Data Collection Survey on Promoting Research and Development and Local Manufacturing Bases of Vaccines and Pharmaceuticals for Emerging/Reemerging Infectious Diseases

Final Report

February 2024

Japan International Cooperation Agency (JICA)

Deloitte Touche Tohmatsu LLC

HM
JR
24-031

Exchange Rate

1 U.S. Dollar (USD) = 147.488 yen

1 Indian Rupee (INR) = 1.774370 yen

1 Vietnamese Dong (VND) = 0.006040 yen

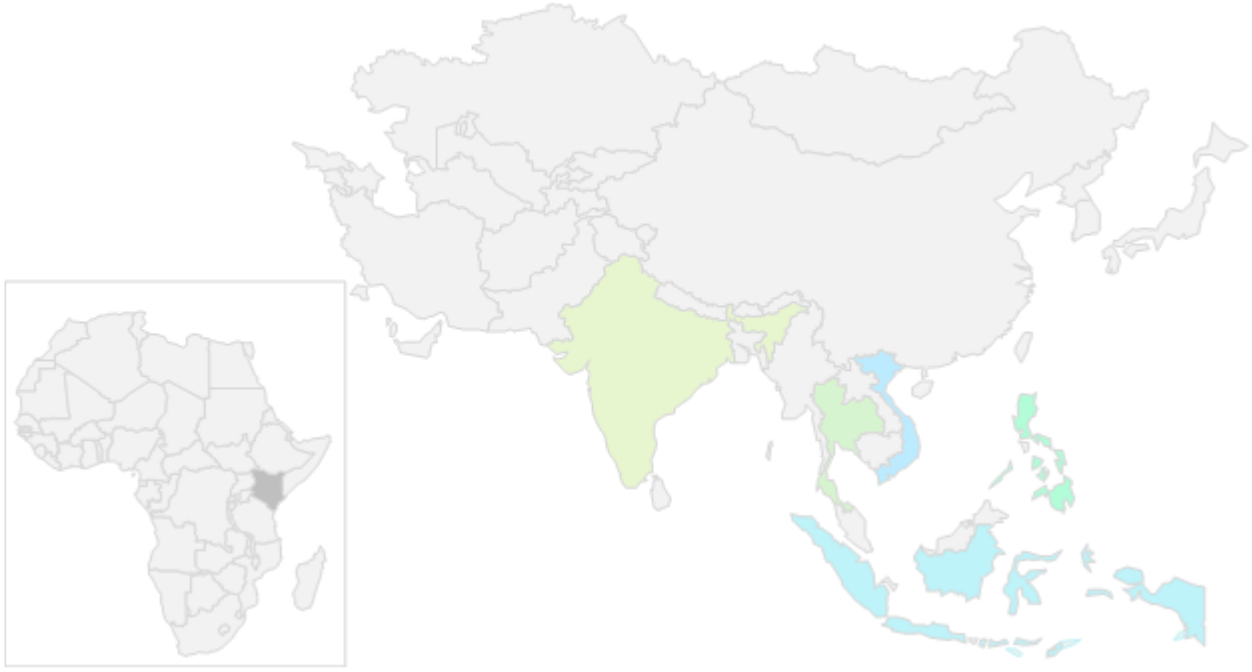
1 Thai Baht (THB) = 4.171570 yen

1 Philippine Peso (PHP) = 2.617810 yen

1 Indonesian Rupiah (IDR) = 0.009340 yen

1 Kenyan Shilling (KES) = 0.917770 yen

(JICA Rate as of February 2024)



Target Countries

(India, Vietnam, Thailand, Philippines, Indonesia, Kenya)

Abbreviations

Abbreviations	Meaning
ACTD	ASEAN Common Technical Dossier
ACTR	ASEAN Common Technical Requirement
ADB	Asian Development Bank
ADMA	Ayurvedic Drug Manufacturers Association
AFD	Agence Française de Développement
AIIMS	All India Institute of Medical Sciences
AMR	Antimicrobial Resistance
AMSPARE	Advanced Metagenomics, Sensors and Photocatalysis for Antimicrobial Resistance Elimination
APAC	Asia Partnership Conference of Pharmaceutical Associations
API	Active Pharmaceutical Ingredient
APVAX	Asia Pacific Vaccine Access Facility
ARDS	Acute Respiratory Distress Syndrome
ASEAN	Association of South-East Asian Nations
ASEAN-NDI	ASEAN Network for Drugs, Diagnostics, Vaccines and Traditional Medicines Innovation
ASTT	Administration of Science, Technology, and Training
AVSSR	ASEAN Vaccine Security and Self-Reliance
BCG	Bacillus Calmette–Guérin
BDMAI	Bulk Drug Manufacturers Association India
BE	Bioequivalence
BJGMC	Byramjee-Jeejeebhoy Government Medical College
BMZ	Federal Ministry for Economic Cooperation and Development (Bundesministerium für wirtschaftliche Zusammenarbeit und Entwicklung)
BPOM	National Agency of Food and Drug Control (Badan Pengawas Obat & Makanan)
B&MGF	Bill & Melinda Gates Foundation
CAGR	Compound Annual Growth Rate
CDC	Centers for Disease Control and Prevention
CDSCO	Central Drugs Standard Control Organization
Chula4DR	Chulalongkorn Drug Discovery and Drug Development Research Center
CIDI	Center for Infectious Diseases in India
CLA	Central Licensing Authority
CMC	Chemistry and Manufacturing Control
CMC	Christian Medical College
CMO	Contract Manufacturing Organization
COMESA	Common Market for Eastern and Southern Africa
COVID-19	Coronavirus Disease 2019
CPP	Certificate of Pharmaceutical Product
CPSU	Central Public Sector Undertaking
CRO	Contract Research Organization
CT	Clinical Trial
CTMS	Clinical Trials Management Systems
CTU	Clinical Trials Unit
c-TRIUMPh	Cohort for Tuberculosis Research by the Indo-US Medical Partnership
DAV	Drug Administration of Vietnam
DBT	Department of Biotechnology
DCGI	Drug Controller General India
DENV	Dengue virus
DOST	Department of Science and Technology
DST	Department of Science and Technology
EC	European Commission
EC	Ethics Committee

ECCT	Expert Committee on Clinical Trials
EECBR	Ethical Evaluation Committee in Biomedical Research
EIMB	Eijkman Institute for Molecular Biology
EOCRU	Eijkman-Oxford Clinical Research Unit
ERB	Ethical Review Board
ERC	European Research Council
EU	European Union
EUL	Emergency Use Listing Procedure
FDA	Food and Drug Administration
FDI	Foreign Direct Investment
FIF	Fondazione Italiana FEGATO
FMUI	Faculty of Medicine University of Indonesia
FOPE	Foundation of Pharma Entrepreneurs
GCLP	Good Clinical Laboratory Practice
GCP	Good Clinical Practice
GDP	Good Distribution Practice
GIZ	German Agency for International Cooperation
GKII	Gupta-Klinsky India Institute
GMP	Good Manufacturing Practice
HHS	U.S. Department of Health and Human Services
HIV	Human Immunodeficiency Virus
IATF-EID	Inter-Agency Task Force for the Management of Emerging Infectious Diseases
ICH-GCP	International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use-Good Clinical Practice
ICMR	India Council of Medical Research
ICRC	International Collaborative Research Center
ICRI	Institute of Clinical Research India
IDMA	Indian Drug Manufacturers' Association
IISER	Indian Institutes of Science Education and Research
IIT	Indian Institutes of Technology
INA-RESPOND	Indonesia Research Partnership on Infectious Disease
IOCRL	Universities of Indonesia and Oxford Clinical Research Laboratory
IPA	Indian Pharmaceutical Association
IPC	Indian Pharmacopoeia Commission
IRB	Institutional Review Board
ISCR	Indian Society for Clinical Research
JHU	Johns Hopkins University
JIPMER	Jawaharlal Institute of Postgraduate Medical Education & Research
KAVI	Kenya AIDS Vaccine Initiative
KEM	King Edward Memorial Hospital
KEMRI	Kenya Medical Research Institute
KfW	KreditanstaltfürWiederaufbau
KUTRRH	Kenyatta University Teaching, Referral & Research Hospital
KWTRP	KEMRI-Wellcome Trust Research Program
LSHTM	London School of Hygiene & Tropical Medicine
LTO	License to Operate
MEAE	France Ministry of Europe and Foreign Affairs (Ministère de l'Europe et des Affaires Etrangères)
MESRI	The Ministry of Higher Education, Research and Innovation (Ministère de l'Enseignement supérieur, de la Recherche et de l'Innovation)
MHRP	U.S. Military HIV Research Program
MoPH	Ministry of Public Health
MoHFW	Ministry of Health and Family Welfare

MORU	Mahidol Oxford Tropical Medicine Research Unit
MoU	Memorandum of Understanding
MRC	Medical Research Council
mRNA	Messenger Ribonucleic Acid
NDP	National Drug Policy
NDSDC	National Drug System Development Committee
NEPI	National Expanded Program on Immunization
NIAID	National Institute of Allergy and Infectious Diseases
NIH	National Institutes of Health
NIHRD	National Research Institute of Department of Health
NIRT	National Institute for Research in Tuberculosis
NRF	National Research Fund
NSF	National Science Foundation
ODA	Official Development Assistance
OPPI	Organisation of Pharmaceutical Producers of India
OUCRU	Oxford University Clinical Research Unit
PAT	Pharmaceutical Association of Thailand
PCHRD	Philippine Council for Health Research and Development
PD	Pharamcodynamics
PFDA	Food and Drug Administration Philippines
PHREB	Philippines Health Research Ethics Board
PIC/S	Pharmaceutical Inspection Convention and Pharmaceutical Inspection Co-operation Scheme
PK	Pharmcokinetics
PLI	Production Linked Incentive
PMDA	Pharmaceuticals and Medical Devices Agency
PPB	Pharmacy and Poisons Board
RBD	Receptor Binding Domain
RNA	Ribonucleic Acid
SATREPS	Science and Technology Research Partnership for Sustainable Development
SCG	Siam Cement Group
SEACTN	South and Southeast Asian Community-based Trials Network
SEACTN-HHS	Rural South and Southeast Asia Household Health Survey
SEAICRN	Southeast Asia Influenza Clinical Research Network
SEC	Subject Expert Committee
SICRES	Siriraj Institute of Clinical Research
SJREB	Single Joint Research Ethics Board
SMO	Site Management Organization
TB	Tuberculosis
TFDA	Thai Food and Drug Administration
UP Manila	University of the Philippines Manila
USAID	United States Agency for International Development
USAMRD-A	U.S. Army Medical Research Directorate-Africa
VNPCA	Vietnam Pharmaceutical Companies Association
WHO	World Health Organization
WHO PQ	WHO Prequalification

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Chapter 1 Survey Summary

1.1 Background of the survey

In March 2020, the novel COVID-19 spread around the world, causing enormous damage to human health, the economy and society. While Europe, the United States, China and India made rapid progress in developing and commercializing vaccines, Japan lagged behind in vaccine development. In addition, domestic trials were necessary to import vaccines made overseas, and therefore it took time to provide vaccines[1].

In response, in June 2021, the Japanese government formulated “The Strategy for Strengthening the Vaccine Development and Production System” and established the Strategic Center of Biomedical Advanced Vaccine Research and Development for Preparedness and Response (SCARDA) to strengthen vaccine development and production. “The Strategy for Strengthening the Vaccine Development and Production System" mentions the enhancement of clinical research and clinical trial networks in the Asian region, the development of the ICH-GCP (International Council for Harmonization-Good Clinical Practice) standard clinical trial implementation infrastructure at base medical institutions in the Asian region, the development of human resources for clinical trial support, and the use of Official Development Assistance to support the clinical trial implementation infrastructure overseas.

The global pharmaceutical market is expanding steadily (compound annual growth rate 2.7%), and the growth in the Asian market is particularly remarkable (compound annual growth rate 7.9%). However, although the pharmaceutical market in Japan is the third largest by country, the growth rate has remained high (-0.2% from 2014 -2019), and it is expected that overseas clinical trials and manufacturing will be meaningful for the Japanese pharmaceutical industry. On the other hand, there are various issues including insufficient information on partners and medical facilities for conducting international clinical trials in the field, and a lack of rapid progress in applying for clinical trials to pharmaceutical authorities of partner countries.

In addition, although the market for pharmaceuticals in Asia is expanding, there are insufficient bases for research and development, approval review, manufacturing and distribution, and proper use. Therefore, cooperation among countries is desirable for the establishment and improvement of a stable supply system. It is expected that international networking will further facilitate the sharing of previously unavailable information, such as the review process by clinical trial partners and regulatory agencies.

Under such circumstances, in order to create an environment and system in which clinical trials and local manufacturing can be conducted rapidly even during a pandemic, JICA will identify the roles that they can play in the future and examine specific business activities based on the past activities of JICA and the efforts and future prospects of relevant organizations such as the ASEAN East Asia International Joint Clinical Research Alliance (ARISE), which is being promoted mainly by NCGM, and the Asia Training Center for Pharmaceuticals and Medical Devices Regulatory Affairs established by PMDA.

