? (Probe: Policy attention, Norms, rules, policies, guidelines, institutional frameworks for promoting innovative capacity and competitiveness, Tax, fee and incentives that are needed to run the R&D activities? Is it a difficult for the industry, Renewal policy?)

5b What are the steps to apply for R&D?

Block 6– Pricing and Availability

6a What is your organisation's approach to pricing and registration of the existing and innovative products that may result from your funding?

6b What kinds of conditions do you include in your funding agreements that may shape the affordability or availability of any products that may result? (e.g., equity or revenue sharing, royalties, licensing)

Block 7 – Prospect and challenges

7a In your opinion, what are the prospects and challenges faced by pharmaceutical industries for R&D activities in Bangladesh?

7b To promote R&D what is done by DGDA, or other ministry, or organization?

(Probe- Prospects and facilitating factors- Investments, Incentives- financial and other, push and pull incentives, data-sharing platforms, patent pools, intellectual property, product development partnerships, matchmaking efforts, and analysts)

Probe- Challenges- risks, lack of skill human resource and scientific physical infrastructure, lack of biotechnical capabilities, more investment in promotion, market commitment, technology transfer, ability to conduct clinical trials, approaches for antibiotics)

Block 8 -- Recommendations

8a What else is essential for the research team to understand your organisation's business model (i.e., any key topic we have not discussed yet)?

8b Any specific recommendation for pharmaceutical R&D in Bangladesh?

8c Who else would you recommend we try to speak with within or outside your organisation?

C. Target KI: "Facilitators."

Definition: those seeking to advance, improve or otherwise shape the R&D process, but not directly conducting or financing R&D (e.g., policymakers, intergovernmental organisations, data-sharing platforms, patent pools, product development partnerships, matchmaking efforts, and analysts)

Block 1 - Context and Prioritisation of R&D activities

1a What is your role within your organisation?

1b How do you see your organisation's role in the R&D ecosystem? What are the unmet needs or gaps the pharmaceutical R&D trying to cover and how your organization can contribute to meet the gap?

1c In your opinion, what is pharmaceutical R&D, what type of activities it usually includes? Usually how R&D priorities are set? (Probe: innovation, use of technology, priority issues- access, quality, price etc.)

1d What unmet needs or gaps in the health technology R&D system is trying to cover? (Probe: Focus, therapeutic areas, process, steps, types)

1e What do you think what are the strategic difference among different companies (national, MNCs- Multinational Companies and Government) which have some level of R&D activities? (Probe: product and process innovations, use and transfer of technology).

1f Given your experience, what is your opinion of pharmaceutical R&D in Bangladesh? (Probe: History of initiation, current status, current focus, current capacity, any major outcomes for public health etc.)

Block 2- Business model

2a How are the different actors or stakeholders (e.g. academics, DGDA, Industry, etc.) of our pharmaceutical system interacting, and how does it impact Bangladesh's pharmaceutical R&D activities and output?

2b We have seen that substantial new molecules were considered as Global Public Goods (GPG) during the pandemic. What is your opinion on the significance of GPG over National Public Good (NPG) in pharmaceutical R&D?

2c What do you think about the scope of introduction of a new business model in the Pharmaceutical R&D of Bangladesh to make innovative medicine accessible to all?

2d What can other business models be implemented for pharmaceutical R&D considering the context of Bangladesh?

2e Is there any other organization like DGDA which is looking after R&D? (Probe: DGHS/ BIOTECHLOGY/ ministry)

2f What are the pre-clinical and clinical research organization in Bangladesh? What are the researches currently going on (Probe: Pre-clinical/ Clinical)?

2g Do you have any partner outside Bangladesh to run R&D?

Block 3 - Financing, Sustainability and Incentives

3a For organisations that provide (non-financial) resources to R&D initiatives: What requirements or conditions are expected to be met by R&D organisations to whom you provide resources? How do you decide on these conditions, and how do you ascertain whether they have been met?

3b What do you think should be the % of GDP spent on Pharmaceutical R&D? (Probe: Govt role/ fund in R&D? Allocation for research?)

3c What other source of finance can be considered for the sustainability of pharmaceutical R&D in LMIC like Bangladesh? (Probe- SME, R&D efforts may include direct grants, tax credits and priority review vouchers, Funding/grants for R&D, public funding, government funders, firms, investors, foundations)

Block 4 – IP and Data

4a What should be the pharmaceuticals' approach to IP management (e.g., patenting, in- or out-licensing, march-in rights, geographical coverage, enforcement) to make innovative medicine accessible to all? What is your opinion on the benefit?

4b How is the TRIPS agreement impacting our pharmaceutical industry and its R&D? (Probe- Extension, obligation, opportunities, challenges, TRIPS waiver longevity, what will happen after that? What are the pharmaceuticals and Government doing towards that issue?)

Block 5- Regulation

5a How does the regulation from the authorities impact pharmaceutical R&D in Bangladesh? (Probe: Policy attention, Norms, rules, policies, guidelines, institutional frameworks for promoting innovative capacity and competitiveness)

5b What are some of the prime R&D regulation in the country? How does the regulation from the authorities impact pharmaceutical R&D in Bangladesh? (Probe: Policy attention, Norms, rules, policies, guidelines, institutional frameworks for promoting innovative capacity and competitiveness, Tax, fee and incentives that are needed to run the R&D activities? Is it a difficult for the industry, Renewal policy?)

