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Report No: PAD2049

INTERNATIONAL BANK FOR RECONSTRUCTION AND DEVELOPMENT

PROJECT APPRAISAL DOCUMENT

ON A

PROPOSED LOAN

IN THE AMOUNT OF US$125 MILLION

TO THE

REPUBLIC OF INDIA

FOR AN

INNOVATE IN INDIA FOR INCLUSIVENESS (I^3) PROJECT

May 8, 2017

Trade and Competitiveness Global Practice
South Asia Region

This operation is part of the Agile Pilots initiative and uses a short version of the Project Appraisal Document.

CURRENCY EQUIVALENTS
(Exchange Rate Effective April 10, 2017)

Currency Unit = Indian Rupee (INR)

US$ = INR 64.55

FISCAL YEAR
April 1 – March 31

ABBREVIATIONS AND ACRONYMS

BIRAC	Biotechnology Industry Research Assistance Council
CAG	Comptroller and Auditor General
CEPI	Coalition for Epidemic Preparedness Innovations
CMC	Chemistry, Manufacturing, and Controls
CPS	Country Partnership Strategy
CRVMF	Clinical Research Validation and Management Framework
CTN	Clinical Trial Network
DBT	Department of Biotechnology
EMF	Environmental Management Framework
GAVI	Global Alliance for Vaccines and Immunization
GCP	Good Clinical Practice
GDP	Gross Domestic Product
GMP	Good Manufacturing Practice
GoI	Government of India
GPP	Good Participatory Practice
HPV	Human Papillomavirus
IFR	Interim Financial Report
IP	Intellectual Property
LMIC	Low- and Middle-income Country
MSMEs	Micro, Small, and Medium Enterprises
NCD	Non-communicable Disease
PCV	Pneumococcal Conjugate Vaccine
PD	Project Director
PDO	Project Development Objective
PIM	Project Implementation Manual
PMU	Project Management Unit
PPSD	Project Procurement Strategy for Development
R&D	Research and Development
RTTP	Registered Technology Transfer Professional
SDG	Sustainable Development Goal
SMEs	Small and Medium Enterprises
TTO	Technology Transfer Office
TPP	Target Product Profile
UN	United Nations
VC	Venture Capital

Regional Vice President:	Annette Dixon
Country Director:	Junaid Kamal Ahmad
Senior Global Practice Director:	Anabel Gonzalez
Practice Manager:	Esperanza Lasagabaster
Task Team Leader/Co-Task Team Leader:	Manju Haththotuwa/Jorge Coarasa

INDIA
Innovate in India for Inclusiveness (I^3)

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India

Innovate in India for Inclusiveness (P156241)

PROJECT APPRAISAL DOCUMENT

SOUTH ASIA

GTC06

Report No.: PAD2049

Basic Information		
Project ID P156241	EA Category B - Partial Assessment	Team Leader(s) Bharatha Manju S. Haththotuwa, Jorge A. Coarasa
Lending Instrument Investment Project Financing	Fragile and/or Capacity Constraints [ ] Financial Intermediaries [ ] Series of Projects [ ]	
Project Implementation Start Date 03-Jul-2017	Project Implementation End Date 30-Jun-2023	
Expected Effectiveness Date 01-Aug-2017	Expected Closing Date 30-Jun-2023	
Joint IFC No		

Practice Manager/Manager	Senior Global Practice Director	Country Director	Regional Vice President
Esperanza Lasagabaster	Anabel Gonzalez	Junaid Kamal Ahmad	Annette Dixon

Borrower: Republic of India					
Responsible Agency: Biotechnology Industry Research Assistance Council					
Contact:	Dr. Renu Swarup		Title:	Senior Adviser, DBT and MD, BIRAC	
Telephone No.:			Email:	swarup@dbt.nic.in	

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Project Financing Data(in US$, Millions)					
[X]	Loan	[ ]	IDA Grant	[ ]	Guarantee
[ ]	Credit	[ ]	Grant	[ ]	Other

Total Project Cost:	250.00	Total Bank Financing:	125.00
Financing Gap:	0.00		

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Financing Source	Amount
Borrower	125.00
International Bank for Reconstruction and Development	125.00
Total	250.00

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Expected Disbursements (in US$, Millions)

Fiscal Year	2018	2019	2020	2021	2022	2023
Annual	7.72	15.34	26.33	28.33	29.58	17.70
Cumulative	7.72	23.06	49.39	77.72	107.30	125.00

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Institutional Data

Practice Area (Lead)

Trade & Competitiveness

Contributing Practice Areas

Health, Nutrition & Population

Proposed Development Objective(s)

The proposed Project Development Objective (PDO) is to facilitate innovation in biopharmaceutical products and medical devices that address public health priorities in India.

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Components

Component Name	Cost (US$, Millions)
Strengthening the pilot-to market innovation ecosystem	125.00
Accelerating the pilot-to-market process for specific products	120.00
Project management and monitoring and evaluation	5.00

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Systematic Operations Risk-Rating Tool (SORT)

Risk Category	Rating
1. Political and Governance	Low
2. Macroeconomic	Low
3. Sector Strategies and Policies	Moderate
4. Technical Design of Project or Program	Substantial
5. Institutional Capacity for Implementation and Sustainability	Moderate
6. Fiduciary	Moderate
7. Environment and Social	Low

8. Stakeholders	Low
9. Other	
OVERALL	Substantial

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Compliance		
Policy		
Does the project depart from the CAS in content or in other significant respects?	Yes [ ]	No [X]

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Does the project require any waivers of Bank policies?	Yes [ ]	No [X]
Have these been approved by Bank management?	Yes [ ]	No [ ]
Is approval for any policy waiver sought from the Board?	Yes [ ]	No [X]
Does the project meet the Regional criteria for readiness for implementation?	Yes [X]	No [ ]

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Safeguard Policies Triggered by the Project	**Yes**	**No**
Environmental Assessment OP/BP 4.01	**X**	
Natural Habitats OP/BP 4.04		**X**
Forests OP/BP 4.36		**X**
Pest Management OP 4.09		**X**
Physical Cultural Resources OP/BP 4.11		**X**
Indigenous Peoples OP/BP 4.10		**X**
Involuntary Resettlement OP/BP 4.12		**X**
Safety of Dams OP/BP 4.37		**X**
Projects on International Waterways OP/BP 7.50		**X**
Projects in Disputed Areas OP/BP 7.60		**X**

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Legal Covenants

Name	**Recurrent**	**Due Date**	**Frequency**
Transfer of Funds	**X**		CONTINUOUS

Description of Covenant

To facilitate the carrying out of the Project, the Borrower shall make the proceeds of the Loan available to BIRAC through its Department of Biotechnology, in accordance with the Borrower's standard arrangements for development assistance in India.

Name	**Recurrent**	**Due Date**	**Frequency**
Institutional Arrangements	**X**		CONTINUOUS

Description of Covenant

BIRAC shall establish and thereafter maintain throughout the period of implementation of the Project, a Steering Committee, a Technical Advisory Group and a Project Management Unit, with functions and resources satisfactory to the Bank and with staff in adequate numbers and with qualifications, experience and terms of reference satisfactory to the Bank.

Name	Recurrent	Due Date	Frequency
Project Implementation Manual and Clinical Research Management Framework	**X**		CONTINUOUS

Description of Covenant

BIRAC shall implement the Project, and cause it to be implemented, in accordance with the Project Implementation Manual and the Clinical Research Validation and Management Framework; and refrain from amending, suspending, waiving, and/or voiding any provision of the Project Implementation Manual and/or the Clinical Research Validation and Management Framework whether in whole or in part, without the prior written concurrence of the Bank.

Name	Recurrent	Due Date	Frequency
Full and informed consent	**X**		CONTINUOUS

Description of Covenant

Prior to the commencement of any clinical trials under the Project, BIRAC shall ensure that: (a) full and informed written consent of all participants in clinical trials is obtained, recorded and retained by all Grantees; and (b) a grievance mechanism is set up, and implemented throughout Project implementation, in order to track complaints related to all Project activities (including clinical trials) and guide resolution of such complaints.

Name	Recurrent	Due Date	Frequency
Grant Agreement	**X**		CONTINUOUS

Description of Covenant

1. BIRAC shall provide Project Grants to Grantees who have fulfilled the requirements set forth in the Project Implementation Manual.
2. BIRAC shall, prior to making any Project Grant, enter into an agreement with a Grantee, whereby BIRAC shall agree to provide such Grantee with any of the aforementioned Project Grants and the Grantee shall agree to carry out its respective Project activities, on terms and conditions satisfactory to the Bank ("Grant Agreement").

Name	Recurrent	Due Date	Frequency
Safeguards Instruments	**X**		CONTINUOUS

Description of Covenant

BIRAC shall, and shall cause Grantees to carry out the Project in accordance/compliance with the EMF and the relevant instruments (to be) prepared pursuant to the objectives, policies, procedures and other provisions set forth therein, in a manner and substance satisfactory to the Bank.

Name	Recurrent	Due Date	Frequency
Safeguards Implementation	**X**		CONTINUOUS

Description of Covenant

Prior to the carrying out of any Project activity, BIRAC shall: (a) carry out and/or cause to be carried out an environmental screening and/or an environmental assessment (as the case may be) of the pertinent activities to be financed under the Grant Agreement; (b) approve, and/or cause the Grantee to approve an environmental/social management plan, acceptable to the Bank, for each said activity all in accordance with the provisions of the EMF; and (c) immediately after such approval, implement and/or cause to be implemented (as the case may be) the corresponding environmental/social management plan in accordance with its terms.

Name	Recurrent	Due Date	Frequency
Safeguards Monitoring	X		CONTINUOUS

Description of Covenant

BIRAC shall, throughout the period of implementation of the Project maintain monitoring and evaluation protocols and record keeping procedures acceptable to the Bank and adequate to enable BIRAC and the Bank to supervise and assess, on an ongoing basis, the implementation of/compliance with the EMF and each environmental management plan and/or social management plan prepared thereunder, as well as the achievement of the objectives thereof.