1.2 Overview of the survey

1.2.1 Objective of the survey

In this survey, we will collect information on legal systems, local implementation systems, cooperation trends of other aid agencies, and research and development cases with other countries in relation to clinical trials and manufacturing of vaccines and other pharmaceuticals in Indonesia, the Philippines, Thailand, Vietnam, India, Kenya, and other target countries, and will identify issues that hinder rapid clinical trials and manufacturing. It will also conduct online and on-site interviews with stakeholders in the six target countries, and determine and implement the content of the pilot activities based on the results. In addition, based on the opinions of domestic stakeholders, such as related organizations and private companies in

[1] Prime Minister's Office (Headquarters for Health and Medical Care Strategy Promotion), Strategy for Strengthening Vaccine Development and Production System (https://www.kantei.go.jp/jp/singi/kenkouiryou/tyousakai/dai28/siryou1-2.pdf)

Japan, we will present proposals for support activities for the issues identified, as well as collaborate and build networks. This will have a development effect on target countries, such as eliminating drug lag, and will contribute to the rapid development and manufacturing of vaccines and other pharmaceuticals by Japanese companies in the future.

1.2.2 Overview of the survey

(1) Collection and analysis of relevant information

In order to achieve the objectives of this survey, the following information will be collected and analyzed through literature surveys, online interviews and field visits to the target countries. In doing so, NCGM, PMDA, and other relevant organizations will conduct a thorough review of the information already collected and provided by NCGM, PMDA, and other relevant organizations, and examine additional information to be collected in this investigation.

i. Collection and analysis of information on relevant policies, legal systems, application and approval procedures, etc.

Information will be collected on the relevant policies and legal systems, the process from application to approval for clinical trials and local manufacturing through literature surveys, interviews with pharmaceutical authorities, clinical trial implementing organizations, drug manufacturers, and site visits. The information obtained will be organized for pharmaceutical companies and other Japanese organizations considering overseas expansion. In addition, we will identify the legal and procedural issues involved in clinical trials of new vaccines and other pharmaceuticals originating in Japan, as well as in future local manufacturing.

ii. Collecting and analyzing information on clinical trials and facilities and human resources that can be manufactured locally

Information on universities and research institutions involved in clinical trials, medical facilities serving as sites for clinical trials, implementation systems of manufacturing facilities, conditions of facilities and human resources, past results and future plans in the countries covered by this survey will be collected through literature surveys, interviews and site visits, and information obtained will be arranged to be useful to Japanese institutions. In addition, issues related to the local implementation system, such as related facilities and human resources, will be identified when considering clinical trials and local manufacturing of vaccines and other pharmaceuticals originating in Japan.

iii. Collection and analysis of information on efforts by aid agencies, research institutions, and companies in other countries

The following information will be collected through literature surveys, interviews, and site visits, and will be organized into useful information for relevant Japanese organizations.

① Promotion of local manufacturing in regions including the countries covered in this survey

② Donors supporting clinical trials and local manufacturing in the target countries

③ Progress and good practices of universities, research institutions, and pharmaceutical companies in Europe and the United States

In addition, based on the above, we will consider efforts that would be desirable for Japanese organizations to take part in when entering the market.

(2) Formulation of project activity proposals and pilot implementation of support activities (Pilot activities)

Through information collection and analysis, priority issues to be addressed will be identified, and based on these issues, proposals for cooperation will be formulated for the target countries and Japanese

stakeholders. In addition, part of the proposed cooperation will be implemented as pilot activities and verified empirically.

(3) Preparation of operational progress reports and final reports

We will summarize quarterly progress in operational progress reports and submit them along with collection materials and data. At the completion of the project, the final report will be prepared and submitted to JICA, summarizing the collection and analysis of relevant information, the formulation of project activity proposals, and the results of the investigation of the pilot implementation of support activities.

1.2.3 Methodology for conducting domestic surveys

From the end of August 2022, information from previous surveys conducted by PMDA, the Cabinet Secretariat, and the Ministry of Health, Labour and Welfare will be examined, and items not found in the existing literature will be identified. After the scope of the survey has been set, issues in the target countries will be extracted jointly with a multilingual research team from our organization. At the same time, preparations will be made for interviews with domestic and foreign stakeholders, and hypothetical questions will be formulated. Interviews will be conducted with government agencies, private companies and industry associations in Japan using the results of the literature survey. After compiling the information collected during the hearings, we will delve into issues in each target country and conduct interviews with the support of subcontractors in each target country to understand issues and needs in the field.

1.2.4 Methodology for conducting field surveys

From the end of November 2022 to February 2023, we will arrange site visits with each target country, and then explain the issues, needs, and proposed pilot activities that we compiled during the domestic survey. After the stakeholders have gained an understanding of the outline and purpose of the survey, we will ask for specific requests. For each of the six target countries, two survey team members will make a site visit. In order to coordinate the date and time with the meeting party, we will utilize the network of the subcontracting party and work together as necessary.

1.2.5 Methodology for developing and implementing proposed support activities (pilot activities)

(1) Delving into proposed support activities and pilot activities (Late February to late May 2023)

We will reorganize the information gathered through the site visit and begin additional research on items that require further research. Based on the results of the site visit, another interview will be held with relevant organizations in Japan, and plans for implementation of pilot activities to resolve issues will be reviewed. In addition, the four pilot activity methods (Matching promotion, data management, networking promotion, capacity strengthening) prepared in advance will be used to formulate specific support activity plans.

(2) Implementation of pilot activities (Late May to late December 2023)

After the preparation of the implementation plan for the pilot activities, the date and time of the meeting will be adjusted again with the relevant parties in each target country, and the details of the plan will be presented and revised according to the request of the other parties. For countries with a high level of confidence in their proposed support activities, we will consider conducting a survey based on requests, if necessary. The status of the pilot activities will be monitored in cooperation with the subcontractor when

the pilot activities are carried out locally. In addition, if the program is to be implemented in Japan, such as inviting visitors to Japan, preparations for travel will be made by the survey team. Depending on the progress of the study, additional activities based on the results of the pilot activities will also be considered.

1.3 Survey team structure and work schedule

1.3.1 Composition of the survey team and external advisors

The survey team will utilize a multilingual research team in our organization to conduct literature research and share the results with relevant stakeholders in the target countries. We will also contact the NCGM International Trial Division, the Japan Agency for International Medical Cooperation, and the Pharmaceutical Manufacturers of Japan, and hold regular meetings to exchange opinions.

In this study, external advisors with expertise in local clinical trials and drug manufacturing will be assigned to each target country. Each advisor has a rich network and will contact the potential candidates. The sub-contractors in each country are shown below.

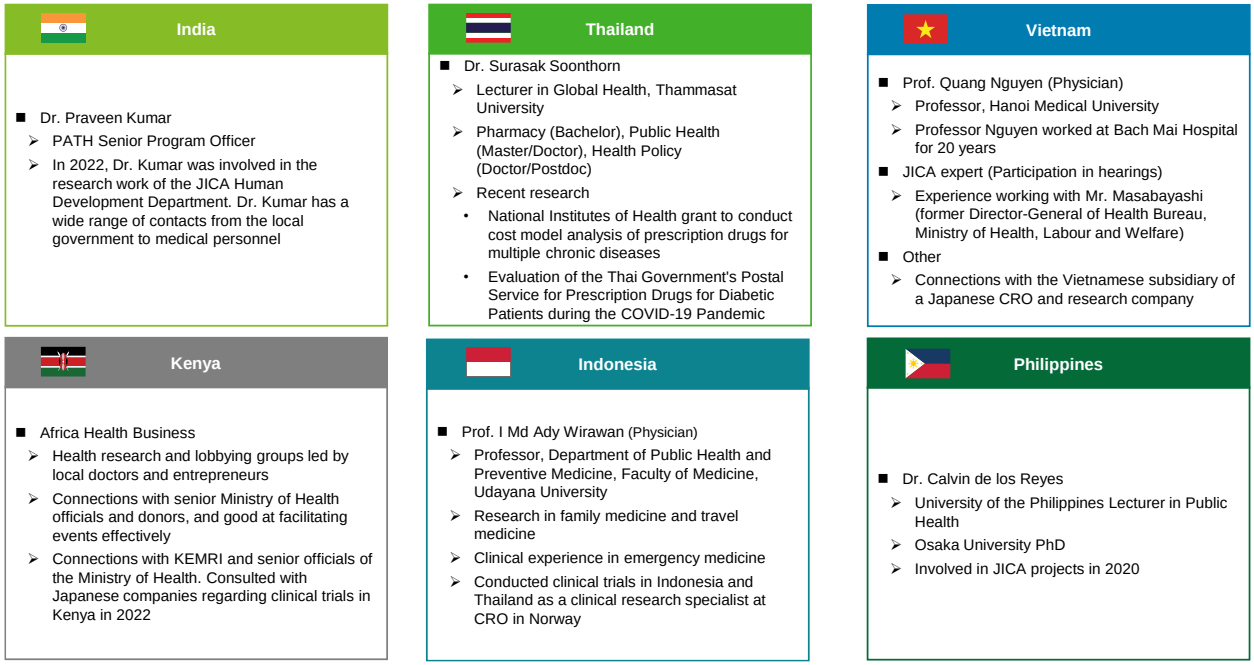


Figure 1-1 Sub-contractors in each target country

1.3.2 Relevant institutions in Japan

There are several stakeholders involved in clinical trials and pharmaceutical manufacturing, including Japanese regulatory authorities, clinical trial institutions, academia, private companies, and industry associations. The organizations that are expected to conduct specific interviews are as follows.

Category	Organization Name
Regulatory authority	PMDA
Clinical trial sites	National Cancer Center (NCC), Tokyo Women's Medical University and University of Tokyo Hospital

Clinical trial implementation promotion organizations and networks	REMAP-CAP, NCGM, SCARDA
Private companies	Multiple pharmaceutical companies
Industry associations	Pharmaceutical Manufacturers Association of Japan, Clinical Trialists' Training Council

1.3.3 Relevant institutions in target countries

Relevant organizations in each of the target countries will be asked to share their contacts with the subcontractor and request interviews. The organizations to be approached are as follows.

・Indonesia

Category	Organization Name
Government agencies	Ministry of Health (MoH), National Research and Innovation Agency (BRIN), Regional Research and Innovation Agency (BRIDA)
Regulatory authorities	National Agency of Food and Drug Control (BPOM)
Clinical trial sites	Hasan Sadikin Hospital, Kariadi Hospital
Academia	Universitas Indonesia, Universitas Gadjah Mada, Udayana University
Private companies	Biofarma, Otsuka Pharmaceutical Indonesia, Prodia the CRO

・The Philippines

Category	Organization Name
Government agencies	Department of Health (DOH), Department of Science and Technology (DOST), Philippine Council for Health Research and Development (PCHRD)
Regulatory authorities	Food and Drug Administration Philippines (PFDA), Health Technology Assessment Council (HTAC)
Clinical trial sites	National Clinical Trials and Translation Center (NCTTC), Research Institute for Tropical Medicine (RITM), National Children's Hospital, Center for Basic Science Research, Research and Biotechnology, St. Luke's Medical Center
Academia	Philippine General Hospital (UP-PGH), National Institutes of Health (NIH-UP Manila)
Private companies	George Clinical, AstraZeneca, Syneos Health, Icuvia (IQVIA)

Industry associations	Philippine Clinical Research Professionals

・Thailand

Category	Organization Name
Regulatory authorities	Thai Food and Drug Administration (TFDA), Medical Council
Clinical trial sites	National Vaccine Institute, Medical Research Foundation
Academia	Chula Research Clinical Center, Chulalongkorn University, Siriraj Institute of Clinical Research
Private companies	Baiya Phytopharm
Industry associations	Thai Pharmaceutical Manufacturers Association, Pharmaceutical Research and Manufacturers Association, the Pharmacy Council, Thailand Towards Excellence in Clinical Trials

・Vietnam

Category	Organization Name
Government agencies	Vietnam Ministry of Health, Ministry of Health's Administration of Science, Technology and Training
Regulatory authorities	National Institute for Control of Vaccines and Biologicals
Clinical trial sites	Choray Hospital, the Pasteur Institute in Ho Chi Minh City, Institute of Vaccine and Medical Biologicals
Academia	Hanoi Medical University, University of Medicine and Pharmacy, Ho Chi Minh City
Private companies	POLYVAC, VABIOTECH

・India

Category	Organization Name
Clinical trial sites	Indian Council of Medical Research (ICMR), (Translational Health Science and Technology Institute (THSTI), National Institute of Animal Biotechnology (National Institute of Animal Biotechnology (NIAB)
Academia	All India Institute of Medical Science (AIIMS)