5c What are the steps to apply for R&D?

Block 6 - Pricing and Availability

6a What should be the approaches by the pharmaceutical industries to make medicines' affordability and/or availability? (Probe- neglected tropical diseases and other diseases considered as the disease of LMIC (scabies, helminthiasis, filariasis etc.)

6b What are the most critical constraints or limitations do you think industries have to achieve its goals?

6c In your opinion, what factors should be considered to decide on the price of the existing products and innovative products if any (e.g., at which stage of development is pricing considered? How does the approach to financing affect the approach to pricing, if at all?)

6d In your opinion, how do pharmaceutical industries decide on where and when it will make products available (e.g., registration, volumes, supply agreements)?

Block 7 - Closing questions

7a In your opinion, what are the challenges faced by pharmaceutical industries for R&D activities in Bangladesh? (Probe- risks, lack of skill human resource and scientific physical infrastructure, lack of biotechnical capabilities, more investment in promotion, market commitment, technology transfer, ability to conduct clinical trials, approaches for antibiotics)

7b What else is important for the research team to understand regarding your organisation (i.e., any key topic we have not discussed yet)?

7c Who else would you recommend we try to speak with within or outside your organisation?

7d To promote R&D what is done by DGDA, or other ministry, or organization?

Annex 04: Consent Forms of KII

New Business Model for Pharmaceutical R&D in Global South

Informed Consent Form

Greetings. My name is ……...and I am a member of the Centre of Excellence research team for Universal Health Coverage (CoE-UHC), BRAC James P Grant School of Public Health, BRAC University. We are currently conducting a study on **'New Business Model for Pharmaceutical R&D in Global South',** supported by Open Society University Network (OSUN).

Faced with the global COVID-19 pandemic, countries are racing to develop new technologies and medicines. However, the systems that develop and scale these tools often fall short of actual needs. The current system of pharmaceutical R&D produces globally unequal access to medicines, with some innovative needs unmet and high prices built into the system. Different approaches to organizing, financing or incentivizing R&D –"new business models" – have demonstrated they can address some of these problems. Understanding of their potential and challenges is limited, particularly for initiatives in developing countries. This project seeks to illuminate whether and how alternative approaches to conducting R&D can produce better global public health outcomes. We will map and analyze Bangladesh's rapidly-changing pharmaceutical R&D sectors from a systems perspective, identifying the main actors, purposes, funding flows, and outcomes for public health. This project will engage scholars, civil society, and policymakers in discussions at national and international levels on reform approaches to technological innovation. As you are a stakeholder of this system, we would like to interview you regarding your view, perception, opinion and recommendations regarding pharmaceutical R&D sectors in Bangladesh. The interview will take approximately 45-60 minutes to answer those questions.

For your information, it will not bring you any direct benefit, but the information you provide will be valuable to understand the perspective and may help in the future. This information will remain anonymous and confidential and will only be used for research purposes. Your personal information (including name, address, designation etc.) is for identification purposes only and will not be shared with other parties. Participation in this research is voluntary, and you may withdraw at any time during the study. Participants are also free not to answer any questions that they do not like or want to answer. If you allow, we would like to record the interview for research purposes.

If you understand what you have been told and agree to participate, may we begin the interview now?

Signature of the Respondent	Name and Signature of Interviewer

Date:

Time of interview:

Annex 05: Extraction template for KIIs

Study identifier		Methods	Key findings							
Title	*Author*	*Objective*	*Concept and context of pharmaceutical R&D/ Innovative activities*	*prioritization of R&D/ PURPOSE OF INNOVATION*	*Business model / FUNDING FLOW*	*Business model/ Actors*	*Outcome of R&D*	*TRIPS &Post-TRIPS context*	*challenges of BD Pharma R&D*	*Recommendations*

Annex 06: IRB approval form

24 March, 2022

IRB References No. (Please quote this ref in all correspondence)	IRB-21 December'21-048
Project Title:	Project 2: New business models for medicines R&D in the Global South
Principal Investigator:	Dr. Suerie Moon

The proposal was considered by the Institutional Review Board (IRB) of the BRAC James P GrantSchool of Public Health, BRAC University. The following documents were reviewed:

1. Protocol
2. IRB Checklist
3. Consent Forms
4. Study tools

The Institutional Review Board gives approval to the study from ethical point of view with the understanding that the researchers satisfactorily addressed the concerns raised by the IRB members and reviewers if any, and the 'Guidelines for the BRAC JPGSPH IRB' will be strictly adhered.

Approval for this study is given for one year from the issuance of this letter. Any research activitiesunder the purview of this approval beyond the study period will require prior written notification andsubsequent approval from the IRB. It is the applicant's responsibility to obtain review and continuedapproval before the expiration date. You may not continue any research activity beyond the expiration date without approval by the Board.

Amendments: If you wish to change any aspect of this study, such as, but not limited to, the procedures, the consent forms, or the survey instruments, please communicate your requested changes to the Board. The new procedure is not to be initiated until the IRB approval has been given.

Adverse Reactions: Investigators are required to promptly report any unanticipated problems or complaints to the committee. If the problem is serious, approval may be withdrawn pending IRB review.

Yours sincerely,

Mrittika

Mrittika Barua, PhD
Assistant Professor
Co-Chairperson, Institutional Review Board BRAC James P Grant School of Public HealthBRAC University