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Conditions

Source Of Fund	Name	Type

Description of Condition

Team Composition

Bank Staff

Name	Role	Title	Specialization	Unit
Bharatha Manju S. Haththotuwa	Team Leader (ADM Responsible)	Lead Private Sector Specialist		GTC01
Jorge A. Coarasa	Team Leader	Senior Economist (Health)		GHN06
Satyanarayan Panda	Procurement Specialist (ADM Responsible)	Procurement Specialist		GGO06
Dhirendra Kumar	Procurement Specialist	Consultant		GTC06
Arvind Prasad Mantha	Financial Management Specialist	Financial Management Specialist		GGO24
Albert Sole Canut	Team Member	Senior Private Sector Specialist		GTC06
Andreas Seiter	Peer Reviewer	Lead Health Specialist		GHNDR

Farah Dib	Team Member	Young Professional		GTC07
Harinath Sesha Appalarajugari	Safeguards Specialist	Senior Environmental Specialist		GEN06
Jorge Luis Alva-Luperdi	Counsel	Senior Counsel		LEGES
Juan Sebastian Saez	Team Member	Lead Economist	T&C CMU lead	GTC06
Justin Piers William Hill	Peer Reviewer	Senior Private Sector Specialist		GTCIE
Karamath Djivede Sybille Adamon	Team Member	Young Professional		GHNGE
Marianne Ellen Anderson	Team Member	Monitoring and Evaluation Specialist	M&E specialist	GTCOS
Ramesh Govindaraj	Peer Reviewer	Lead Specialist, Health, Nutrition and Population		GHN02
Samuel Thangaraj	Safeguards Specialist	Consultant		GSU06
Satish Kumar Shivakumar	Team Member	Finance Officer		WFALA
Shiny Jaison	Team Member	Program Assistant		SACIN
Srividya Jagannathan	Peer Reviewer	Principal Investment Officer		CMGC1
Tanya Cubbins	Team Member	Program Assistant		SACIN
Victor Manuel Ordonez Conde	Team Member	Senior Finance Officer		WFALA

Extended Team

Name	Title	Office Phone	Location
Anya Eldan	External peer reviewer	972544781204	Tel Aviv
Kannan Vijayaraghavan	Industry Expert	919866522111	Hyderabad
Robert Levine	Clinical Trials Expert	2033140476	New Haven

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Locations

Country	First Administrative Division	Location	Planned	Actual	Comments

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Consultants (Will be disclosed in the Monthly Operational Summary)

Consultants Required?	Consultants will be required.

I. STRATEGIC CONTEXT

A. Sectoral and Institutional Context

1. While India is recognized as a leading global manufacturer of high-quality generic drugs, industry gaps and market failures constrain its innovation capabilities, limiting its competitiveness and ability to address its disease burden. The Indian pharmaceutical sector accounts for about 2.4 percent of the global pharmaceutical industry in value terms and 10 percent in volume terms. India also accounts for 20 percent of global exports in generics, making it the largest provider of generic medicines globally. In 2014, Indian manufacturers provided nearly 60 percent of vaccine volume, representing just over 30 percent of the total value of procurement by the Global Alliance for Vaccines and Immunization (GAVI). However, the strategic focus of the global pharmaceutical and medical device industries has gradually shifted from reverse-engineering manufacturing toward product innovation, primarily owing to breakthroughs in translational research, bio-manufacturing, and medical technology. With this shift, however, diseases that disproportionately affect low- and middle-income countries (LMICs) and the poor, many of which are public health priorities in India,[1] are largely ignored as companies tend to allocate research and development (R&D) funding to high-profit markets.

2. Under this new paradigm, innovation capabilities, quality of research, and transparency in the regulatory validation of product efficacy become increasingly relevant for the long-term competitiveness of the industry. While India is a leader in innovation in South Asia, innovation in India is mostly incremental or imitative, as illustrated by the strong generics industry. India's output of patents and trademarks is small, business expenditure on R&D is low, and there is a limited skills base for innovation.[2] With the exception of world-class players in a few sectors and localized centers of excellence, there is a low degree of novelty innovations in India, and the economy underperforms relative to other middle-income peers on several related indicators.

3. While India has strong capabilities and resources in basic research and manufacturing (Figure 1), market failures limit its capabilities in pilot-to-market stages of product development. To successfully transition toward world-class innovation in biopharmaceuticals and medical devices, India needs to overcome these market failures that currently undermine private incentives to invest in R&D and negatively affect the performance of innovative entrepreneurs. These are:

(a) **Investment in pilot-to-market stages of product development is perceived as too risky for private investors.** Lack of investment in product-oriented discovery and translational research limits innovation capacity (FFigure 1) and impedes the industry's ability to provide affordable solutions to neglected diseases that constitute public health priorities. Access to private capital (venture capital [VC], private equity, and so on) is extremely limited at this stage due to the perception of high risk. While a few large companies have the means to fund product development and scale up, these investments can be prohibitively costly for smaller firms, and network and market financing failures can prevent their acquisition. Globally, substantial government grants are available for scale-up funding, especially in the European

[1] India accounts for 20 percent rotavirus, pneumococcal, and measles deaths and about 25 percent of cervical cancer deaths globally.
[2] Organisation for Economic Co-operation and Development 2014.

Union, the United States, and Asian countries such as the Republic of Korea, but the dearth of such options in India affects the competitiveness of the industry and the ability for critical products to reach the market in a reasonable timeframe and at an affordable price.

(b) **Suboptimal investment in public goods critical to translational research.** India has strong and well-developed capabilities in the pre-validation and large-scale manufacturing stages where the industry's research and the bulk of private investment have focused; however, critical technology and knowledge gaps exist in pilot-to-market stages of the product development lifecycle. India lacks the hard and soft infrastructure to support these stages of the value chain. First, firms, and in particular micro, small, and medium enterprises (MSMEs), lack access to technology and equipment tailored to specific needs across poorly developed stages of drug development, such as basic and applied research, clinical trials, and validation. Second, despite strides in developing strong capabilities in basic research, bio-manufacturing, and medical services, India lacks a workforce—including scientists, researchers, and staff trained in a broad set of skills across the different stages of product development—equipped to provide the skills base for a well-functioning innovation ecosystem. While infrastructure, technology, and human capital are critical to successful innovation and deliver substantial economic benefits, the levels of investment required and appropriation problems make it prohibitive for individual firms to pursue these investments. In countries that have been successful in building effective innovation ecosystems, partnerships among government, the private sector, and academia have eased access to these shared facilities and public goods.

(c) **There is a gap between private and social returns to collaboration.** Research shows that relative to other regions, a much larger share of innovation in South Asia (including in India) takes place in-house, limiting productive collaboration across firms and possibly explaining high rates of imitation instead of radical innovation.[3] Cooperation to strengthen interactions and linkages across the various stakeholders in innovation processes is an essential pillar in the innovation ecosystem. Government organizations are ideally placed to build noncompetitive collaborations toward accelerated and cost-effective product development, in which the division of risk-taking aligns with the social and private returns of participating actors. These include filling in process gaps between large companies with manufacturing expertise and the discovery and validation capabilities which currently lie within academia and research institutes.

(d) **Institutional failures in management of innovation systems.** Globally, successful experiences highlight the importance of strong and efficient institutional arrangements for knowledge creation and diffusion. In countries with well-functioning innovation systems, technology transfer offices (TTOs) assist stakeholders in the facilitation and adoption of new global innovations, technologies, and licensing models; manage

[3] Lopez-Acevedo, Gladys, Denis Medvedev, and Vincent Palmade. 2016. *South Asia's Turn: Policies to Boost Competitiveness and Create the Next Export Powerhouse.* South Asia Development Matters. Washington, DC: World Bank. https://openknowledge.worldbank.org/handle/10986/25094 License: CC BY 3.0 IGO.

intellectual assets; and provide relevant legal monitoring and support. Yet, India lacks TTOs that can identify research which has potential commercial interest and develop strategies to exploit it.

(e) **Private returns do not provide sufficient incentives for R&D in diseases of the poor.** In the current market-driven R&D system, a high number of medicines for diseases that disproportionately affect populations in LMICs are not available or not affordable. Pharmaceutical companies are typically reluctant to invest in developing medicines for patient populations that do not represent a profitable market or for diseases predominantly affecting LMICs, given the low and unpredictable expected private returns on investment. This 'directionality' failure means that with regard to addressing societal challenges, governments have to provide direction and public funding of R&D to achieve a socially optimal level of R&D. This can be done by influencing the incentives of and reducing the risk for the private sector of undertaking R&D activities deemed to have significant social benefits and thus delinking the price of solutions for public health priorities from their R&D cost.

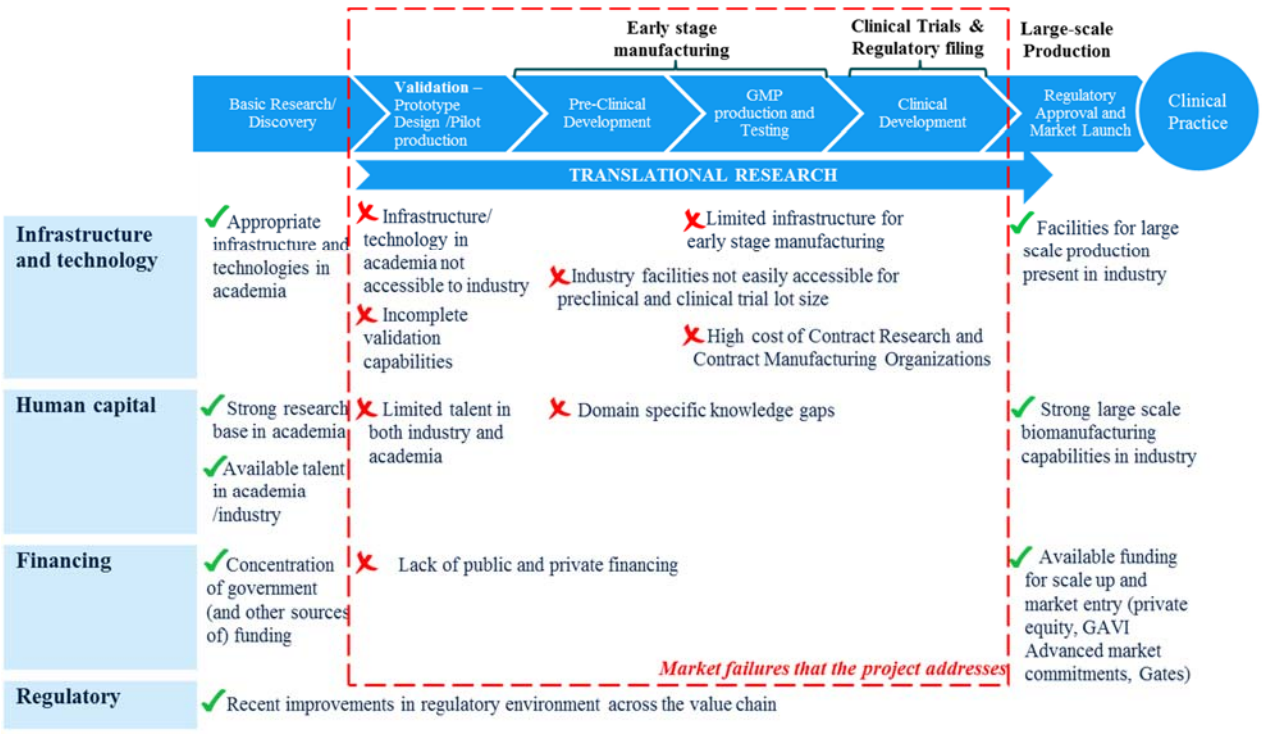
4. India has recognized the need for strong innovation policies particularly in support of the biopharmaceutical sector. India's strategy, 'Decade of Innovations 2010–20', aims at strengthening innovation capacities including by increasing gross expenditure on R&D to 2 percent of gross domestic product (GDP) by 2020. The Make in India initiative, an ambitious countrywide program launched in September 2014 to encourage manufacturing, identifies the pharmaceuticals, biotechnology, and medical device industries as priority sectors and aims at addressing a number of policy challenges and improving the business environment to foster India's competitiveness. Finally, the 12th Five-Year Plan encourages states and central ministries to promote 'R&D outputs leading to public and social goods' such as ensuring access to good quality health care and alleviating the burden of communicable and non-communicable diseases (NCDs).