Private companies	Bharat Biotech, ImmunitiasBio, PremasBiotech, Novartis, Novartis, Biological E. Limited, Panacea Biotech
Industry associations	India Vaccine Manufacturers Association, Indian Pharmaceutical Association
International organizations	World Health Organization, Country Office for India

・Kenya

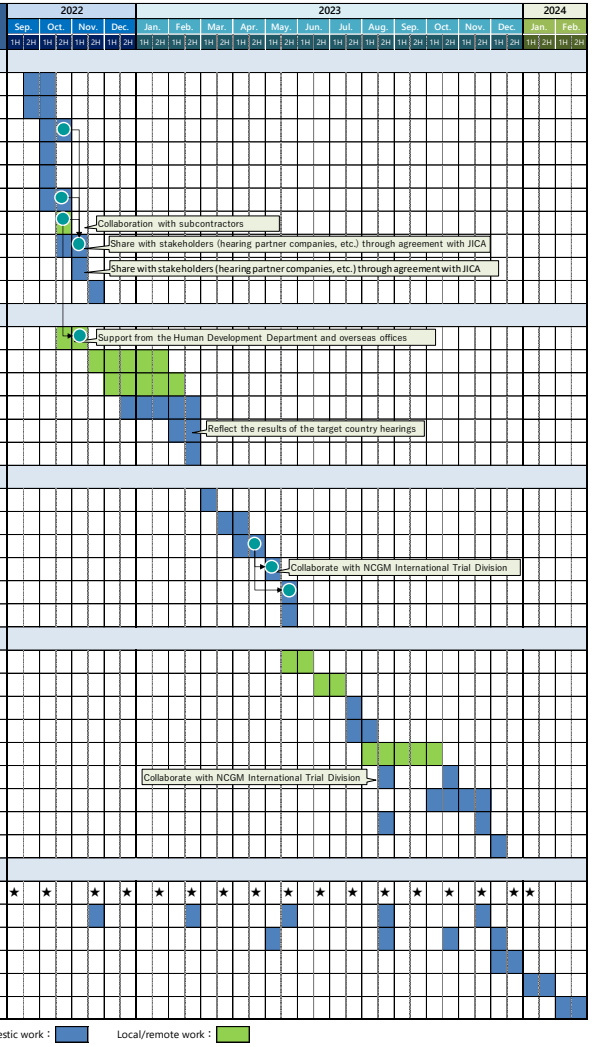
Category	Organization Name
Government agencies	Ministry of Health (MoH)
Regulatory authorities	Pharmacy and Poisons Board (PPB)
Clinical trial sites	Kenya Medical Research Institute (KEMRI), Kenya AIDS Vaccine Initiative (KAVI), National Quality Control Laboratory (NQCL)
Private companies	Cosmos Pharmaceuticals Limited, Regal Pharmaceuticals, Dawa Life Sciences, ClinWin Research Services
Industry associations	Pharmaceutical Society of Kenya (PSK), Kenya Association of Pharmaceutical Industry (KAVI), Federation of Kenyan Pharmaceutical Manufacturers (FKPM)
International organizations	World Health Organization, Country Office for Kenya

1.3.4 Survey schedule

The purpose of this survey is to collect information on the clinical trials and manufacturing processes of vaccines and other pharmaceuticals in the target countries. In addition to the literature research, the survey also compiles interviews with local implementation systems of regulatory authorities, clinical trial implementing organizations, academia, private companies, and industry associations in each target country. After identifying the needs and issues facing each country, the survey aims to formulate proposals for support activities and establish networks with domestic and overseas stakeholders to resolve issues. The overall schedule is as shown in the table below.

Table 1-1 Overall Schedule

	Classification	Work Content	Preparation Materials
Step 1.	**Domestic work/Hypothesis Setting**		
1-1.	Determine the items to be studied in literature review	Check items that are not in the existing literature	Draft bibliography entry
1-2.	Work Plan	Summary of surveyed data, business policies and schedules	Work Plan
1-3.	Initial literature review on each target country	Digging into related policies, systems, and issues	Summary of Extraction Issues
1-4.	Preparation for domestic interviews	Prepare a list of Interviewees and list of questions	Call list and questionnaire (domestic)
1-5.	Preparation for local interviews	Prepare a list of Interviewees and list of questions	Interviewees and Questionnaire (Country)
1-6.	Conducting domestic interviews	Conduct interviews with the government agencies, private sector and industrial associations in Japan	Minutes
1-7.	Conducting local interviews (online)	Conduct (online) interviews with local agencies and relevant parties to understand the challenges	Minutes
1-8.	Summarize issues identified in previous processes and rough draft of support activities	Make hypotheses for support activities and share it with JICA	Summary of Challenges and Proposed Support Activities
1-9.	Proposals of pilot support	Draft plans for implementing pilot support based on the proposed support activities and share it with JICA	Trial support implementation plan
1-10.	Progress Report (1st)	Summarize the issues, possible idea of support activities, and interests of Japanese companies	Progress report
Step 2.	**Field survey/Hypothesis Confirmation**		
2-1.	Development and coordination of field survey guidelines	Advance adjustment through subcontractors	Field Survey Guide
2-2.	Digging and Reorganizing Challenges	Briefing on issues and interests of Japanese companies	Minutes
2-3.	Exchange of views on proposed support activities	Explanation of the proposed cooperative programs/ Gathering requests for the pilot activities	Minutes
2-4.	Field survey report	Identify gaps with hypotheses before traveling	Field survey report
2-5.	Proposals to implement pilot support	Draft of a proposal of trial activity	Minutes
2-6.	Progress Report (2nd)	Challenges in target countries, proposed cooperative programs , and plan for pilot activities	Progress report
Step 3:	**Drill Down on the plans of support activities and pilot activities / Revise hypotheses**		
3-1.	Additional Survey Items for Challenges	Review additional items to be delved into after field study	Draft additional items of investigation
3-2.	Conduct additional research on issues	Literature and company interviews	Results of the issue-drilling survey
3-3.	Modification of hypotheses	Restructuring of support activities and trial support implementation plans	Draft plan for cooperative programs and pilot activities
3-4.	Briefing for Japanese companies (seminar)	Presentations and exchange of views on issues and support and trial activities	Seminar materials and minutes
3-5.	Final decision on proposed trial activities	Coordinate with JICA based on the results of the seminar	Pilot activity plan
3-6.	Progress Report (3rd)	Summary of challenges, draft support and trial activities plan, seminar results	Progress report
Step 4:	**Conduct pilot support activities**		
4-1.	Notification and announcement of trial support implementation plan	Initiating coordination through local subcontractors	Guide to the trial implementation plan
4-2.	Local implementation of trial support (about two countries)	Travel to and implementation of field trials in target countries (tentatively two countries)	Records of trial data and results
4-3.	Field survey report	Sharing the results of local trials	Field survey report
4-4.	Response to a request survey	Accurate proposals for support activities must be preceded by a request survey	Revised support plan
4-5.	Monitoring Trials	Conduct questionnaires and follow up activities through local subcontractors	Monitoring Results
4-6.	Briefing for Japanese companies (seminar)	Online implementation of domestic trials (matching seminars, etc.)	Seminar materials and minutes
4-7.	Summary of survey results	Finalization of cooperative programs based on the results of pilot activities (final hearing of related parties)	Support measures and minutes
4-8.	Progress Report (4th and 5th)	Status of trial implementation (4th), implementation of trial support and summary of support measures (5th)	Progress report
4-9.	Briefing for Japanese companies (seminar)	Publication of findings	Seminar materials and minutes
Summarization:	**Compile results / Prepare deliverables**		
M-1.	Regular meetings with JICA	Regular progress reports with JICA and concerned parties	Progress report materials and minutes
M-2.	Progress report	Compilation of each stage	Progress report
M-3.	Sharing progress for Japanese stakeholders	Survey progress (verification of issues and hypotheses)/Survey results seminar	Seminar materials and minutes
M-4.	Draft Final Report	Including the reflection of the final support proposal	Draft Final Report
M-5.	Final Report	Modified from Draft Final Report	Final Report
M-6.	Correspondence after termination	Report, etc.	Settlement report



Chapter 2 Results of survey and analysis and issues in considering clinical trials and future local manufacturing of new vaccines and other pharmaceutical products from Japan

2.1 India

2.1.1 Legal systems and procedures in target countries

(1) Related policies and legal systems

i. National organizations and legal systems for drug regulation, including vaccines

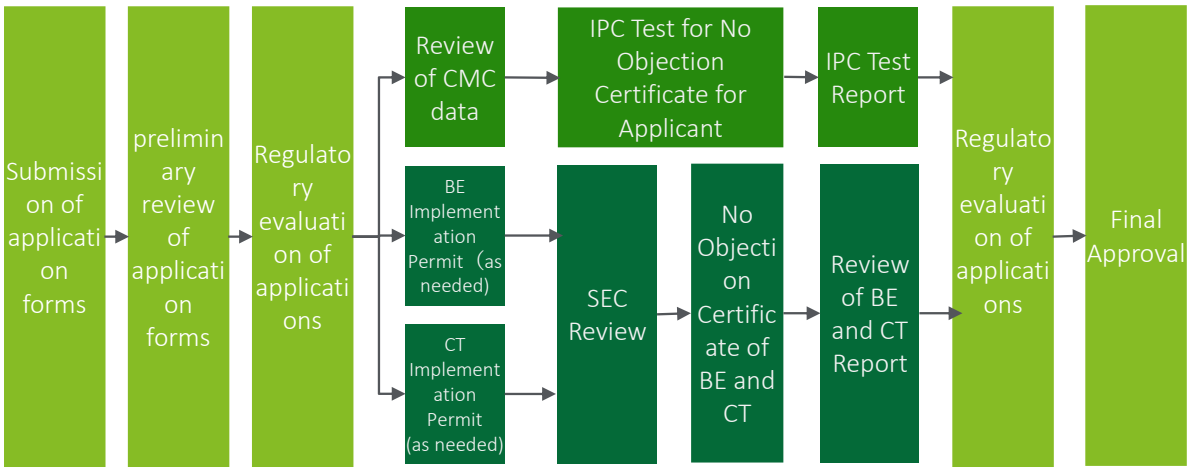
The pharmaceutical regulations for drugs in India are based on the "Drugs and Cosmetics Act,1940" enacted in 1940 and the "Drugs and Cosmetics Rules, 1945" revised in 1985. In addition, the "New Drugs and Clinical Trials Rules,2019" were enacted in 2019 and replaced Part XA "Importation of New Drug Manufacturing for Clinical Trials and Marketing" and Schedule (Annex) Y of the Drugs and Cosmetics Rules, 1945. The new Regulation is intended to promote clinical research in the country and changes the regulatory landscape regarding the approval of new drugs and the conduct of clinical trials in the country. (Details are given in subsequent v. "Policy Trends in Clinical Trials and Production".)

Under these laws, the Central Drugs Standard Control Organization (Hereinafter referred to as CDSCO), under the umbrella of the Ministry of Health and Family Welfare (Hereinafter referred to as MoHFW), is the regulatory agency for pharmaceutical products. CDSCO is responsible for the approval of new drugs, approval of clinical trials, licensing and quality control of imported drugs, prohibited drugs, market monitoring of drugs, revision of the above-mentioned regulations and laws, and supervision of local drug control organizations.[2]

ii. Drug approval system

The figure below shows the drug substance/drug approval process in India. These approval processes are based on the Drugs and Cosmetic Rules, 1945. The process for approval of generic drugs is largely the same, except there are no steps for conducting clinical trials for the generic drugs.

[2] PMDA 「FY 2020 Study report on Pharmaceuticals and Medical Devices Regulations in Asian Countries (India)」



CMC・・・Chemistry and Manufacturing Control
BE・・・Bioequivalence
CT・・・Clinical Trial
SEC・・・Subject Expert Committee
IPC・・・Indian Pharmacopeia Commission

Figure 2-1 Approval process for APIs/Drugs in India

iii. Regulations concerning clinical trials

Good Clinical Practice (Hereinafter referred to as GCP) [3] in India is based on the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use- Good Clinical Practice (Hereinafter referred to as ICH-GCP). In addition, under the New Drugs and Clinical Trials Regulations 2019, clinical trials of new drugs are subject to approval by the Drug Controller General India (DCGI).

iv. Systems and regulations for local manufacturing

The Good Manufacturing Practice (Hereinafter referred to as GMP) [4] is described in the Drugs and Cosmetic Rules. The India's GMP are based on WHO guidelines. India's GMP impose GMP obligations on all licenced manufacturers (manufacturing facilities, domestic drug manufacturing requires a license in India , and manufacturing companies must be based in India to obtain a license.).[5] Since 2018, the GMP has been revised in line with WHO-GMP standards, imposing finer GMP standards.

In order for Japanese pharmaceutical companies to set up local factories and export drugs to Japan, they must also comply with "The Industries Act, 1951" and "The Trade and Merchandise Marks Act, 1958."

v. Policy trends in clinical trials and manufacturing

In 2013, following allegations of unethical conduct of pharmaceutical clinical trials by the media[6], CDSCO tightened regulations on the conduct of clinical trials. At that time, a number of new regulations were introduced, many of which led to confusion among pharmaceutical companies conducting

[3] Abbreviation for Good Clinical Practice. Refers to international standards for conducting, prescribing, documenting, and reporting clinical trials with potential human participants.