5. To implement its strategy, the Government of India (GoI) created the Biotechnology Industry Research Assistance Council (BIRAC) five years ago under the Department of Biotechnology (DBT). BIRAC has supported 539 companies (mainly start-ups and MSMEs) that are implementing 360 projects, with funding support of over US$100 million and commitments of over US$160 million from the private sector. These projects have delivered 26 affordable products and 19 new technologies in addition to creating 53 new intellectual properties (IPs). BIRAC efforts can be broadly divided into three verticals: (a) providing innovation funding to entrepreneurs, small and medium enterprises (SMEs), start-ups, and other biotechnology companies; (b) supporting entrepreneurship through mentorship, capacity building, technology transfer facilities, and IP management; and (c) developing strategic partnerships with national and international entities. BIRAC's schemes encourage collaboration among stakeholders and provide a conducive environment for collaborative R&D, with a particular focus on the health care sector (including drugs, devices/diagnostics, biosimilars, and vaccines/clinical trials). The proposed project would further BIRAC's work in transforming the biopharmaceutical and medical devices industries in India.

6. The World Bank can leverage its experience in financing and supporting the implementation of innovation, competitiveness, and public health projects to help the GoI unlock India's potential for increased innovation. Drawing from global best practices adapted to the

strategic and institutional context of India, the design of the project is based on a holistic approach to product-driven innovation in the biopharmaceutical and medical device industries. The project will focus on the sections of the biotechnology value chain where critical gaps which impede the development of the industry exist (see Figure 1 for a visualization of the market failures along the value chain and where the project seeks to intervene). The project helps fill financing, infrastructure/technology, and human capital gaps where there is limited public or private resources. It also facilitates collaboration among the various stakeholders, which would not otherwise occur. While not directly supporting the regulatory environment (including IP), the project will inform ongoing GoI efforts in this space, which is considered adequate in its current state, to facilitate project interventions. The project specifically will support concerted public-private efforts toward product development combined with upgrades in related soft and hard infrastructure to reinforce and sustain the transformation of the industry. Consortia of public-private stakeholders will be the recipients of grants to accelerate development and improve success rates of select products tackling major public health priorities. These consortia will also benefit from additional project support aimed at improving overall factor conditions in the business environment, which will be implemented in tandem with the product-driven initiatives. Namely, the project will support improved technical skills, advanced research-oriented facilities, and technology transfer processes which, combined, will foster improved innovation capabilities and collaboration within the ecosystem. These efforts are expected to provide strong demonstration effects and to crowd-in additional private sector financing and participation in the sector going forward.

Figure 1. Biotechnology Value Chain, Market Failures, and Areas of Project Intervention



Note: GMP = Good manufacturing Practice.

B. Higher Level Objectives to which the Project Contributes

7. The project aligns with the Sustainable Development Goals (SDGs) and the United Nations (UN) High Level Panel on Access to Medicines recommendations. The SDGs adopted in 2015 (specifically SDG 3) include an explicit focus on Universal Health Coverage and access for all to safe, effective, quality, and affordable medicines and vaccines for both communicable diseases and NCDs. However, the innovation gap in diseases that predominantly affect neglected populations, particularly in LMICs, and high costs of existing health technologies, due to the profit-driven innovation models, are barriers to achieving these goals. Target SDG 3b includes "support the research and development of vaccines and medicines for the communicable and non-communicable diseases that primarily affect developing countries." The UN High Level Panel on Access to Medicines convened in 2015 finds that "adequate investment in R&D by the public sector is crucial if governments are to fulfil their obligations with respect to the right to health" and calls for new approaches to close the health innovation and access gap, including mechanisms that "delink the costs of R&D from end prices to promote access to good health for all."[4]

8. India's growth potential[5] will contribute toward ending extreme poverty and boosting shared prosperity, the World Bank's twin goals, to the extent it effectively promotes and sustains inclusive growth and raises global competitiveness. With low-income households highly vulnerable to health shocks, empowering the poor to participate in the growth process requires continued efforts to remove barriers to affordable healthcare. Affordability becomes a binding constraint to economic inclusion in a country with 640 million people unable to access essential medicines, 75 percent of the population uninsured, and out-of-pocket health expenditures which rank as one of the highest in the world.

9. The project will contribute to the World Bank Group's Country Partnership Strategy 2013-2017 (CPS), Report No. 76176-IN, discussed by the Executive Directors on April 11, 2013. The development of innovation capabilities of the pharmaceutical industry aiming at providing access to new vaccines and biosimilar products, medical devices, and diagnostics, is consistent with the objectives of the inclusion pillar insofar as it targets basic public health priorities. More indirectly, the project will also support growth in manufacturing, a central topic in the integration pillar, and capitalize on agglomeration economies, a guiding principle within the transformation pillar.

II. PROJECT DEVELOPMENT OBJECTIVES

A. Proposed Project Development Objective

10. The proposed Project Development Objective (PDO) is to facilitate innovation in biopharmaceutical products and medical devices that address public health priorities in India.

[4] Report of the United Nations Secretary-General's High-Level Panel on Access to Medicines: promoting innovation and access to health technologies. Released September 14, 2016.

[5] Underpinned by the largest youth population in the world, the third-largest domestic market in purchasing power parity terms, and a steady implementation of trade and regulatory reforms, India is expected to average 8 percent annual GDP growth in the upcoming years, the fastest growth rate projections among large economies in the world.

B. Project Beneficiaries

11. The project's direct beneficiaries are the companies, research and academic institutions, researchers, and field practitioners receiving grants or training. Product development grants will benefit companies or public sector entities with product leads that meet the selection criteria for the targeted vaccines, biosimilars, and devices and diagnostics. Public and private sector entities with R&D and/or manufacturing facilities can qualify for grants to establish shared facilities needed for product development. Researchers can qualify for research grants to provide inputs into the product development process. Clinical sites will benefit from capacity building to conduct clinical trials. Practitioners will benefit from domain-specific and business training to fill knowledge and managerial skills gaps. Additionally, a few practitioners will benefit from technology transfer training to generate a set of registered technology transfer practitioners (RTTPs) who will manage newly set up TTOs in the various biotechnology clusters around India.

12. Indirect project beneficiaries include researchers, start-ups, MSMEs, and other companies who can access the shared facilities set up under the project to advance their products (regardless of whether they also benefit from product development grants). The ultimate project beneficiaries are the millions of Indians, including women and children, particularly those from vulnerable sections of society, who will benefit from low-cost health products because of expected reduction in out-of-pocket expenses when these reach the market, developed through the ecosystem set up under the project. Products will be accessed for the first time either because they previously did not exist or were unaffordable to those who need them the most. These products could also benefit people outside of India, such as in Africa for example, where the need for affordable medicines is equally significant.

III. PROJECT DESCRIPTION

A. Principles of Project Design and Implementation

13. The project is designed to support consortia of public, private, and academic institutions to overcome the key market failures currently holding back the development of an innovative biopharmaceutical and medical device industry in India. Through Component 1, the project will provide grants to collaborative consortia to fill critical gaps in the biologics (namely vaccines and biosimilars) and medical devices value chains. Through Component 2, the project will provide grants to institutions (public and private) currently in the pilot-to-market stages of development for a targeted set of products that have been identified as public health priorities for India. Both components have been designed following a set of principles derived from international best practice and lessons learned from prior initiatives in and outside the World Bank:

(a) Industry associations, academic institutions, and public sector undertakings have been convened by BIRAC to identify and prioritize both the gaps and the products targeted by the project (see section VI. C for details).

(b) Grants provided by the project will be leveraged to bring together top Indian institutions with cutting-edge international players including private firms, individual experts, and contract research organizations as well as universities and other research centers. These international partners will be engaged through knowledge transfer

agreements, technology licensing and acquisition, and other innovative mechanisms tailored to each activity.

(c) The grant-based design of the project leverages market demand by allocating performance-based funds through open, competitive calls for proposal with transparent eligibility and selection criteria.

(d) Sustainability has been a key criterion in the design as the project aims to build an ecosystem for the future. The investments in Component 1 are aimed at public goods and shared facilities that will be first tested by the products supported by Component 2. However, those assets will become available to multiple other products in the pipeline for years to come. In that sense, while accelerated innovation will be measured by project end through the products supported by Component 2, the impact of Component 1 is expected to continue long after the project closes (see section IV. C for further details).

B. Project Components

Component 1: Strengthening the pilot-to-market innovation ecosystem (US$125 million)

14. The interventions under this component will be targeted at critical gaps in infrastructure, human capital, and technology transfer that have been identified as weak areas in the pilot-to-market innovation ecosystem for biopharmaceuticals and medical devices. The project will not address the overall regulatory and institutional framework for biopharmaceutical and medical devices in India, which has already undergone significant reforms in the last three years that improved its robustness, but will have targeted interventions within that framework to improve areas where gaps have been identified (clinical trials and technology transfer).

15. The project will provide grant funding to support the creation of centers of excellence for validation, early stage bio-manufacturing, clinical development, training, and technology transfer. Funding will be used to procure specialized equipment, services, and technologies required for the different stages of the pilot-to-market process. Grant recipients under this component will be primarily private and autonomous public entities, selected through open and competitive calls for proposal with transparent selection criteria. Grantees are expected to be top institutions from both the public and private sectors that already have a successful track record in the biotechnology space but lack specific capabilities required to enable faster, lower-cost validation, clinical development, and early stage manufacturing.