[4] Abbreviation for Good Manufacturing Practice. It refers to the standard of manufacturing control and quality control of pharmaceutical products, and is a standard that defines the control and compliance requirements at the time of manufacture in order to supply high-quality pharmaceutical products that can be used with confidence.

[5] Institute for Humanities and Social Sciences, Doshisha University, "Implementation of Standards for Manufacturing Control and Quality Control (GMP) of Pharmaceuticals in India" https://doshisha.repo.nii.ac.jp/?action=pages_view_main&active_action=repository_view_main_item_detail&item_id=18167&item_no=1&page_id=13&block_id=100

[6] A 2012 report by a parliamentary committee in India noted that CDSCO had legally approved the sale of several untested medicines to Indian patients.

international clinical trials in India and resulted in a reduction in the number of clinical trials approved by regulatory authorities[7].

Therefore, the New Drugs and Clinical Trials Regulations, enacted in 2019, provide for the promotion of clinical research and change several topics, including orphan drugs, post-trial access, and pre- and post-submission meetings, to be more comprehensive and accelerate the drug development process. The new regulations aim to expedite time-limited reviews from application to review completion, to make the regulatory process predictable and transparent, and to promote domestic clinical research. The main points of the 2019 revision are as follows[8].

1) Shortening the review schedule

In principle, clinical trials of drugs developed outside India are evaluated and reviewed for approval within 90 working days. The clinical trial application review schedule for drugs developed, researched and manufactured in India is reduced within 30 working days. If no communication is received from the regulatory authority within the fixed working days, implementation of Bioavailability study (BA test) and Bioequivalence study (BE test) for new drugs or existing drugs is deemed to be permitted.

2) Conducting pre-application meeting

In 2015, CDSCO announced the introduction of a formal system of pre-application meetings between applicant, CDSCO officers and relevant experts on the regulatory process, but this was never put into practice. The the New Drugs and Clinical Trials Regulations in 2019 include provisions for pre-application meetings regarding licensing procedural requirements for manufacturing processes, clinical trials and so on. The pre-application meeting is designed to provide mutual clarity on the application process before applicant companies begin to apply to regulatory authority. The opportunity for a pre-application meeting also applies when a company undertakes clinical research that has not been approved by regulatory authority, or when a specific study is additionally required from a regulatory perspective[9].

3) Post-marketing surveillance

Post-marketing surveillance is conducted according to the dosage and administration approved by regulatory authority. It does not apply if the durg has already been approved for manufacturing and sales in accordance with Indian regulations guidelines.

4) Registration of Orphan Drugs

Orphan drugs are defined as "drugs intended to treat conditions that have not affected more than 500,000 people in India." In order to promote clinical research on orphan drugs, the following provisions were made in the new regulations of 2019:

- Provisions on the accelerated approval process and exceptional measures for orphan drugs, including fee waivers for clinical trial applications.
- Provisions for an accelerated review process. (If all clinical trial phases have not been completed, the sponsor or applicant can still able to apply to the Central Licensing Authority (CLA) for an accelerated review process. After accelerated approval, the applicant may be required to conduct a Phase IV clinical trial to test the clinical efficacy)
- Exemptions from Phase IV trials or clinical trials on Satisfaction with CLA

In the United States, the Orphan Drug Designation program defines orphan drugs and biologics for the treatment of diseases affecting fewer than 200,000 people and provides a list of rare diseases. Similarly, in

[7] The Wall Street Journal, https://jp.wsj.com/articles/SB10001424127887324195104578600851030750938

[8] Regulatory Focus, “India’s New Drugs and Clinical Trials Rules: An Industry Perspective,” https://www.raps.org/news-and-articles/news-articles/2019/7/indias-new-drugs-and-clinical-trials-rules-an-in

[9] Regulatory Focus, “India’s New Drugs and Clinical Trials Rules: An Industry Perspective”, (https://www.raps.org/news-and-articles/news-articles/2019/7/indias-new-drugs-and-clinical-trials-rules-an-in)

India, it has been suggested that the CDSCO should develop a similar means of listing rare diseases[10].

5) Access to new / investigational drugs after clinical trials

The new 2019 regulations stipulate that "A new drug or investigational drug that has been found to be beneficial to the subjected patient during the clinical trials should be provided to him/her for a period of time that the investigator and the ethics committee deem necessary after completion of the clinical trials."

However, the sponsor is not responsible for the post-trial use of the study drug or new drug by the subjected patient. Therefore, it has been pointed out that there are some problems that are not clear in the regulations, such as the appropriate period for providing drugs and the method for monitoring safety during the period for providing drugs.

6) Exemption from clinical trials

The new drugs must be approved through clinical trials carried out in India before they can be imported. Rule 75 provides specific conditions under which the requirement for clinical trials can be exempted when new drugs are imported. The exemption applies if ;

- The drug is approved and marketed in a specific country[11] designated by the regulatory authority.
- An international clinical trial with the drug is underway in India, during which the new drug has been approved in a specific country designated by the regulatory authority (Rule 101).
- Unexpected serious adverse events are not reported.

In addition, exemption from clinical trials requires the absence of factors affecting the safety and efficacy of new drugs, such as differences in the Indian population, enzymes or genes involved in the metabolism of new drugs, and factors affecting pharmacokinetics (PK) and pharmacodynamics (PD). If such factors are present, a Phase IV clinical trial should be conducted with a CLA-approved design. Requirements for the Phase IV clinical trial include life-threatening or serious diseases, diseases that are particularly prevalent in India, unmet needs in India, and rare diseases for which drugs are unavailable or expensive (However the requirement may be mitigated in case of orphan drugs).

Rule 80 provides the specific conditions under which clinical trial requirements may be exampeted for locally originated new drug manufacturing licenses. For new drugs that have been approved and marketed in other countries for several years, the conditions are similar to those for importation of new drugs, except that mitigation of data submission for animal toxicity studies, reproductive and developmental toxicity studies, teratogenicity studies, perinatal studies, mutagenicity studies, and oncogenicity studies.

These provisions for clinical trial exemptions and relaxations shorten the time between the global launch of a drug and the delivery of said drug to patients in India.

7) Shortening the approval process in times of disaster

The new 2019 regulations also include provisions to facilitate approval of the use of new drugs for diseases with high morbidity in India, particularly for disaster and special defensive uses. The new regulations now allow marketing authorization to be granted based on Phase II rather than Phase III clinical trial data if there is a demonstrated need for such a product in these circumstances. However, even in this case, post-approval Phase IV clinical trials (post-marketing clinical trials) are mandatory.

[10] Regulatory Focus, “India’s New Drugs and Clinical Trials Rules: An Industry Perspective”, (https://www.raps.org/news-and-articles/news-articles/2019/7/indias-new-drugs-and-clinical-trials-rules-an-in)

[11] At the Third Japan-India Symposium on Medical Product Regulation held in 2018, institutionalization of an exemption in principle for additional clinical trials to be conducted in India for new drug applications by Indian side. To achieve this, CDSCO will include Japan as an exempt country in its new draft rules on clinical trials and import and marketing of drugs.

(2) Process from application to approval for clinical trials and local manufacturing

i. Process from application to approval for clinical trials

Clinical trials in India are evaluated and approved or denied by the Subject Expert Committee (Hereinafter referred to as SEC) of the CDSCO and the Ethics Committee within 90 days of receipt of the application. DCGI must evaluate clinical trial applications within 90 days for drugs developed outside India and within 30 days for drugs discovered, researched, and manufactured in India. If a response from DCGI to a clinical trial application for a drug is not received within 30 days, the applicant may assume that permission to conduct the trial in question has been granted. The approval process is illustrated in the figure below.

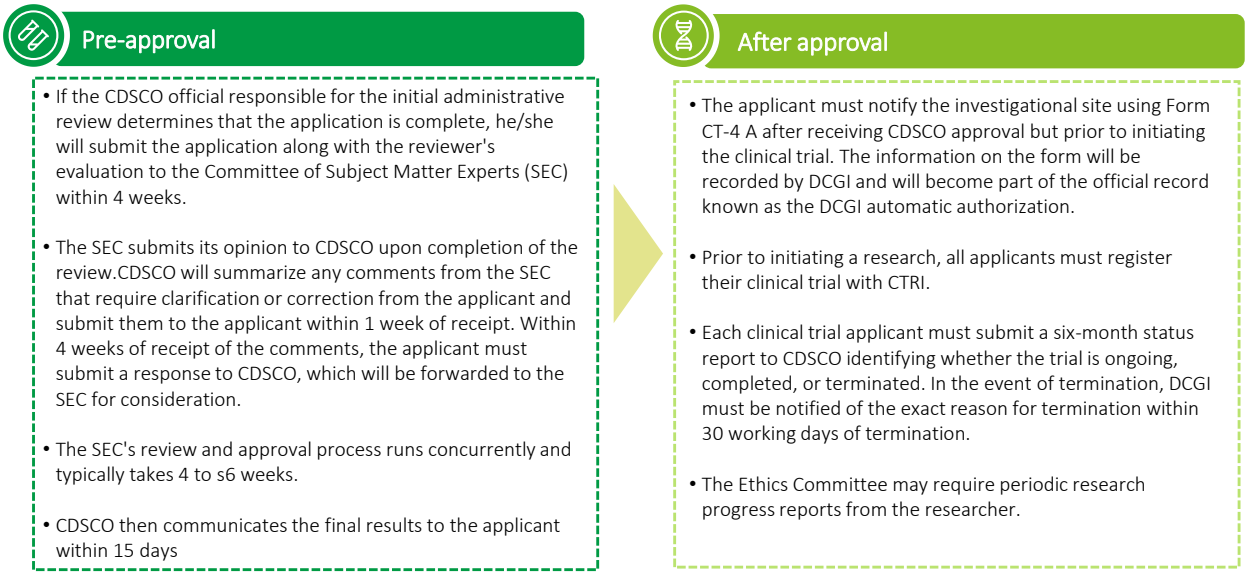


Figure 2-2 Application/approval process for clinical trials

ii. Process from application to approval for local manufacturing of drugs

The Drugs and Cosmetics Act, 1940 is the law that regulates the manufacture of pharmaceuticals in India. There are four types of drug manufacturing licenses, as shown in the figure below: Test license for manufacturing, Licence to manufacture notificed medical device, Loan license, and Manufacturing license post successful clinical trials.

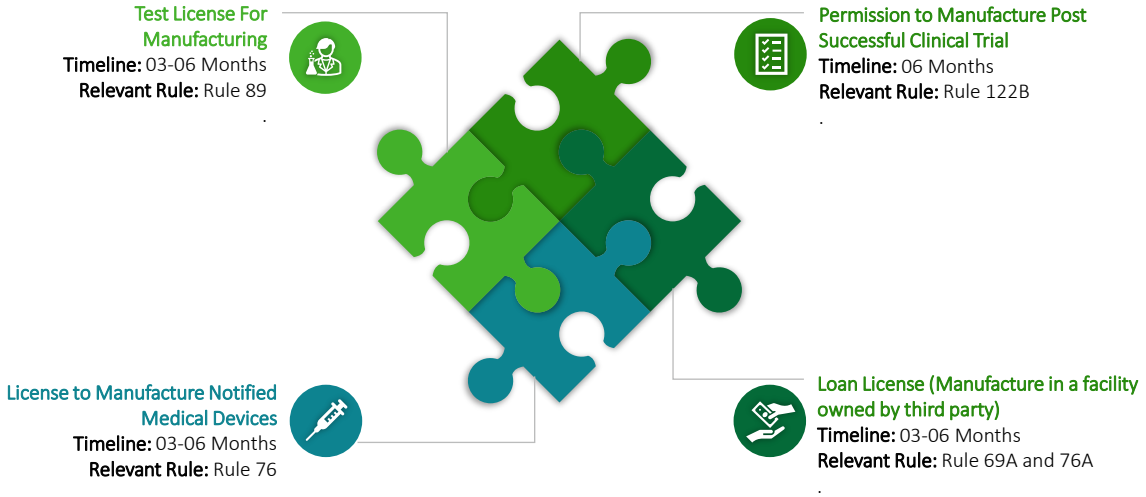


Figure 2-3 Types of drug manufacturing licenses

The process from license application to approval for drug manufacturing is shown below. Drug manufacturing licenses are valid for five years.