Subcomponent 1.1: Shared facilities

16. **Validation and reference facilities.** Once a product lead has been identified through the process of scientific discovery, it enters the validation stage where it is further tested for efficacy, safety, and scalability. The project aims to support two validation and reference facilities for biologics (vaccines and biosimilars) and one facility for validation of medical devices (instruments and diagnostics). This will be done by providing grants to public and private R&D institutions (both academic research centers and commercial entities) in existing biotechnology clusters for upgrading equipment and expanding their know-how. No land acquisition or major civil works will be supported. Once these new capabilities are in place, they will be offered in the form of

shared facilities to any player in the industry and, therefore, they will be used to advance the development of products under Component 2 as well as support products not directly funded through the project. MSMEs will be able to use these facilities at lower rates than currently available in the market.

17. **Early stage manufacturing.** The project aims to support existing institutions to set up or upgrade three chemistry, manufacturing, and controls (CMC) facilities to support early stage manufacturing for vaccines and biosimilars. Products manufactured in CMC facilities will then go back to the validation facilities for further testing before they can go to clinical development.

18. **Cell line repository.** A key input for lead and product validation is cell culture, a process by which cells are grown under controlled conditions, generally outside of their natural environment. These cells are used to test products and product leads and this is done by maintaining cell lines—a population of cells descended from a single cell and containing the same genetic makeup separated from their original tissue. The project will support the upgrading of an existing institution into a national cell line repository that will allow ready access to quality-controlled cell lines across the different stages of the validation process.

Subcomponent 1.2: Scientific research

19. In addition to the shared facilities described, accelerating and lowering the cost of validation and early stage manufacturing will require the development of new scientific research tools such as biomarkers, assays, cell lines, and technologies for efficient processing. The project will provide research grants to scientific institutions that will lead a consortia of Indian and global researchers to develop these novel tools. The new tools will be initially used for the development of products supported by Component 2, but they can be subsequently applied to other products, permanently expanding the knowledge and competency of the ecosystem in the process.

Subcomponent 1.3: Clinical trial network

20. Following the validation and early bio-manufacturing stages, products undergo clinical development, which includes confirming their efficacy and safety in humans through clinical trials. Clinical trials are currently an important bottleneck in the product development process as companies and institutions usually have to go through an ad hoc process of finding sites with access to the required population that meet internationally accepted clinical and ethical standards. The project will support the establishment of a clinical trial network (CTN) which connects various clinical sites together giving researchers and manufacturers ready access to a wide population sample across India on which to conduct trials required to obtain regulatory approvals and certifications. The project will provide grant funding to carefully selected individual clinical sites which already have a strong track record of conducting high-quality trials to achieve and maintain internationally accepted Good Clinical Practice (GCP) and Good Participatory Practice (GPP) compliance. This may entail upgrading of technology used to manage data and monitor trial implementation, equipment, and minor repairs and renovations required to ensure patient safety as well as consulting services from individual experts to develop and implement the protocols and procedures required to comply with the highest clinical and ethical standards. It will also provide grant funding to develop shared support services across sites such as data management.

Subcomponent 1.4: Training

21. The project will provide grant funding to existing academic institutions to connect them with global centers of excellence and help them develop new training programs to fill scientific, business, and R&D management knowledge gaps that have been identified as current weaknesses in the industry. Training will target young professionals (from recent PhD graduates to middle managers, including women) working in the sector with the following objectives:

(a) Enabling suitable human resources for product development needs under Component 2 and able staffing of the facilities under Component 1;

(b) Generating the next generation of trainers in each identified area; and

(c) Training next generation scientists (academic researchers—PhDs and postdoctoral fellows) for interdisciplinary skills across the product development value chain.

Subcomponent 1.5: Technology transfer

22. This subcomponent will include acquiring the specialized technical skills and the institutional knowledge, networks, and know-how to establish a few TTOs with the target of having one TTO in each biotechnology cluster in India (six to eight). TTOs are key to translating scientific research results into patentable and marketable products. The process will include Indian personnel going through formal training in IP and technology transfer and securing the Registered Technical Transfer Professional (RTTP) status and undertaking internships in successful TTOs overseas as well as bringing key experts from overseas to embed them in the start-up TTOs in India. Twinning arrangements with successful TTOs elsewhere will also be pursued. Domain expertise in technical; legal (for example, patent writing, technology valuation, commercialization mentoring and advice); financial; and commercial aspects will be imparted to a core cadre of Indian professionals who will pioneer this subcomponent.

Component 2: Accelerating the pilot-to-market process for specific products (US$120 million)

23. The project will provide grant funding to consortia of private, public, and academic institutions, led by cutting-edge institutions in their respective field, to accelerate the development of low-cost, select vaccines, biopharmaceuticals, diagnostics, and medical devices that address public health priorities in India. By extending financing to consortia, the project seeks to foster a more collaborative R&D environment which leverages the expertise of local and international players from both the public and private sectors. Additionally, consortia present an opportunity to link MSMEs in the field with larger companies. This funding will be used by grantees to cover the cost of critical aspects of the product development process such as acquisition or licensing of proprietary technologies, equipment, and specialized services, as well conducting clinical trials and meeting other regulatory requirements. In addition to funding, the products supported under this component will benefit from access to the research infrastructure, scientific research tools, and a CTN that will be developed under Component 1, at reduced costs. Finally, the products directly supported by the project will be those that address public health priorities, have market potential, and are already in the critical validation to early bio-manufacturing stages of product development. In addition to reflecting the lower cost of development in lower market prices, the recipients of

grants under this component will commit to delivering agreed quantities at agreed prices to the public health sector in India. Finally, any technologies developed in the process of product development will be treated as non-proprietary and will be accessible to other users.

Subcomponent 2.1: Vaccines

24. The project will finance the development of select vaccines through grant funding. Three disease areas of focus for vaccine development have been selected through a filtering exercise based on criteria including public health requirements (disease morbidity and mortality and unmet demand) and market relevance (industry focus based on national demand, opportunity for accelerated access and affordability, community demand). Selected diseases are human papillomavirus (HPV), dengue, and pneumonia.

25. For each of these disease areas, a Target Product Profile (TPP) will be established based on further scientific consultations. Potential candidates for support will be selected for each disease area through an open call for proposals and based on a transparent set of criteria, as set out in the Project Implementation Manual (PIM).

Subcomponent 2.2: Biosimilars

26. The project will finance the development of select biosimilars through grant funding. A short list of 11 potential biosimilars, focused on NCDs, has been identified. The process started with a list of 135 biotherapeutics that are due to be off-patent in the next few years and that could be developed as biosimilars in India. The short list was then compiled through a consultative process including experts from industry, academia, and government. Selection criteria included public health needs (India's disease burden), market feasibility (ability of licensure in India and high global demand), and scope for Indian licensure in the next three to five years (existing Indian leads).

27. Potential candidate(s) for support will be selected through an open call for proposals with transparent selection criteria established in the PIM.

Subcomponent 2.3: Medical devices (instruments and diagnostics)

28. As a result of a landscaping exercise with industry stakeholders, it was decided that the project would be focused on platform technologies rather than specific devices. The aim is to use the grants under this subcomponent as catalytic investments that allow further development of multiple products. The subcomponent will leverage grants to promote collaboration among medical and information technology researchers and entrepreneurs to further develop the selected platforms, including, for example, digital health.

Component 3: Project management and monitoring and evaluation (US$ 5 million)

29. This component will cover the operating costs incurred by BIRAC in the implementation of the project. It includes

(a) Salaries and honoraria for staff, consultants, and members of the different technical committees;

(b) Stakeholder and scientific consultations, including with international experts, at different stages of the project;

(c) Consulting services such as clinical data auditing and others required in discharge of clinical research oversight and validation;

(d) Travel costs for supervision visits; and

(e) Other operating costs as needed.

C. Project Cost and Financing

30. The total cost of the project is US$250 million, co-financed by the World Bank Group for US$125 million through Investment Project Financing. Table 1 describes the financing support.

Table 1. Estimated Project Cost and Financing (US$, millions)

Project Components	Project Cost	IBRD Financing	% Financing
1. Strengthening the pilot-to-market innovation ecosystem	**125.0**	**62.5**	**50**
1.1. Shared facilities	50.0	25.0	50
1.2. Scientific research	36.0	18.0	50
1.3. Clinical trial network	12.0	6.0	50
1.4. Training	15.0	7.5	50
1.5. Technology transfer	12.0	6.0	50
2. Accelerating the pilot-to-market process for specific products	**120.0**	**60.0**	**50**
2.1. Vaccines	80.0	40.0	50
2.2. Biosimilars	30.0	15.0	50
2.3. Medical devices (instruments and diagnostics)	10.0	5.0	50
3. Project management and monitoring and evaluation	**5.0**	**2.5**	**50**
Total Project Costs	**250.0**	**125.0**	**50**

D. Lessons Learned and Reflected in the Project Design

31. The project design reflects lessons from ongoing operations, international good practice, and thematic evaluations. It draws on lessons learned from similar World Bank-funded innovation projects in Argentina (Unleashing Productive Innovation Project, P106752, approved in June 2008, and rated Satisfactory both on the development outcome and implementation progress with additional financing currently being processed) and Kazakhstan (Technology Commercialization Project, P090695, which closed in December 2015 with Moderately Satisfactory development outcome and implementation progress and which has a follow-on operation—Kazakhstan: Fostering Productive Innovation Project, P150402—approved in 2014). The project also draws on lessons from a recent Independent Evaluation Group review of World Bank Group support for Innovation and Entrepreneurship as well as an impact evaluation of In-Tech, a program offered by Poland's National Center for Research and Development to support research entities and businesses in carrying out innovative projects in scientific and industrial areas through grant funding. Finally, the design draws on lessons from the experiences of other countries in facilitating innovation in biotechnology and medical devices: on the one hand is Israel with a thriving life sciences innovation sector, and on the other hand is Malaysia with a less successful experience. The following lessons have been considered:

(a) **Public sector funding can make a useful contribution to the development of technology financing and the creation of knowledge-based companies.** The project in Argentina piloted an early stage VC fund, based on other countries' experiences. The goal was to provide a demonstration effect of the commercial viability of early stage funds for technology start-ups, with the expectation of attracting other VC companies. Similarly, this project fills a financing gap in India for companies going from pilot scale to markets and early stage. BIRAC's grant funding is expected to provide a demonstration effect for investors to enter this space, in a field perceived as particularly risky. In fact, in Israel, through the Israel Innovation Authority, the Government initiated a life sciences VC fund (allocating US$40 million) that invests mainly in pharmaceuticals and which catalyzed the formation of other, purely private funds without Government support.

(b) **Government subsidies can also provide an incentive for increased collaboration between science and industry which is essential for innovation in biotechnology.** There are several barriers that inhibit collaboration, including financing constraints, information asymmetries which prevent researchers and firms from interacting, and transaction costs in negotiating collaboration agreements. In Poland, In-Tech funding provided grants mostly to scientific consortia consisting of at least one research unit and at least one enterprise with the intention of taking ideas from the research stage through to commercialization. This resulted in increased likelihood of having a product ready to sell. The proposed project builds on this success story by funding grants to both private enterprises and public research entities to form consortia that will allow the acceleration of product development through increased collaboration.

(c) **The success of early stage funding depends on the availability of 'deal flow', or investment-ready projects**. In Argentina, the World Bank Group helped set up consortia assisting entrepreneurs in all stages of the incubation cycle. Similarly, this project will provide training not only in technical areas but also in managerial and business skills to help start-ups grow. Through the TTOs, the project also aims to increase the rate of translation of research ideas into marketable products that could serve as potential investments. Israel recognized the importance of creating a deal flow: the Government helped create an early stage incubator for pharmaceutical companies managed by a private sector operator and investing in early stage investors. It also created over 10 medical devices incubators. Thus far, around 200 early stage life sciences companies have been supported through Israel's incubator programs, creating a deal flow for the various VC funds in the country.

(d) **Experience and lessons learned point to the importance of competitive financing of science, technology, and innovation programs to enhance their efficiency and promote quality research.** In Argentina, the implementing agency provided grant funding through an open and competitive call for proposals where the centers and institutes would present proposals and would be selected on the basis of predefined criteria included in the Operational Manual. This model will be replicated in India and is a model already practiced by BIRAC in its existing funding schemes. Particular attention will be paid to involving international experts in the grant selection process.

(e) **Science and technology projects are most successful when executed by an 'agency-champion', that is, an agency that has experience, capacity, and high commitment to the project.** In this case, BIRAC is the champion of the project, which it has been designing for some time along with champions from the DBT. Although only five years old, BIRAC has already had significant experience running funding schemes and supporting entrepreneurs and clusters around India. BIRAC has strong institutional capacity backed by a significant number of experienced scientists and practitioners who are on its Board and among its staff.

(f) **International expert advice and support are essential for successful innovation project implementation.** In Kazakhstan, the professional coaching provided to the groups benefiting from project support proved to be critical in promoting a culture of innovation and linking academic researchers and markets. Creating professional expert bodies to apply international best practices at different stages of implementation (including grant selection processes and supervision of the selected groups) proved to be instrumental in achieving the PDO. As such, the proposed project includes a training subcomponent to bring state-of-the-art technical and managerial skills to the professionals leading innovation in the field. Also, the implementation arrangements include a Technical Advisory Group made up of global and Indian academic and industry experts who will provide scientific and technical guidance for the project throughout implementation.

(g) **Private sector participation is key in facilitating innovation with market potential.** In the case of Malaysia, the Government poured millions of dollars to create three Government-owned companies that were supposed to secure Malaysia's place as an advanced country in biotechnology. These efforts have not led to the desired outcome for a number of reasons, namely, a disconnect between acquiring technology and using it to create products. A lack of commercialization vision led to suboptimal use of state-of-the-art technology which is for the most part now obsolete. In contrast, Israel's initiatives have all involved the private sector (either as VC partner, manager of incubators, or even research partner). The Government has funded technology and laboratories as well as provided grants to universities and research centers, always with the objective of translating research into a commercial product. In fact, Israeli government grants require the participation of a business party contributing a percentage of the funding and providing commercial guidance to researchers. The proposed project therefore leverages private sector participation in all aspects of its design (in the selection of products and grantees, in product development, and so on) and ensures collaboration between the public and private sectors as well as within the private sector between MSMEs and larger firms.

(h) **Investing in human capital is as important as investing in equipment, buildings, and technologies.** In Malaysia, the Government realized a little too late that innovation in biotechnology is mainly driven by people, both scientists and administrators, and not by technologies. The Government underinvested in the human capital needed to use the state-of-the-art technology it had purchased. Keeping this in mind, the project allocates funding to develop and deliver training programs to fill key

knowledge and skills gaps in India's biopharmaceutical and medical devices sector today, both technical and managerial.

IV. IMPLEMENTATION

A. Institutional and Implementation Arrangements

32. The project will be implemented by BIRAC, a public sector unit under the DBT, Ministry of Science and Technology, the GoI. It was registered in March 2012 as section 8 'not-for-profit company' under the India Companies Act 2013. The institution functions through a formal Board of Directors headed by a chairman at the rank of Secretary in the GoI and supported by directors with sectoral knowledge from premier academic institutions. BIRAC will serve as the implementing agency as per the Project Agreement to be signed with the World Bank Group. Implementation of the project will be led by a project management unit (PMU) within BIRAC. The PMU will be staffed by a dedicated Project Director (PD) as well as a mix of dedicated and part-time staff, including technical coordinators (one for each subcomponent); procurement, financial management, social, environmental, and monitoring and evaluation specialists; a legal/compliance team; a communications team; a quality control officer; and other administrative staff. In addition, a Steering Committee made up of senior DBT representatives (both civil service and career scientific officers) will provide strategic direction for the project and have final decision authority. A Technical Advisory Group made up of global and Indian academic and industry experts will provide scientific and technical guidance for the project.

33. Most of the funding for the project will be in the form of grants following open, competitive, and transparent calls for proposals. The eligibility and selection criteria, application formats, and other details of the calls for proposals as well as grant disbursement, implementation, and monitoring are detailed in the PIM.

B. Results Monitoring and Evaluation

34. Monitoring and evaluation of project indicators will rely on the data and information provided by grantees as part of their obligations under the Grant Agreement. BIRAC will collect, compile, validate this information, and use it to track progress toward achievement of project outcomes and intermediate results targets. Most of the outcomes are linked to either specific milestones along the product development cycle, such as regulatory approvals, and/or concrete events, such as a shared facility being used. Therefore, validation of the project by BIRAC as well as the World Bank team through implementation support missions is not expected to pose a major challenge. Results monitoring and evaluation will be one of the key responsibilities of the PMU and a primary accountability for the PD.

C. Sustainability

35. World Bank Group financing under this project is a small fraction of funding needs for the overall biotechnology industry in India. The project directly leverages DBT funding 1:1 and leverage is manifold once other private, public, and philanthropic resources that go into product development are considered. Component 1 is designed to remove key bottlenecks in the value chain that have public goods characteristics and/or positive externalities and once removed should lower the risk of future investments and accelerate time to market for biotechnology products. All

the investments in Component 1 will be sustained through revenue from future users of upgraded facilities, new research tools and clinical trial sites, TTOs, and training programs. Market prices will apply except for products developed under Component 2, which will benefit from concessionary rates. The project aims, through Component 2, to serve as a catalyzer that results in increased fund mobilization through, among others, a demonstration effect that helps investors (public and private) better assess the risk of future investments in product development and encourages further private sector participation in the sector.

36. The project will also leverage synergies with other initiatives going forward. Such initiatives include the Coalition for Epidemic Preparedness Innovations (CEPI)[6] which aims to galvanize the development of new vaccines against diseases that can cause devastating epidemics by funding vaccine candidates through late preclinical studies to proof of concept and safety in humans. CEPI-supported vaccine developers could benefit from the investments in the biopharma ecosystem made under the project.

37. Lessons learned during project implementation will be applied by the Ministry of Science and Technology to other sector-specific innovation ecosystems in which the combination of product-driven R&D investments and targeted improvements in the business environment can upgrade existing innovation capabilities. The ministry aims to support industry initiatives with potential "paradigm-shifting influence in the Science and Technology landscape," particularly in knowledge- and capital-intensive industries where the lack of rapid private sector funding, prototyping, and testing capabilities constitutes major constraints to growth. Sectors where public institutions are particularly well-suited to fill gaps in R&D funding and innovation capabilities across the business fabric include, in addition to health care, education, waste management, space exploration, or energy. Similar approaches to public-led development and transfer of technologies and innovations can also be applied to facilitate cross-cutting breakthroughs in enabling and advanced manufacturing, such as robotics, automation, nano-materials, or precision manufacturing.

V. KEY RISKS

A. Overall Risk Rating and Explanation of Key Risks

38. **Political and governance.** The PDO is in line with the GoI's 12th Five-Year Plan focusing on 'R&D outputs leading to public and social goods' such as ensuring access to good quality health care and alleviating the burden of communicable diseases and NCDs. BIRAC has a good track record of successfully supporting grantees in accordance with the three governance principles of transparency, accountability, and participation, which this project will adopt as well and will be outlined in the PIM. The project has robust leadership within BIRAC, strong support from the DBT as well as from the Ministry of Health, the Indian Council for Medical Research, and the broader public health community. The risk in this area is rated Low.

39. **Macroeconomic.** India is expected to average 8 percent annual GDP growth in the upcoming years, the fastest growth rate projection among large economies in the world. According

[6] CEPI is a global partnership to stimulate, finance, and coordinate vaccine development against priority threats, particularly when development is unlikely to occur through market incentives alone. The Secretary of DBT (India) currently chairs the CEPI board.

to the World Bank Group CPS FY13–17, "India's long-term prospects remain bright owing to favorable demographics, rising average educational attainments, and high savings rates." The risk in this area is rated Low.

40. **Sector strategies and policies.** BIRAC's vision is to "stimulate, foster, and enhance the strategic research and innovation capabilities of the Indian biotech industry, particularly start-ups and SME's, for creation of affordable products and addressing the needs of the largest section of society." This vision is in line with the GoI's 12th Five-Year Plan and the country's overall priorities. Targeted products to be developed under the project have been identified as addressing public health priorities, as defined by the GoI. India has established a clear regulatory pathway for most products falling under this project, in line with international practice, and is working toward regulating all product types. Any risks related to clinical trials will be mitigated through project funding for a GCP-compliant CTN as well as a Clinical Research Validation and Management Framework (CRVMF) to ensure product development follows best practice. The risk in this area is rated Moderate.

41. **Technical design of project or program.** R&D in general and collaborative R&D in particular, given the long product development lifecycles in this sector, is inherently risky. Not all products supported through the project will reach advanced stages by project-end. However, the project aims to maximize chances of success by focusing on products in more advanced stages of the development life cycle, that is, beyond proof of concept, acknowledging that only a handful of products may be ready for commercialization by project-end. In the case of biosimilars, the development process is much less risky and lengthy than for patented products. Selected products address diseases already identified by the GoI as public health priorities and in some cases (including for all vaccines) will enter the public health system. Finally, while the project supports, in part, the development of specific products, it also supports (through more than 50 percent of the financing) strengthening of the overall ecosystem. Interventions to set up shared facilities, training programs, and TTOs, among others, will support a much wider pipeline of products and will be sustained beyond the end of the project. The risk in this area is rated Substantial.