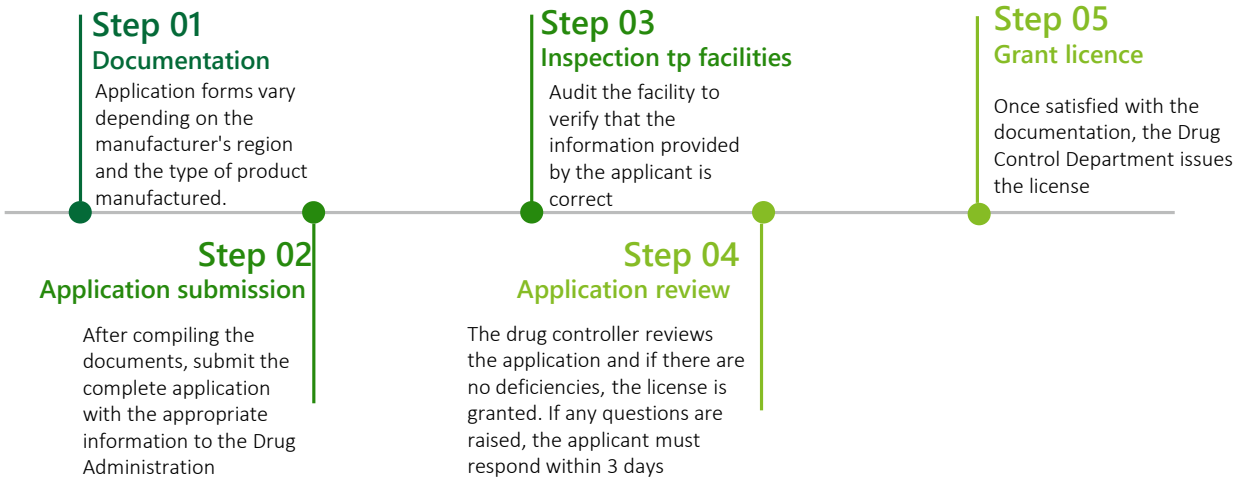


Figure 2-4 License approval process for drug manufacturing

(3) Issues in target countries (Policies, regulations and legal systems for clinical trials and local manufcturing)

i. Delay of approval process

Sponsors of clinical trials must receive written approval from the DCGI to proceed with a clinical trial, and the process for approving clinical trials in India can take months or longer. Factors behind the delay in DCGI approval include the lack of a sufficient number of skilled staff in the regulatory authority. Another reason for the delay in the approval process is that because the regulations are only described in general terms, applicants should directly consult with CDSCO on specific application procedures or should understand industry practices well. Another issue is that the CDSCO has not published a guidance document that provides an official interpretation on the regulations.

Delays in the clinical trial approval process can cause Indian clinical trial sites to lag far behind their counterparts in other countries in international clinical research collaborations.

ii. Necessity of monitoring legislation for clinical research and clinical trials

There is no independent legislation in India to monitor clinical research and clinical trials. Such laws are necessary to ensure that subjects participating in clinical trials are informed about adequate safeguards so that they are not exploited or exposed to significant risks. In addition, the lack of knowledge among subjects about the types, phases, and coverage of the clinical trials has led to a shortage of subjects due to fear of adverse side effects.

iii. Clinical trial system for drugs and vaccines for rare diseases and emerging diseases

Few clinical trials for rare diseases are currently being conducted in India. India has one of the highest numbers of clinical trials in the world but compared to common chronic diseases such as diabetes and hypertension, clinical trials for rare diseases in India account for less than 3% of all trials. The small number of patients with rare diseases forces an increase in the number of sites to recruit potential subjects, which complicates the research process and increases the cost burden. Conversely, reducing the number of subjects limits the robustness of clinical trial data.

While India has established a clinical trial system for generic drugs, the regulatory framework for clinical trial approval of new drugs is weak, and the application data required by the Indian regulatory authority may only follow the template for existing drugs and not necessarily be adapted to new drugs. In such cases, regulatory approval of clinical trials for new drugs may not proceed expeditiously. The same can be said for drugs of rare diseases, where it is difficult to obtain approval for clinical trials for new drugs, although approval in India is relatively easier if the drug has already been approved overseas. It is necessary to promote regulatory harmonization and a regulatory framework for drug development for rare diseases for which no cure has been found and for emerging diseases that could cause pandemics in the future.

2.1.2 Local implementation system including related facilities and human resources in target countries

(1) Implementation system including facilities, human resources, etc. for clinical trials and local manufacturing at related facilities

i. Local clinical trial system

A) Clinical trial institutions

There are several CROs in India, and the following six companies are introduced as examples. Other CROs are listed in the figure below.

① Clinigene (Biocon)

Clinigene is a 100% subsidiary of Biocon, India's first clinical research organization, and a full-service CRO for end-to-end clinical development of biopharmaceuticals, with extensive experience in new biopharmaceuticals and biosimilars.

② Reliance Life Sciences

Headquartered in Mumbai, it is research-oriented and engaged in the fields of biological therapy (plasma proteins, biosimilars, and novel proteins), pharmaceuticals (late oncology generics), clinical research services, regenerative medicine (stem cell therapy) and molecular medicine.

③ Lotus Clinical Research Academy Pvt. Ltd. (LCRA)

Founded in 2001, it provides specialized services for numerous clinical pharmacology studies, including food effects, drug interaction studies, and pharmacokinetic/pharmacodynamic studies. To date, the company has completed 350 pain trials, 10 analgesic approvals and 12 FDA approvals.

④ Anovus Institute of Clinical Research

The Annovus Institute of Clinical Research is an educational institution that provides a variety of academic curricula for rapid clinical trials of new drugs to combat diseases worldwide and for more effective and efficient clinical research education. In addition, it aims to network with clinical research professionals in Japan and abroad to share industry knowledge and feedback, and to freely exchange views with academia, pharmaceutical industry leaders and regulatory bodies.

⑤ Apejay Svran Institute for Biosciences & Clinical Research

It is part of the Apeejay Group and collaborates with industry participants Martin & Harris Pvt. Ltd., ASG Biochem Pvt. Ltd. and Walter Bushnell Health Care Pvt. Ltd., to provide a variety of training programs and workshops that address the needs of different employment levels in the biotech/biopharma/healthcare industry and the needs of academics.

⑥ Institute of Clinical Research India (ICRI)

ICRI is a leading research institution in India with more than 9 campuses and 13 research centers in the country. Through its unique university-industry partnership model, ICRI offers undergraduate and graduate programs at top universities in India and around the world.

Table 2-1 Examples of CROs in India

Aagami	Oasis Institute of Health Sciences&Research Centre (OIHSRC)	Global Clinical Trials (GCT)
Jubilant Clinsys (Jubilant Organosys)	Accutest Global	ICON
WellQuest (Nicholas Piramal)	APCER Life Sciences	Indus Biotherapeutics
Synchron	Clinical Research Education and Management Academy (CREMA)	Max India
Vimta Labs Lambada (Intas)	Asian Institute of Health Sciences (AIOHS)	GVK Biosciences
SRL Ranbaxy	Asiatic Clinical Research	Navitas Life Sciences
Accelsiors	Covance	Novotech
Asian Clinical Trials (Suven Life Sciences)	Altree Healthcare	Quanticate
Metropolis	Dishman Group	Spectrum Clinical Research
Novartis	Eurofins Advinus	Synchron
Torrent		Syngene

B) Local capacity for clinical trials

The market for clinical trials in India is expected to expand at a compound annual growth rate (CAGR)

of 8.2% from 2022 to 2030. Globalization of clinical trials, utilization of new technologies in clinical research, diversification of diseases, and increasing research and development are the key factors projected to drive the market.

India has a large number of institutions that conduct clinical trials, including universities and research institutes. Examples include the All India Institute of Medical Sciences (AIIMS) and the India Council of Medical Research (ICMR). ICMR has conducted a clinical trial of "Randomized Evaluation of COVID-19 Therapy" in collaboration with Oxford University and has collaborated with various overseas research institutes. There are also many cases of clinical trials conducted by Indian pharmaceutical companies in collaboration with foreign companies. To rapidly co-develop a live attenuated vaccine against the novel coronavirus, Codagenix, a US clinical-stage biotechnology company, has formed a development and manufacturing partnership with the Indian Serum Institute to co-develop clinical trials for the COVID-19 vaccine CoviLiv.

C) Examples of recent clinical trial research

All India Institute of Medical Science (AIIMS, All India Institute of Medical Sciences) conducted a clinical trial of COVAXIN, India's first domestically manufactured vaccine. Preclinical studies showed promising results in terms of safety and immunogenicity, and phase I and II clinical trials involving 755 participants also showed a high safety profile for the vaccine. The phase III trial of COVAXIN, conducted in November 2020 in collaboration with Bharat Biotech and ICMR, tested 25,800 subjects and showed a preliminary vaccine efficacy of 81% in preventing COVID-19. The Department of Biotechnology of the Indian Ministry of Science and Technology has implemented the COVID Suraksha scheme to accelerate the development and manufacturing of COVID-19's domestic vaccine. With this initiative, the Government of India provided financial support to vaccine manufacturing facilities to enhance manufacturing capacity, resulting in a sharp increase in COVAXIN vaccine manufacturing.

Biological E conducted a clinical trial of CORBEVAX, COVID-19's first domestic receptor-binding domain (RBD) subunit protein vaccine. A phase I clinical trial was conducted to evaluate the safety and immunogenicity of the vaccine in approximately 360 subjects, and the phase II clinical trial was completed in April 2021. Additionally, in April 2021, India's Directorate General of Medicines Control allowed the vaccine to begin Phase III clinical trials. As of December 2021, Biological E reported positive results, but some experts criticized the lack of published data from phase III trials. The developer of the vaccine claimed that based on antibody levels, the vaccine appeared to be more than 90% effective against the original variant, and on December 28, 2021, India approved the Corbevax vaccine for emergency use.

The Serum Institute of India, an Indian biotechnology company, is conducting a phase III clinical trial of VPM 1002, a candidate Bacillus Calmette–Guérin vaccine (BCG vaccine), to evaluate its efficacy in reducing COVID-19 infection and severe disease in the elderly, those at high risk for comorbidities and health care workers. The phase III trial was conducted on 2,064 elderly subjects to test whether VPM1002, a vaccine candidate developed against tuberculosis by scientists at the Max Planck Institute for Infection Biology, was also protective against COVID-19. As a result, COVID-19 hospitalizations and ICU admissions were reduced after VPM1002 vaccination, and the VPM1002 vaccine was considered to be well tolerated and protective against severe respiratory disease in the elderly.

ii. Local manufacturing system

A) Pharmaceutical manufacturing base

India is the third largest producer of pharmaceuticals in the world, with a total of 3,000 pharmaceutical companies and a total of 10,500 pharmaceutical manufacturing sectors. India has several government-owned pharmaceutical companies, and the companies shown in the chart below are Center Public Sector Undertaking (CPSU), which are funded by the Government of India.

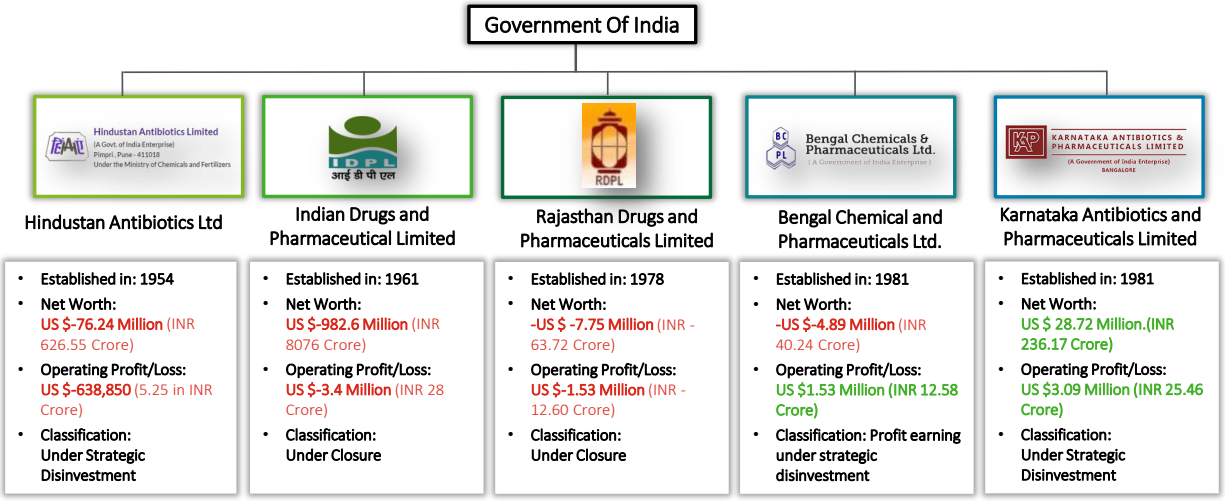


Figure 2-5 Public Industrial Centres funded by the government of India

The Central Drugs Standard Control Organization (CDSCO) is India's regulatory body responsible for approving new drugs, and there are 865 CDSCO approved manufacturing plants. These include Pfizer Healthcare India Private Limited, Emcure Pharmaceuticals Limited, and Cipla Limited as listed below.

- Pfizer Healthcare India Private Limited manufacturing site situated in Aurangabad, Maharashtra
- Emcure Pharmaceuticals Limited manufacturing site located in Pune, Maharashtra
- GSK Pharmaceutical Limited Manufacturing unit in Nashik, Maharashtra
- Cipla Manufacturing plant in North Goa, Goa

India has a large number of industry associations, and the organizations and groups shown in the chart below are important stakeholders in clinical trials in India, and India is bringing together all of these organizations and groups to improve the way healthcare works through innovation. The Pharmaceutical Alliance of India (IPA) and the Pharmaceutical Manufacturers Association of India (OPPI) are representative bodies of the research and development-oriented pharmaceutical industry in India working with various stakeholders, including the government and pharmaceutical companies, to find long-term solutions while supporting the country's healthcare goals.

Asia Partnership Conference of Pharmaceutical Associations (APAC)	• APAC is an industry-led initiative comprising thirteen R&D-based pharmaceutical associations from eleven Asian economies joining forces to achieve the mission: "to expedite the launch of innovative medicines for the people of Asia" • APAC has provided unique chances for constructive dialogue among regulators, academics, and industry on topical subjects to improve "Access to Innovative Medicines" (ATIM) in Asia since its inception in 2012 • Its members include Organization of Pharmaceutical Producers of India (OPPI) and Japan Pharmaceutical Manufacturers Association (JPMA)
Indian Pharmaceutical Alliance (IPA)	• The Indian Pharmaceutical Alliance (IPA) is an association that represents India's research-based pharmaceutical industries. It is a consortium of 24 major Indian pharmaceutical businesses • IPA member companies account for: ➢ Over 85% of the private sector investment in pharmaceutical R&D ➢ Over 80% of the country's exports of drugs & pharmaceuticals ➢ 62% of price-controlled medicines ➢ Over 57% of the domestic market's sales
The Indian Society for Clinical Research (ISCR)	• The Indian Society for Clinical Research (ISCR) is an association of Indian clinical research professionals registered under the Societies Registration Act (1860) • The Society brings together all those involved in clinical research in India and serves as a venue for information sharing and learning • ISCR's mission is to raise awareness of clinical research as a specialty in India and to assist its growth while promoting the highest quality and ethical standards
Indian Drug Manufacturers' Association (IDMA)	• The Indian Drug Manufacturers' Association (IDMA), established in 1961, is the industry association of major pharmaceutical companies based out of India • It collaborates with the Indian government on industry development goals and represents the industry on key issues like pricing, regulatory affairs, and other policy concerns • More than 1,000 companies that make formulations and Active Pharmaceutical Ingredients (API) are members of IDMA
Indian Pharmaceutical Association (IPA)	• The Indian Pharmaceutical Association (IPA) is a national organization that represents over one million pharmacists and pharmaceutical scientists from industry, academia, regulatory, hospital, and community pharmacy. Its mission is to address India's health-care needs • The IPA is a non-governmental organization with official ties to the FIP and the WHO. IPA is a member of the Drug Technical Advisory Board (DTAB) of India's Ministry of Health and Family Welfare • IPA works to support the development of the pharmacy profession, through practice and emerging scientific innovations, as well as the development of the pharmacy workforce
Organization of Pharmaceutical Producers of India (OPPI)	• The Organization of Pharmaceutical Producers of India (OPPI) was founded in 1965 to represent India's research-based pharmaceutical industries • They support India's healthcare goals and work with the government and other stakeholders to find long-term solutions

Figure 2-6 Organizations and associations representing the Indian pharmaceutical industry

In addition, there are pharmaceutical organizations such as the Indian Association of Active Pharmaceutical Manufacturers (BDMAI), Federation of Pharmaceutical Manufacturers (FOPE), Ayurveda Pharmaceutical Manufacturers Association (ADMA) and Ministry of Pharmaceutical Affairs as listed below. For example, the API Manufacturers Association of India serves as a catalyst between the government and industry on various issues for industry growth and as a common forum for developing views on all matters, including national, economic, financial, commercial and related policies, on the growth of the API industry.

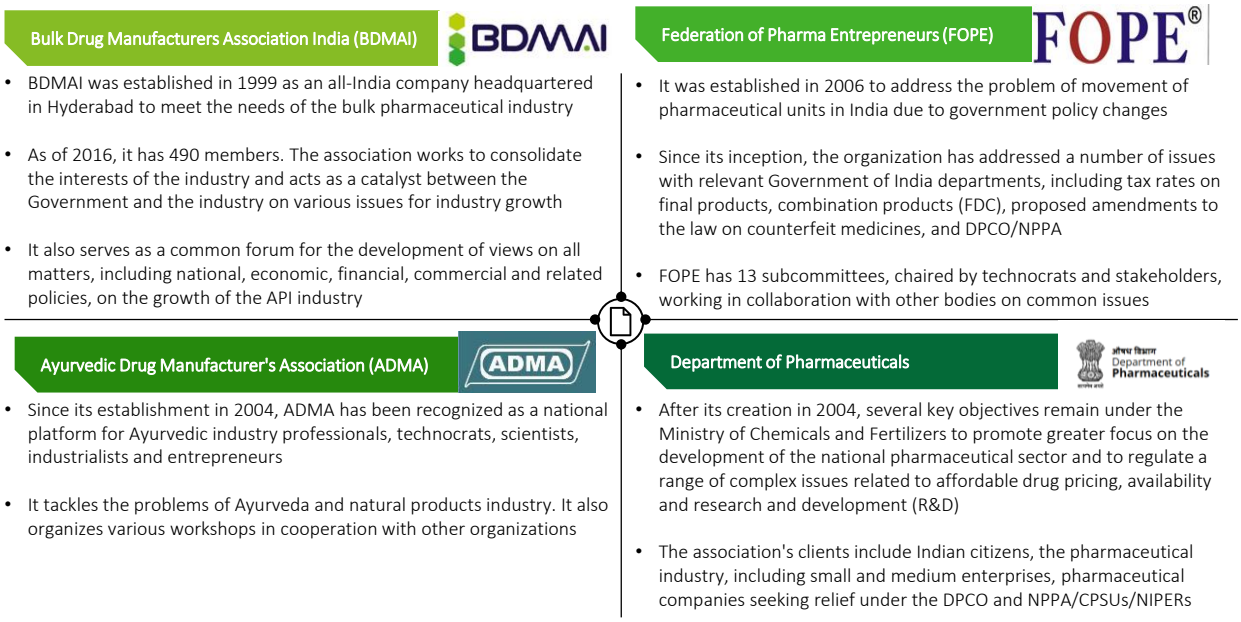


Figure 2-7 List of pharmaceutical organizations in India

B) Types and volumes of locally manufactured drugs

There are 3,889 drugs approved by India's Central Drug Control Organization (CDSCO), as of 2023.

The five center public sector undertakings (CPSU) listed below manufactured a variety of medicines, including generic and branded drugs, through dedicated factories spread across the country. However, in 2016, due to budget constraints, the government closed down Indian Drugs & Pharmaceuticals Limited (IDPL) and Rajasthan Drugs & Pharmaceuticals Limited (RDPL) and disinvested in the remaining 3 PSUs.

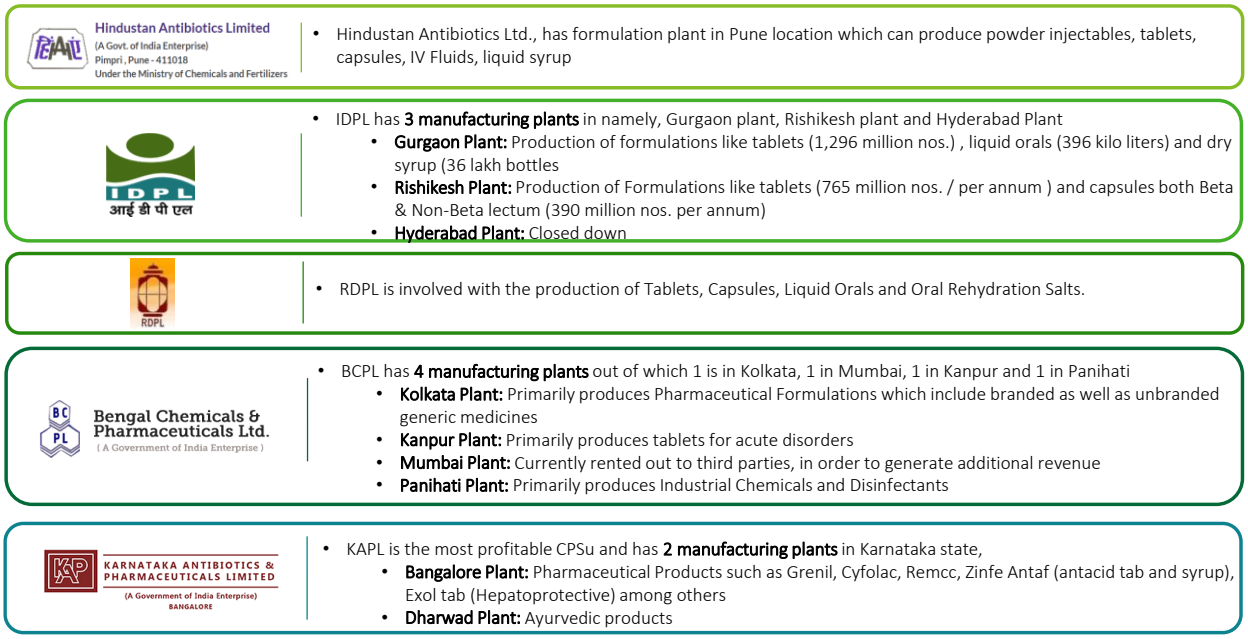


Figure 2-8 Equipment overview and capacity of the CPSUs

Indian pharmaceutical companies are shown in the table below. According to the 2022 earnings report, Sun Pharma is the largest pharmaceutical company in India with more than 8% market share.

Private companies in India also have large manufacturing capacity spread across the country for research and development and API manufacturing. As shown in the table below, each company handles a wide

variety of pharmaceutical products, including specialty drugs, generic drugs, over-the-counter drugs, and biosimilars, and manufactures them at its manufacturing sites across the country.

Table 2-2 Indian pharmaceutical companies with pharmaceutical manufacturing plants

Company	Year of Establishment	Revenue (in mn US $)	Key Offerings		Manufacturing Facilities in India
SUN PHARMA	1983	**4,141.47** (2021)	• Specialty Medications • Generic Medications • Over-The-Counter (OTC) Medications	• Active Pharmaceutical Ingredients (APIs) • Anti Retro Viral Medications	• **15** Finishing Dosage Manufacturing Units • **9** API facilities in India
Dr. Reddy's	1990	**858.87** (2021)	• Generic Active Pharmaceutical Ingredients (APIs)	• Nutraceuticals • Custom Synthesis	• **2** Manufacturing facilities – Hyderabad and Vishakhapatnam
Cipla	1935	**2,398.37** (2021)	• Generic Medications • Over-The-Counter (OTC) Medications • Respiratory Therapeutics	• Active Pharmaceutical Ingredients (APIs) • Oncology Therapeutics	• **34** manufacturing units spread across **8 locations**
Dr.Reddy's	1984	**2,830** (2021)	• Branded Generics • Aurigene Pharmaceutical Services	• Active Pharmaceutical Ingredients (APIs) • Biologics	• **6** manufacturing units in India
glenmark	1977	**1,654** (2021)	• Formulations	• Active Pharmaceutical Ingredients (APIs)	• **7** manufacturing units in India
torrent PHARMA	1959	**1,065.22** (2021)	• Central Nervous System (CNS) Therapeutic • Gastro-Intestinal (GI) Therapeutics	• Women healthcare (WHC) • Cardiovascular (CV) Therapeutics	• **7** manufacturing units in India
ALKEM	1973	**1,331.59** (2021)	• Rx Products • Alkem Generics • Gastro-Intestinal (GI) Therapeutics	• OTC Products • Central Nervous System (CNS) Therapeutic	• **19** manufacturing units in India
LUPIN	1968	**2,054.35** (2021)	• Biosimilars • Active Pharmaceutical Ingredients (APIs) • Over-The-Counter (OTC) Medications	• Generics • Specialty Medication • Therapeutics	• **12** manufacturing units in India

(2) Issues in target countries (regarding capacity to conduct clinical trials and local manufacturing)

i. Securing raw materials for manufacturing pharmaceuticals and vaccines

India imports most of its medicines and vaccines from the United States and Europe, as well as much of the materials and equipment needed for clinical trials. Even if a local supplier is found, the lead time is very long due to the complicated customs procedures, and the import process is generally delayed. During a pandemic, it is difficult to import raw materials and equipment for pharmaceutical manufacturing, and there is a risk of clinical trials and manufacturing stoppages. The COVID-19 pandemic has also made clinical trials and local manufacturing of vaccines and drugs difficult, prompting the Indian government to shift its reliance on imported raw materials to local manufacturing and procurement.

ii. Vulnerability of the quality control system

Known as the "pharmacy of the world," India is the third largest producer of medicines, supplying 60% of global vaccine demand and is expected to reach a $65 billion market by 2024[12]. On the other hand, quality standards have been questioned by some pharmaceutical companies, and there have been cases where requirements have not been met with regards to the practices and quality of medicines manufactured and supplied. 46 pharmaceutical companies had their licenses revoked in 2021, despite ongoing efforts by regulatory agencies to regulate the review of drug applications and to inspect drug manufacturing facilities for compliance with current Good Manufacturing Practices (GMPs).