42. **Institutional capacity for implementation and sustainability.** BIRAC has a good track record of accomplishments, even in the short span of its five-year existence, of successfully completing many donor-funded projects and programs and of managing collaborations. However, it is the first time that BIRAC is implementing a World Bank Group-funded project. To mitigate related risks, the PMU will include, among others, a procurement specialist, a financial management specialist, a monitoring and evaluation specialist, and, as needed, safeguards specialists. The World Bank Group will support the necessary capacity building within the PMU and has already provided procurement-related training. BIRAC has already put together a PIM, based on its experience drafting scheme documents for similar projects, which will facilitate swift implementation once the project is effective. The risk in this area is rated Moderate.

43. **Fiduciary.** The initial procurement risk rating for the project is Substantial and the residual risk after taking proposed mitigation measures is Moderate, given that the level of procurement activity in the project is limited to US$4 million out of a total of US$250 million and that BIRAC, while lacking World Bank procurement experience, has significant experience with consultancy contracts. The financial management risk for the project is assessed as Moderate. BIRAC is a professional institution with sound information/accounting systems and technical capacity to

account for and report on project expenditures. The monitoring and audit mechanisms are robust and would provide fiduciary assurance on the use of project funds. The overall fiduciary risk is Moderate.

44. **Environment and social.** The project does not trigger any social safeguards and is classified as Category B under OP 4.01 (Environmental Assessment). The potential grantees are high-end scientific research institutions with substantial experience on environmental management. The risk in this area is rated Low.

45. **Stakeholders.** The project objective to provide equitable and increased access to affordable vaccines, and life-saving drugs and accelerate local innovation in this sector is consistent with the interests of the GoI, public health priorities, civil society, the private sector, the donor community, and the public in general. Currently investors, including donors, have a well-coordinated effort to address mitigation strategies for life-threatening diseases, and the project investment will be gaining buy-in from these stakeholders. The state administration and the central administration have a strong focus on the prevention of communicable diseases and NCDs for all, and the project will gain from the central- and state-level support. The stakeholder opposition to essential vaccines (vaccine hesitancy) is low in India for infectious diseases and, therefore, public health institutions and civil society engagement in outreach and delivery to the last mile will be forthcoming. Preparation of the project included substantial consultation with stakeholders. The risk in this area is rated Low.

46. The overall risk is rated Substantial.

VI. APPRAISAL SUMMARY

A. Economic and Financial

47. An Economic and Financial Analysis indicates that the development impact benefits of the project are expected to exceed project costs. While product development success is difficult to predict, the potential impact of the project is assessed using the example of accelerating development of two products identified as priorities under the program—the pneumococcal conjugate vaccine (PCV) and HPV vaccine—by one year. The resulting economic benefits are primarily due to the expected health gains (disease prevented) from providing solutions to affected populations that did not previously have access to them. Benefits from accelerating development of the PCV vaccine alone are estimated at US$6 billion in the first year of introduction even assuming a rather conservative 15 percent coverage rate. The HPV vaccine would yield economic benefits estimated at US$586 million in a year. Additional cost savings would be realized by substituting new, affordable solutions to existing, more expensive ones; for example, cost savings for the segment of the population that is using the existing PCV vaccine would amount to approximately US$63 million in one year.

48. Other benefits are not quantified but include (a) providing solutions that are tailored to local needs, thereby increasing their efficacy relative to existing products, and (b) economic benefits to other LMICs, beyond India, that are suffering from a similar significant and unaddressed burden of disease.

49. Finally, investments to fill critical gaps in infrastructure, human capital, and technology transfer identified as key gaps in the pilot-to-market ecosystem for biopharmaceuticals and medical technology products will (a) facilitate the development of a pipeline of products beyond the ones selected for investment under Component 2, (b) foster MSME growth and competitiveness of the local biopharmaceutical and medical technology industry, and (c) enhance India's outsourcing industry to realize its potential of becoming a US$455 million market by 2020.[7]

50. Public sector financing to achieve these benefits is justified, and the World Bank Group involvement offers significant value to the proposed project activities. Project activities address market failures in the pilot-to-market ecosystem for biopharmaceutical and medical technology products that are associated with underinvestment in the sector, including (a) low perceived private returns (due to inadequate purchasing power of affected populations) and excessive risks associated with R&D (time, attrition rates, costs) that make markets provide less financing for developing medicines for patient populations in LMICs and (b) gaps in infrastructure, human capital, and technology transfer and coordination failures associated with scale-up of innovative solutions.

B. Technical

51. The program design was informed by a detailed landscape analysis commissioned by BIRAC to a highly specialized organization and guided by an Expert Advisory Group. The analysis included an overview of the current biopharmaceutical scenario in terms of critical drivers and available technical and operational resources to understand India's strengths and current challenges for growth in this sector.

52. The assessment of the drivers of growth in the biopharmaceutical industry included the following:

(a) The global and Indian biopharmaceutical market, including the current trends in the biosimilars and prospects of the outsourcing market. A comparison of the Indian and global biopharmaceutical market size and annual growth rates of different product categories was conducted, based on which India's strengths and potential opportunities to grow in the field were analyzed.

(b) India's burden of communicable diseases and NCDs and the preventive and therapeutic biopharmaceuticals currently available for these diseases were examined to gain an insight into specific public health needs in India.

(c) An understanding of the product development portfolio of the country was gained by analyzing the products already in the market as well as those being developed by major industries, academia, and MSMEs.

53. The landscaping analysis provided an overview of the resources present in the country across the biopharmaceutical value chain, including discovery, validation, and early bio-

[7] "Outlook of India Biopharmaceutical Outsourcing Market", by JZMed Inc., July 2013.

manufacturing. These resources were covered under two subcategories—technical and operational resources:

(a) Technical resources included the talent, infrastructure, technologies, and patents and publications. The analysis looked at talent available by focus area both in academic institutions and the private sector. Analysis of talent covered talent distribution based on skills and focus area across industry and academia and critical talent with national fellowships present in the country. Analysis of infrastructure and technologies helped in identifying relevant players with current capacity for biopharmaceutical development and also in gaining an understanding of the technologies being developed in the country. An assessment of patents and publications was conducted, based on which strengths and gaps in biopharmaceutical development across the biopharmaceutical value chain were identified.

(b) Operational resources included the funding landscape across public, private, and philanthropic ventures; global and national collaboration modes and analysis of their success factors; analysis of product development partnerships; and current training modules in India relevant to skills required for biopharmaceutical development.

54. Critical analysis, along with advisory group recommendations, led to focusing on the pilot to market segment of the value chain and allowed short-listing of the specific disease areas and types of products to be supported by Component 2 and the types of activities to be supported by Component 1. The design of the project plays to BIRAC's strengths as a highly technical grant-making organization and facilitator of government-industry-academia collaboration.

55. **CRVMF.** The processes of validation and clinical development, especially clinical trials, are likely to have social issues and impacts that are not covered by the World Bank Group's social safeguards. These issues include, among others, the process of obtaining informed consent of those participating in clinical trials, potential loss of income, adequate compensation, risk of disability, and adequate follow-up health care. To ensure these issues are managed adequately by the project, a CRVMF has been developed by BIRAC. The framework aims to ensure that both clinical trials conducted with funding from Component 2 grants as well as the CTN funded under Component 1 follow adequate clinical and ethical standards and that the oversight mechanisms are in place to monitor that entities receiving funding actually comply with these standards. The GoI's Central Drugs Standard Control Organization, among other regulatory agencies, has a robust regulatory framework for product development (including for clinical trials), in accordance with international regulatory regimes and practices. Furthermore, BIRAC has a track record of successful oversight of clinical research and compliance with national regulations. Nevertheless, as part of appraisal, the World Bank Group engaged one of the world's leading bioethical experts to independently review the CRVMF and suggest areas for strengthening to bring it in line with international best practices. The project will represent an opportunity for India to not only ensure compliance but actually push the frontiers of clinical and ethical standards in biotechnology research. For example, one of the activities proposed under the CTN is to develop a framework to ensure GPP in pluripotent (multidisease) clinical trial sites. Thus far the only GPP guidelines available are for sites focused specifically on HIV/AIDS and tuberculosis. As the main implementing agency for the project, BIRAC will develop a suitable framework for clinical studies compliance by the grantees, which will be a precondition for dispensing the grants and create an oversight mechanism

that monitors grantees' compliance. BIRAC will retain competent experts to monitor clinical studies and compliance to the CRVMF.

C. Financial Management

56. **Budget and fund flow.** BIRAC, immediately after the Cabinet Committee on Economic Affairs approval (scheduled in March 2017), will open an identifiable budget head in the 'Demand for Grants' of FY16–17 within the DBT (Demand no. 79) and budget provision will be made to implement project activities of FY17–18. The yearly budget provision/estimate under this budget head from the subsequent year will be made by the DBT in the month of March (before the beginning of each GoI fiscal year) based on approved annual work plans and procurement plans submitted by BIRAC. The budget utilization will be monitored by the DBT and any additional demand for budget during the fiscal year will be met through a revised estimate in the month of December. BIRAC will obtain administrative sanction from the DBT to draw funds from the budget into its bank account. The payments will be made by BIRAC for the following key activities: (a) disbursement of grants to grantees under Components 1 and 2 according to the terms and conditions stipulated in the Grant Agreement and (b) consultancy and project management expenses under Component 3. The grantees will be selected through a competitive process and Grant Agreements will be signed between BIRAC and the grantees to govern the use of funds. The grantees will open a separate bank account for the receipt of grant funds and will maintain books of accounts to account for expenses incurred out of such funds. At the end of each financial year, the grantees will provide audited utilization certificates to BIRAC. The technical team of BIRAC will visit the grantees to monitor the use of funds. Additionally, the Financial Due Diligence (auditors) empaneled with BIRAC will review the books of accounts maintained by grantees and submit a report to BIRAC management. The PIM will document the operating procedures on use, accounting, and monitoring of grant funds.