Between 2022 and the first half of 2023, 9 warning letters were issued to Indian drug manufacturers by the US FDA, a situation that could affect drug imports from India into the US. In fact, since 2009, India's rate of US FDA inspections has been 83%, lagging behind China's 90%, European Union's 98% and the

[12] INVEST INDIA "India Pharmaceuticals" (https://www.investindia.gov.in/ja-jp/sector/pharmaceuticals)

United States' 93%[13]. In 2021, the WHO also issued a Toxic Substances Detection Report and Warning Notice to the DCGI, alleging that 4 cough syrups from New Delhi-based Maiden Pharmaceuticals were linked to kidney damage and 66 deaths in Gambian children, and that the main cause was suspected to be the use of diethylene alcohol or drugs contaminated with ethylene alcohol[14].

In India, the quality management system is currently weak as there is nobody responsible for quality management assessment delegated to regulatory bodies to ensure quality. Currently, Indian pharmaceutical companies have to comply with various standards (state-level GMP, WHO-approved GMP, USFDA) to obtain drug approval, but they are not members of "Pharmaceutical Inspection Convention and Pharmaceutical Inspection Co-operation Scheme (PIC/S)" or "International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH)". There is a need for streamlined regulation to ensure quality and accelerate approval, reduce duplication of inspections by multiple regulatory bodies, and disseminate high-quality medicines in an efficient and cost-effective manner.

2.1.3 Reasearch results on initiatives taken by aid agencies, research institutes, and companies in other countries, including the target country

(1) Overview of promotion of local manufacturing of vaccines and pharmaceuticals

i. Domestic policies and measures to promote local manufacturing

To promote local manufacturing of vaccine medicines, in 2020, the Government of India has launched three support schemes, described in the figure below. The aim of these policies is to minimize dependence on imported bulk drugs from abroad, incentivize global and domestic players, and enhance investment and manufacturing. The three policies are Production Linked Incentive Scheme for Bulk Drugs (PLI 1.0), Production Linked Incentive Scheme for Pharmaceuticals (PLI 2.0), and the Bulk Drug Park Scheme, which aim to promote local manufacturing capacity in the country, make API manufacturing self-sustaining, and revitalize the industry, respectively.

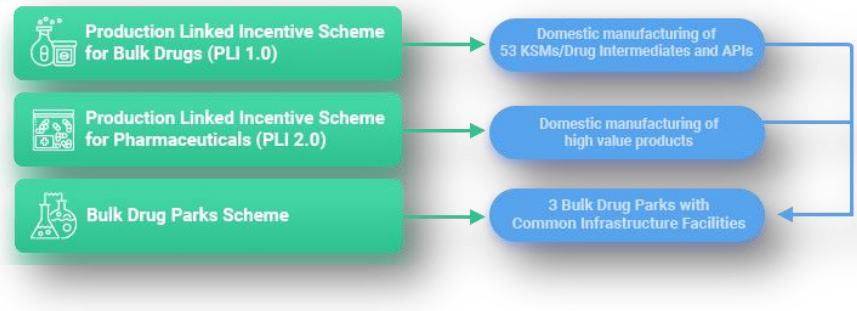


Figure 2-9 Policies to promote local manufacturing of vaccines and pharmaceuticals

The objective of the API Production Linkage Incentive Scheme (PLI 1.0) is to attract large investments in bulk drugs[15]/APIs and promote the domestic manufacturing of key starting materials (KSM)[16], bulk drugs and APIs in India, thereby reducing India's import dependency on critical APIs. The period of the production-linked incentive scheme is from FY 2020-21 to FY 2029- 30, and the eligibility criteria for the scheme is to cover greenfield projects. A production-linked incentive of up to US $849 million (INR 69

[13] Deccan Herald " FDA uncovers failures in Indian pharma factories" (https://www.deccanherald.com/opinion/us-fda-uncovers-failures-in-indian-pharma-factories-1225810.html)

[14] Reuters "India Tests Maiden Syrup, Suspects Death From Kidney Injury" (https://jp.reuters.com/article/idUSKBN2R20GP/)

[15] Ingredients and intermediates of pharmaceuticals

[16] Key Starting Material: a raw material, intermediate, or API used in the manufacture of the API and incorporated as an important component of the API structure.

billion) was also approved for 4 key segments: major fermentation-based KSM/pharmaceutical intermediates, niche fermentation-based KSM/pharmaceutical intermediates/APLs, major chemosynthesis-based KSM/drug intermediates, and other chemosynthesis-based KSM/drug intermediates/APLs.

The objective of the Pharmaceutical Production Linked Incentive Scheme (PLI 2.0) is to strengthen India's manufacturing capacity by increasing investment and manufacturing in this sector and contributing to product diversification into high value commodities in the pharmaceutical sector. The period of the incentive scheme is from FY 2020 -21 to FY 2028-29, and the target segments are classified as Class 1: biopharmaceuticals, complex generics, patented drugs or drugs about to expire; Class 2: active pharmaceutical ingredients/main starting materials/drug intermediates; and Class 3 (drugs not covered by Classes 1 and 2). The total incentives (including administrative expenditures) under the scheme as incentives amount to approximately US $1.8 billion (INR 150 billion), with incentive allocations of US $1.3 billion (INR 110 billion) for Group A, US $275 million (INR 22.5 billion) for Group B and US $214 million (INR 17.5 billion) for Group C[17].

The objective of the Bulk Drug Park Scheme is to make India self-reliant in bulk medicines and to reduce the manufacturing cost of bulk medicines. The scheme, which runs from FY 2020-21 to FY 2024-25, funds infrastructure facilities common to the 3 bulk drug parks, requiring US $366 million (INR 30 billion) from 2020 to 2021. Note that the maximum grant assistance for a single bulk drug park is capped at US $122 million (INR 10 billion).

According to a 2021 economic report by the Ministry of Finance of India, the Indian pharmaceutical market was estimated at about US $42 billion (6 trillion yen), with a compound annual growth rate of about 17.7%. The growth of the pharmaceutical market in India is expected to continue. Behind this steady industry growth are high economic growth (approximately 5~10% annual GDP growth since 2005), an increase in national income, expansion of the middle class, improvements in the health care system, and changes in the disease structure. In addition to the domestic market, India also has a global presence in pharmaceutical exports, with an estimated pharmaceutical output of over US $30 billion, of which about half is reported to be exported (30~40% to the United States). India's exports of pharmaceuticals and precision chemicals between 2015 and 2016 were reported to be around US $17 billion, while imports of pharmaceuticals were estimated to be around US $4 billion during the same period. Based on exports, which are several times larger than imports, India's trade in pharmaceuticals exceeds exports by more than US $10 billion, in contrast to India's overall trade balance, which exceeds imports by US $100 billion. In India, the share of primary industry in GDP is higher than that of Western countries, and secondary industry is still around 20%, and the share of secondary industry is lower than that of emerging countries such as Russia and China. This suggests that pharmaceuticals, which have a high global presence, have become a major export industry in India at a time when India's industrialization is relatively low. This industrial structure itself has been a factor in supporting local manufacturing of pharmaceuticals throughout the country, and a major factor has been the fact that overseas companies have been allowed to acquire Indian pharmaceutical manufacturers continuously since 2002. For example, Abott in the US became a top-grossing company in India in 2010 when it acquired the generics division from local giant, Piramal Healthcare. On the other hand, some point out that Indian pharmaceutical manufacturers are making strategic profits from sales in their mid-long-term management strategies to invest in new drugs. In this way, acquisitions by foreign companies have become a means of boosting financing, expanding business, and technology transfer, and have been a driving factor in increasing the pharmaceutical manufacturing share.

[17] Applicants in Group A are those with global pharmaceutical manufacturing revenues (FY 2019–20) of INR 50 billion or more. Group B is an applicant whose global manufacturing revenue (FY 2019–20) of pharmaceuticals is between INR 5 billion (inclusive) and INR 50 billion. Group C is an applicant whose global pharmaceutical manufacturing revenue (FY 2019–20) is less than INR 5 billion. Within this group, a subgroup for MSMEs will be created, taking into account the unique challenges and circumstances of MSMEs.

(2) Donor initiatives to support clinical trials and local manufacturing of vaccines and other pharmaceutical products in target countries

i. Trends of supports from the United States

The Department of Biotechnology (heireinafter referred to as DBT) under Indian Ministry of Science and Technology, is implementing several joint programs with the National Institutes of Health (hereinafter referred to as NIH) [18]. For example, the Indo-US Vaccine Action Programme (hereinafter referred to as VAP) is a bilateral program between DBT and the National Institute of Allergy and Infectious Diseases (hereinafter referred to as NIAID) that primarily supports a wide range of activities related to new/improved vaccines. The program has been in place since 1987 and is positioned as an internationally recognized model for bilateral programs in biomedical research.

VAP accomplishments to date include the following[19].

- Under the VAP, the Candidate Vaccine Advisory Committee (CVAC) was established in 2016 to review vaccine candidates for dengue, tuberculosis, chikungunya fever, RSV, influenza, and COVID-19 and provide further support to advance the development pipeline.
- Under the VAP, an initiative called Regional Prospective Observational Research on Tuberculosis ("RePORT-India") was launched to promote TB research in India, including basic and applied research for the development of new diagnostic methods and identification of new improved biomarkers for targeted therapy. In addition, approximately 100 publications were created as a result of projects supported under the RePORT initiative.
- Collaborative research on the immunology of infectious diseases such as typhoid fever, dengue fever, Japanese encephalitis, hepatitis B, and tuberculosis was supported, and 16 papers were published with this support.
- Adjuvant[20] Collaborations are being promoted and vaccines are being developed. One successful example is the development of COVAXIN, an inactivated COVID-19 vaccine candidate currently under development by Bharat Biotech.

ii. Trends of supports from the United Kingdom

India and the United Kingdom are deepening their scientific research collaboration in the area of Antimicrobial Resistance (hereinafter referred to as AMR) control, with five projects planned for September 2020 that will address AMR control, led by UK Research and Innovation (UKRI) and DBT. The UK is contributing £4 million from the UK Research and Innovation Fund for International Collaboration, and India is also contributing funds (£8 million total). One project example is Advanced Metagenomics, Sensors and Photocatalysis for Antimicrobial Resistance Elimination (hereinafter referred to as AMSPARE). AMSPARE is a project that brings together experts in sensor technology and water treatment from the Indian Institute of Technology Bombay and experts in policy, industry regulation and research processes from the University of West Scotland to study AMR[21].

iii. Trends of supports from Europe

Under the India - European Union Science and Technology Cooperation Agreement, the Department of Science and Technology (hereinafter referred to as DST) of Indian Ministry of Science and Technology and the European Commission (hereinafter referred to as EC) have agreed to jointly fund certain joint India-EU research and technology development and deployment project proposals. This allows Indian research institutes and universities in the fields of science, technology and innovation to team up with European

[18] https://dbtindia.gov.in/schemes-programmes/international-cooperation/bilateralmultilateral-cooperations

[19] MINISTRY OF SCIENCE & TECHNOLOGY , GOVERNMENT OF INDIA, Department of Biotechnology HP (https://dbtindia.gov.in/scientific-directorates/global-innovations/global-innovations)

[20] Adjuvant is derived from the Latin word 'adjuvare' meaning 'to help' and is a substance that is administered with a vaccine to increase its effectiveness (immunogenicity).

[21] GOV.UK “UK and India join forces on new £8 million research”(https://www.gov.uk/government/news/uk-and-india-join-forces-on-new-8-million-research)

partner institutions to participate in EU research funding program (Horizon 2020[22]) projects and maximize the use of EU research data, chemical research networks and other resources. Also, DST and EC have also agreed to establish a joint funding mechanism to support joint projects between European and Indian universities and research institutions[23].

The EU and its Member States were also actively providing financial and other assistance to India during the COVID-19 pandemic. In the health sector, for example, the European Investment Bank was scheduled to provide a loan of 300 million euros to focus on medium- and long-term investments in India to pay for pandemic preparedness and to strengthen the public health care system to ensure early prevention, detection, and containment of future pandemics. Germany, through the German Agency for International Cooperation (hereinafter referred to as GIZ), in cooperation with the German national development bank "KreditanstaltfürWiederaufbau" (hereinafter referred to as "KfW") and UNICEF, provided EUR 20 million in aid. The funds were mainly used for capacity building for inspections and infrastructure development to address future challenges. In addition, the French development agency Agence Française de Développement ("AFD"), through Proparco, provided EUR 20 million to support the development of medical facilities in South and Southeast Asia.