57. **Accounting and financial reporting.** BIRAC maintains books of accounts in a computerized environment. It has an accounting manual to guide staff on internal control principles. It has been agreed that a separate ledger account in the accounting system will be opened for the project and a chart of accounts will be configured to classify expenditures based on project components/major activities. Interim financial reports (IFRs) on use of funds will be submitted to the World Bank through the office of the Controller of Aid Accounts and Audit, GoI, within 45 days from the end of each half year. The IFR will form the basis of disbursement to the GoI. The expenditure statements/ledger accounts generated from the accounting system will be used for the preparation of the IFRs. The amounts released as grants under Components 1 and 2 will trigger reimbursements from the World Bank, and the agreed underlying expenditures as stated in the PIM will be construed as eligible expenditures. For Component 3, the amounts paid by BIRAC for consultancy and project management costs will be construed as eligible expenditures.

58. **Staffing.** BIRAC has agreed to depute one existing accounts officer to provide overall financial management oversight for the project. Accountants will be additionally recruited from the market to provide support on financial management functions. Adequate provision for staff costs has been made in the project budget. The finance staff will be provided requisite training on World Bank Group financial management and disbursement procedures.

59. **Audit.** The statutory audit of BIRAC as per the India Companies Act is presently conducted by an external audit firm appointed by the Comptroller and Auditor General of India (CAG). A supplementary audit is further conducted by CAG after the audit is completed by the external audit firm. The audit report, entity financial statements, and forming schedules are exhaustive and provide program-wise financial information on use of funds by BIRAC. The entity audit report is issued within six months from the end of the fiscal year. To obtain fiduciary assurance for this project, it has been agreed with BIRAC that entity audit will also cover project transactions and project financial statements will form part of the entity audit report. The audit of the project will be conducted according to terms of reference agreed with the World Bank Group. The entity audit report and entity financial statements will be shared with the World Bank Group within nine months from the end of each fiscal year.

D. Procurement

60. Project funding will be mostly through competitive grants to private and autonomous public entities. Therefore, procurement will, for the most part, follow commercial best practices, consistent with the World Bank Group's procurement core principles. If the grantees are public sector undertakings, then a one-by-one determination will be made as to the procurement guidelines to be followed depending on the legal status of the institution and in accordance with the World Bank Group procurement regulations, effective since July 1, 2016. The project will be subject to the World Bank Group's Anti-corruption Guidelines, dated October 15, 2006, and revised in January 2011 and July 1, 2016. Direct procurement by BIRAC will be limited to a small number of consulting firms, individual consultants, and non-consulting services. This direct procurement will be governed by the Procurement Regulations, effective from July 1, 2016. Most, if not all, of the procurement of goods and services will be carried out by the grantees.

61. **Procurement risk assessment and mitigation.** Direct procurement by BIRAC will be carried out by the Administration Department under the guidance of the legal counsel. The procurement capacity assessment carried out by the World Bank Group during appraisal concluded that the staff in BIRAC has no prior experience in World Bank Group procurement and, therefore, the PMU will be staffed with an experienced full-time procurement officer. In addition, the World Bank Group has provided training and support to other BIRAC officials who will be involved in project procurement. BIRAC officials are planning to undergo training on the World Bank Group's new Procurement Framework in June 2017. BIRAC has prepared a Procurement Manual, which has been in use since March 2016. It includes all procurement processes, decision making, and safe upkeep and management of records.

62. **Project Procurement Strategy for Development (PPSD).** According to the requirement of the World Bank Group Procurement Guidelines, BIRAC has prepared a PPSD to inform the Procurement Plan. BIRAC has prepared a draft Procurement Plan which provides the basis for procurement methods and review by the World Bank. This Procurement Plan will be disclosed through BIRAC's and the World Bank's external websites. The first Procurement Plan includes all procurement to be taken up during the first 18 months of project implementation and will have to be submitted to the World Bank Group through the Systematic Tracking of Exchanges in Procurement. It will be updated at least annually or as required to reflect the actual project implementation needs and improvements in institutional capacity. The World Bank Group will review the procurement done by BIRAC and those public sector grantees to whom the World Bank

Group procurement guidelines are applicable. Besides confirming that the mitigation measures referred earlier are appropriate, the PPSD concluded that the operational context is considered to be quite good due to the good governing system, sophisticated market, and availability of technical competence as well as research facilities within the country and the strong technical and economic capacity of BIRAC. Furthermore, the procurement trends for BIRAC in selection of grantees in the past have been quite good due to availability of sufficient numbers of competent institutions in the private as well as the public sector. BIRAC has so far supported the implementation of 360 projects, supporting 230 companies and fostering 89 collaborations between industry and academia.

E. Social (including Safeguards)

63. The project activities will be located in public and private research institutions located in urban areas across India. Bioclusters, where many of the grantees are likely to be located, include the National Capital Region, Pune, Bengaluru, Hyderabad, and Chennai and the exact locations in such urban areas will be known at the time of grantee selection. These will be existing centers where project-supported product development or pilot research will be carried out. These centers are sanitized and protected with restricted and authorized entry. In view of this, the project does not include any socially sensitive locations or areas/development blocks where Scheduled Tribes/Indigenous People live. The project components will not involve major civil works/construction activities but could involve renovation of existing buildings and/or establishing support infrastructure for carrying product development, pilot research, and clinical trials within existing buildings and complexes that will not require any land acquisition. This means, the project will not require acquisition of any private land under the provisions of Right to Fair Compensation and Transparency in Land Acquisition, Rehabilitation and Resettlement Act, or Government land under any tenure systems, including forestland on which the Scheduled Tribes depend to meet their social, economic, and cultural needs in Scheduled Areas. In view of this, the World Bank Group's social safeguards policies on Involuntary Resettlement and Indigenous Peoples are not triggered in this project.

64. **Gender.** The project will address some important gender disparities in India that are described below:

(a) One of the main gender gaps in India is that girls face a much higher risk than boys of dying before the age of five. Most of the leading causes of death in children under five were between 12 percent and 72 percent higher in girls than in boys and all-cause mortality rate was about 36 percent higher, with pneumonia and diarrheal diseases accounting for about two-thirds of the excess deaths. Therefore, the addition of vaccines against pneumonia—such as PCV, which will be supported under Component 2—to outreach home-based immunization programs would reduce child deaths and contribute to narrowing the gender gap in child mortality in India.[8]

(b) Cervical cancer is the most common type of cancer causing death among women in developing countries. Mortality due to cervical cancer is also an indicator of health

[8] The Million Death Study Collaborators. 2010. "Causes of Neonatal and Child Mortality in India: A Nationally Representative Mortality Survey." *Lancet* 376 (9755): 1853–1860. http://www.sciencedirect.com/science/article/pii/S0140673610614614.

inequities as 86 percent of all deaths due to cervical cancer are in LMICs. Every year in India, 122,844 women are diagnosed with cervical cancer and 67,477 die from the disease. India has a population of 432.2 million women, ages 15 years and older, who are at risk of developing cervical cancer.[9] A primary approach to preventing cervical cancer is to vaccinate girls against several strains of HPV that are known to increase the chances of getting cervical cancer. Under Component 2, the project will support the development of a low-cost HPV vaccine.

(c) There is a slight gender gap in the burden of NCDs in India—51 percent of years lost to disability due to NCDs are from women.[10] The biosimilars to be supported by Component 2 as well as others that will benefit from investments in Component 1 are targeted toward NCDs and therefore will potentially contribute to closing this gap.

(d) Although women are better represented in biotechnology than in other industries in India, in part due to gender-targeted interventions such as a DBT-supported women biotechnology park in Chennai, in 2016–2017, only about 30 percent of the beneficiaries of DBT schemes were women. The project will contribute to closing this gap by ensuring at least 50 percent of the beneficiaries of Subcomponent 1.4 are women.

65. **Citizen engagement and beneficiary feedback/grievance mechanism.** The project benefits from a two-tier citizen engagement mechanism. The first tier is at the level of BIRAC which has already undertaken stakeholder consultations to facilitate beneficiary feedback in the process of selecting activities and products financed by the project. In addition to these, a second tier will be at the level of the CTN funded through the project. As part of the CRVMF, a mechanism for collecting grievances related to clinical trials will be set up, and the project will closely monitor responsiveness to and resolution of these grievances through the indicator included in the Results Framework.

F. Environment (including Safeguards)

66. The project activities essentially support medical research through innovations in biotechnology. Anticipated environmental safeguard issues for these activities, hence, are management of liquid/solid waste (including hazardous waste) generated from the research activities, occupational health and safety issues in handling various research substances, and overall laboratory safety aspects. These issues are limited to the specific products such as vaccines, biopharmaceuticals, diagnostics, and medical devices that are directly supported by the project. In case of shared infrastructure facilities and the CTN (Component 1) for validation and reference, the issues will be broad based depending on the support they provide such as biological products (vaccines and biosimilars), medical devices (instruments and diagnostics), and CMC.

[9] Sreedevi, Aswathy, Reshma Javed, and Avani Dinesh. 2015. "Epidemiology of Cervical Cancer with Special Focus on India." *International Journal of Women's Health* 7: 405-14.
[10] WHO (World Health Organization). 2016. *Global Health Estimates 2015: Disease burden by Cause, Age, Sex, by Country and by Region, 2000–2015*. Geneva: WHO.
www.who.int/healthinfo/global_burden_disease/estimates/en/index2.html.

67. To address these environmental safeguard issues, the project has developed an Environmental Management Framework (EMF), which outlines environmental due diligence requirements for the activities to be financed by the project for the development of various products and shared facilities. The framework was prepared based on a review of environmental management practices in biotechnology research, visits to some of the research centers, and consultations with stakeholders.[11] In addition to complying with the safeguard policies of the World Bank Group, the due diligence envisages compliance with various regulatory requirements of the GoI (on biomedical waste management, hazardous waste management, Water Act, and so on) and also GCP and Good Laboratory Practices. As the main implementing agency for the project, BIRAC will carry out the environmental due diligence before the approval of grants and regular monitoring during implementation. An environmental safeguards officer will be designated for this purpose, who, in addition to carrying out the due diligence, will carry out annual visits to the project beneficiaries to assess the status for safeguards compliance.

68. Further, appropriate modules on environmental management will be included in the training programs of the project, with an objective to build capacity of the stakeholders in integrating environmental management aspects in biotechnology research.

69. Finally, no climate impacts are foreseen under this project.

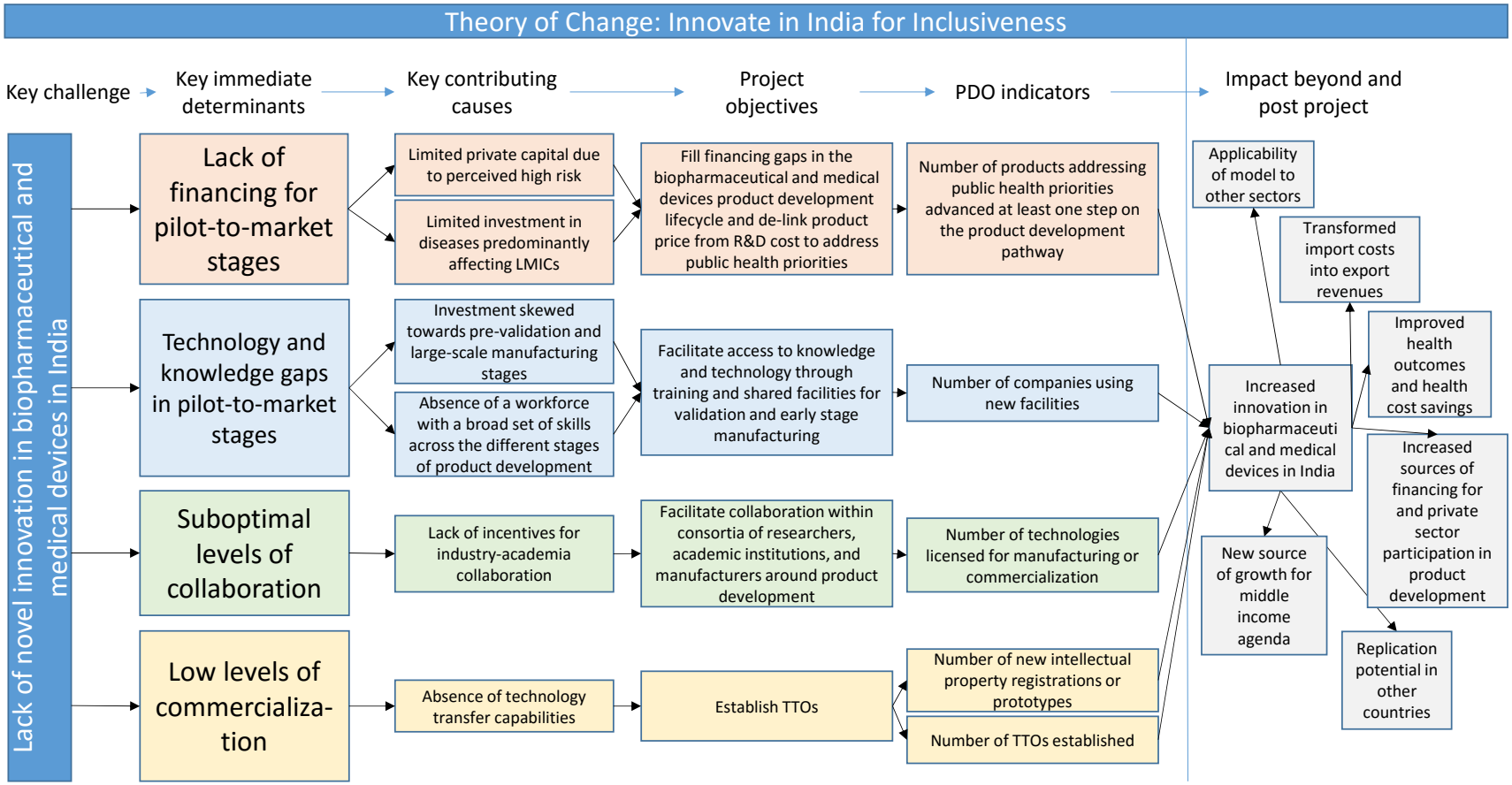
G. World Bank Grievance Redress

70. Communities and individuals who believe that they are adversely affected by a World Bank (WB) supported project may submit complaints to existing project-level grievance redress mechanisms or the WB's Grievance Redress Service (GRS). The GRS ensures that complaints received are promptly reviewed in order to address project-related concerns. Project affected communities and individuals may submit their complaint to the WB's independent Inspection Panel which determines whether harm occurred, or could occur, as a result of WB non-compliance with its policies and procedures. Complaints may be submitted at any time after concerns have been brought directly to the World Bank's attention, and Bank Management has been given an opportunity to respond. For information on how to submit complaints to the World Bank's corporate Grievance Redress Service (GRS), please visit http://www.worldbank.org/GRS. For information on how to submit complaints to the World Bank Inspection Panel, please visit www.inspectionpanel.org.

[11] EMF was disclosed both in-country and on the World Bank website on March 9, 2017. It was redisclosed on April 13, 2017 with updates on institutional arrangements and stakeholder consultations sections.

VII. RESULTS FRAMEWORK

Figure 2: Project Theory of Change



Project Development Objectives								
PDO Statement								
The proposed PDO is to facilitate innovation in biopharmaceutical products and medical devices that address public health priorities in India.								
These results are at	Project Level							
Project Development Objective Indicators								
		Cumulative Target Values						
Indicator Name	Baseline	YR1	YR2	YR3	YR4	YR5	YR6	End Target
Number of products addressing public health priorities advanced at least one step on the product development pathway [a] (Number)	0.00	0.00	0.00	0.00	0.00	0.00	6.00	6.00
Number of new IP registrations or product prototypes (Number)	0.00	0.00	5.00	8.00	11.00	13.00	15.00	15.00
Number of technologies licensed for manufacturing or commercialization (Number)	0.00	0.00	0.00	0.00	0.00	0.00	2.00	2.00
Number of TTOs established (Number)	0.00	0.00	0.00	1.00	3.00	5.00	6.00	6.00
Number of companies using shared facilities supported by the project (Number)	0.00	0.00	20.00	30.00	40.00	50.00	60.00	60.00
Intermediate Results Indicators								
		Cumulative Target Values						
Indicator Name	Baseline	YR1	YR2	YR3	YR4	YR5	YR6	End Target
Number of product development agreements in place (Number)	0.00	4.00	9.00	9.00	9.00	9.00	9.00	9.00
Number of clinical trial sites that are GCP compliant (Number)	0.00	0.00	1.00	3.00	4.00	5.00	5.00	5.00
Proportion of grievances responded to and/or resolved within the stipulated service standards for response times (Percentage)	0.00	0.00	90.00	90.00	90.00	90.00	90.00	90.00
Number of international publications (Number)	0.00	0.00	1.00	3.00	6.00	8.00	10.00	10.00
Number of people trained (Number)	0.00	0.00	165.00	455.00	895.00	1,335.00	1,775.00	1,775.00
Number of people trained who are women (Percentage - Subtype: Supplemental)	0.00	0.00	50.00	50.00	50.00	50.00	50.00	50.00

Number of registered technology transfer professionals qualified (Number)	0.00	0.00	0.00	2.00	6.00	10.00	12.00	12.00

Note: a. Refer to Figure 1 for a representation of steps in product development.

Indicator Description

Project Development Objective Indicators				
Indicator Name	Description (indicator definition)	Frequency	Data Source / Methodology	Responsibility for Data Collection
Number of products addressing public health priorities advanced at least one step on the product development pathway	This refers to the products supported through the product development grants under Component 2. Advanced at least one step on the product development pathway means that the product would have advanced towards 'Regulatory Approval and Market Launch' as per the steps described in Figure 1. The end target assumes two out of three vaccines, one out of two biosimilars, and two out of four devices/diagnostics are advanced.	Biannually	BIRAC	PMU
Number of new IP registrations or product prototypes	Number of new IP registrations as well as prototypes developed with support from the project as reported by grantees and verified by BIRAC in the case of prototypes not yet registered. This assumes two prototypes for each candidate vaccine and two for each biosimilar. It also assumes five to six patents covering the product, methods, and delivery forms for vaccines and biosimilars and covering the design for devices/diagnostics.	Biannually	BIRAC	PMU
Number of technologies licensed for manufacturing or commercialization	New technologies will be developed as an outcome of investments under Component 1 as well as by-products of the specific product development supported by Component 2. This will also include technologies licensed as a result of the work of Technology Transfer Offices (see paragraph 22). Assuming technology transfer for one vaccine and for one device/diagnostic	Biannually	BIRAC	PMU

	(those that will be licensed from the public sector to the private sector).			
Number of TTOs established	This refers to the results of the TTO subcomponent as described in paragraph 22. Assuming one TTO per cluster (six clusters in India).	Biannually	BIRAC	PMU
Number of companies using shared facilities supported by the project	This measures the results of the shared facilities subcomponent as described in paragraphs 16–18. Assuming 11 companies are working on vaccines, 20–30 on biosimilars, and about 30 on devices/diagnostics.	Biannually	BIRAC	PMU
Intermediate Results Indicators				
Indicator Name	Description (indicator definition)	Frequency	Data Source/Methodology	Responsibility for Data Collection
Number of product development agreements in place	This measures outputs of Component 2 as described in paragraphs 23–28. Based on nine products in total targeted by BIRAC.	Biannually	BIRAC	PMU
Number of clinical trial sites that are GCP compliant	This measures intermediate outcomes of Clinical Trials Network subcomponent as described in paragraph 20. BIRAC is targeting five sites to bring under the CTN.	Biannually	BIRAC	PMU
Proportion of grievances responded to and/or resolved within the stipulated service standards for response times	Refers to grievance redress mechanisms in the context of clinical trials and the CRVMF.	Biannually	BIRAC	PMU
Number of international publications	This measures publications as outputs of Components 1 and 2. The target assumes each product will eventually result in at least one publication, more likely for vaccines and biosimilars (relating to their safety assessment, validation model, and so on), but not excluding the possibility of publications for devices/diagnostics, as there may always be design innovations, delivery systems for Point of Application uniqueness, and so on.	Biannually	BIRAC	PMU
Number of people trained	This measures the number of people trained as a result of activities financed under the subcomponents related to training as well as TTOs. Training will focus on four areas:	Biannually	BIRAC	PMU

	1. Discovery and early development: Two professionals from 10 key institutions engaged in product development and Med-tech innovation will be covered, with 20 cohorts undergoing the intensive exposure over the first two years. 2. Clinical development: Three cohorts from 10 institutions will be covered from all entities engaged in the clinical validation pathway that would result in 30 trainers with globally benchmarked competency and having ability to train others over the next three years. 3. GMP manufacturing: Ten companies will be gaining exposure to the skills in this arena with 30 persons exposed to pilot and large-scale GMP compliance and management. 4. Technology transfer: Training imparted to institutions in overall national TTO system. Forty individuals will be trained per year.			
Number of people trained who are women	The subindicator tracks the proportion of people trained who are women.	Biannually	PMU	BIRAC
Number of registered technology transfer professionals qualified	This is an output of the TTO subcomponent as described in paragraph 22. Assumes two RTTPs for each TTO.	Biannually	BIRAC	PMU