(3) Initiatives of European and American universities, research institutes and pharmaceutical companies

i. Initiatives of US universities

Johns Hopkins University (hereinafter referred to as JHU) and the Gupta-Klinsky India Institute (hereinafter referred to as GKII) collaborate with Indian experts and partners primarily across the Indian government, academia, civil society, and private sector to solve issues in India and abroad through research, education, policy and practice. More than 165 JHU faculty members have partnered and collaborated with experts from more than 100 Indian institutions.[24] Health areas of focus for GKII include infectious disease research and clinical processes, maternal and child health, health systems strengthening, and non-communicable diseases. In 2022, the Center for Infectious Diseases in India (hereinafter referred to as CIDI) will be established under the auspices of GKII, with priority research areas including HIV, TB, hepatitis, COVID-19 and other infectious diseases, antimicrobial resistance, cardiovascular disease, diabetes, and malnutrition[25].

JHU also has an organization called IndoUS Clinical Research (IndoUS team). The IndoUS team is based in both Baltimore and New Delhi and has areas of expertise in international clinical research and implementation science[26] and education in the public health field of infectious diseases, HIV/AIDS, TB, vaccine preventable diseases, drug-resistant bacterial infections, and most recently COVID-19. Since 2003, the Indo-US team has been involved in several Indo-JHU and international research collaborations, primarily in India. The Indo-US team is also affiliated with leading medical research institutions in India[27] and actively participates in the VAP-sponsored India RePORT TB Research Consortium[28], among others[29]. One of the Indian TB research consortia of RePORT is the Cohort for Tuberculosis Research by the Indo-US Medical Partnership, consisting primarily of JHU, Byramjee-Jeejeebhoy Government Medical College, and the National Institute for Research and Technology. c-TRIUMPH is studying factors affecting

[22] Horizon 2020 is the EU's research and innovation funding program for 2014-2020 with a budget of approximately EUR 80 billion.

[23] 「Research & Innovation Cooperation between DST and the EU under HORIZON 2020 」

[24] ohns Hopkins Gupta-Klinsky India Institute HP

[25] Johns Hopkins Gupta-Klinsky India Institute 「Bringing the Best of Hopkins and India Together to Benefit the Worl」（https://indiainstitute.jhu.edu/wp-content/uploads/2022/11/JH-India-Institute-2022-8.5x11.pdf）

[26] Implementation science refers to the scientific study of methods and strategies for the everyday use of evidence-based practices and research by practitioners and policy makers.

[27] For example,Byramjee-Jeejeebhoy Government Medical College 、DY Patil、Hinduja Hospital、King Edward Memorial Hospital、Bharati Vidyapeeth、National Institute for Research in Tuberculosis 、JIPMER、Christian Medical College、Medanta、Indian Institutes of Science Education and Research、YRG Care、Indian Institutes of Technology etc

[28] The consortium is funded by the National Institutes of Health (NIH) and the Biotechnology Agency of the Indian Ministry of Science and Technology.

[29] Johns Hopkinds Medicine, “IndoUS Clinical Research“ (https://www.hopkinsmedicine.org/research/labs/indous-clinical-research)

treatment, active TB, and TB transmission[30].

ii. Initiatives of UK universities

In May 2022, the world's largest clinical trial investigating inpatient treatment options for the COVID-19 (RECOVERY trial[31]) was launched in India, and its Indian rollout was made possible by a partnership between Oxford University, the British government and the Indian Council for Medical Research (hereinafter referred to as ICMR). This makes India the seventh country to conduct the RECOVERY trial, following the start of the UK trial in March 2020, in addition to Ghana, Indonesia, Nepal, South Africa and Vietnam. The study was started with five Indian hospitals and will expand to about 40 sites in India in the coming months (as of June 2022). Current locations include AIIMS Rishikesh, Father Muller Medical College Mangalore, D.Y. Patil Medical College Pune, Sagore Dutta Medical College Kolkata and Government Medical College Kolkata[32].

2.2 Vietnam

2.2.1 Legal systems and procedures in target countries

(1) Related policies and legal systems

Two laws form the basis of pharmaceutical regulation in Vietnam: the new Pharmaceutical Affairs Act of 2017 and the old Pharmaceutical Affairs Act of 2005. In addition, In addition, There are Decree 54, which is a detailed regulation implementing part of the New Pharmaceutical Affairs Act, and notifications issued by ministries to determine and issue detailed regulations (for example, there are notifications on the quality of drugs and their materials, and on pharmaceutical clinical trials) [33].

Vietnam's pharmaceutical-related regulations in Vietnam are governed by the Drug Administration of Vietnam (Hereinafter referred to as DAV, in charge of overall pharmaceutical affairs) which is an internal agency of the Ministry of Health, the Administration of Science Technology & Education (in charge of clinical trials of new drugs), and the Traditional Medicines Administration (in charge of regulation of traditional medicines). The Drug Control Administration, the National Institutes of Drug Quality Control, and the Pharmaceutical Inspectorate, which is also an internal agency of the Ministry of Health, are the three agencies responsible for the implementation of drug control. These three agencies responsible for implementing drug control are similarly constituted at the local government level in Vietnam.

i. Drug approval system

The figure below shows the process for registration of in vitro diagnostic biologics and other pharmaceuticals (except for locally manufactured medicines for external use)[34].

[30] Jonhs Hoplind Center for Global Health “Bringing together people and opportunities to solve global health problems” (https://hopkinsglobalhealth.org/faculty-research/project-map/c-triumph--cohort-for-tb-research-by-the-indo-us-medical-partnership/)

[31] Recovery trials are clinical trials that test existing drugs and therapies that have been used to treat common diseases to see if they are also effective for COVID-19.
[32] RECOVERY “RECOVERY Trial launched in India “ (https://www.recoverytrial.net/news/recovery-trial-launched-in-india)

[33] Pharmaceuticals and Medical Devices Regulatory Information Collection and Analysis Project Report for 2020 (Vietnam), FDA

[34] Pharmaceuticals and Medical Devices Agency, "Report of the 2020 Project for the Collection and Analysis of Regulatory Information for Drugs and Medical Devices in Asian Countries (Additional Survey)"

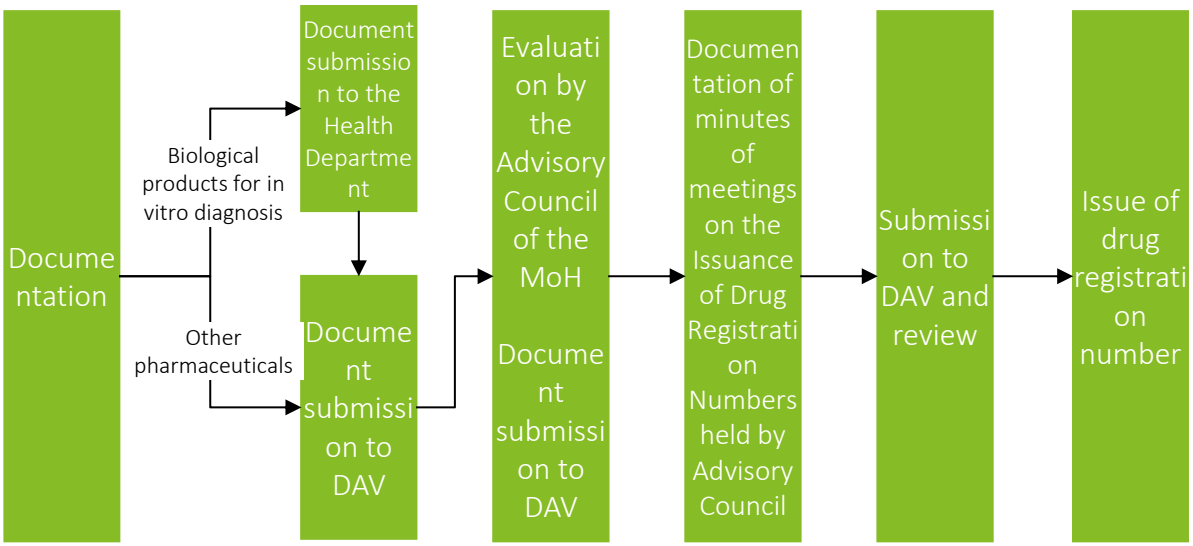


Figure 2-10 Drug Registration Process in Vietnam

For drugs newly registered in Vietnam, clinical trials must be conducted except in the following three cases[35]:

1) Generic drugs
2) The countries of origin or reference countries are the United Kingdom, France, Germany, the United States, Japan, Australia, Canada, or the European Medicines Agency, and the product has been in market for at least five years and has been confirmed as safe and effective by the authorities in these countries.
3) Foreign-made drugs that have obtained a distribution registration number in Vietnam and have been legally distributed in the country of origin for at least five years, even if the new designation, route of administration, or dosage form has been changed or supplemented.

In addition, if an overseas company is applying for registration of a pharmaceutical product in Vietnam for the first time and has not obtained a certificate of registration for the pharmaceutical product or raw material in Vietnam, the company must undergo a GMP inspection by the Vietnamese authorities.

ii. Regulations concerning clinical trials

Clinical trials in Vietnam are regulated by Circular 3. In addition, compliance with Vietnam's own GCP and compliance with ICH-GCP are also permitted.

According to annoucement by the Ministry of Health in Vietnam, clinical trial sites are required to apply for a new GCP standard whenever there is any change in the site. In addition, GCP inspections of clinical trial sites are first conducted to obtain a GCP certificate of compliance, followed by inspections every three years.

iii. Systems and regulations for local manufacturing

In Vietnam, a regulatory agency under the Ministry of Health enforces regulations on local manufacturing based on the WHO's GMP standards (WHO-GMP). Pharmaceutical companies must consider four requirements to comply with the regulations: human resources, design and enforcement, clean environment, and product distribution. One of the benefits of these standards is that in addition to being able to prove the capabilities of each company, it will also help ensure the quality and safety of drugs. The specific content of each guideline is shown in the chart below. The Drug Administration conducts GMP inspections as the inspecting authority and licenses domestic pharmaceutical companies' manufacturing

[35] the Ministry of Health, Labour and Welfare "2014 Review System for Drugs and Medical Devices Overseas, Review Status Survey and Analysis Report"

sites by issuing GMP compliance certificates. The license is valid for two years. On the other hand, foreign pharmaceutical companies are also required to meet WHO-GMP standars or submit a certificate that meets equivalent requirements. GMP inspections are not conducted for foreign pharmaceutical companies once a certificate is submitted. In Vietnam, there are no restrictions on foreign capital for foreign pharmaceutical companies, and local manufacturing in Vietnam by 100% foreign capital is possible.

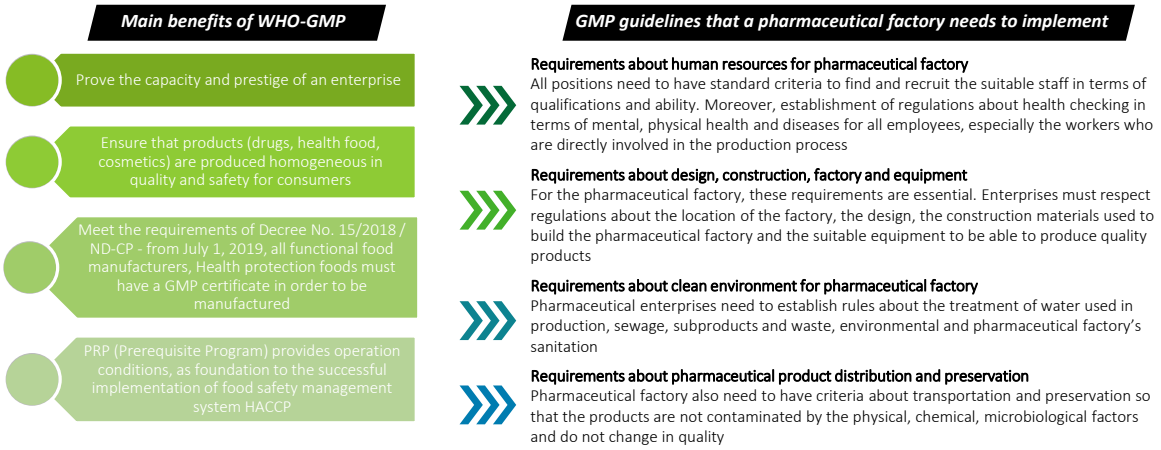


Figure 2-11 Requirements for GMP guidelines

iv. Policy trends in clinical trials and manufacturing

Recent changes in regulations for clinical trials and manufacturing are aimed at easing regulations and speeding up the regulatory process in order to promote the manufacture and sales of drugs in Vietnam (including entry from overseas). Here are some examples of recent changes:

- New regulations for drug registration

In 2022, instead of Circular No: 32/2018/TT-BYT, Vietnam's Ministry of Health issued a new Circular No: 08/2022/TT-BYT to revise drug registration regulations in the country. The revised regulations streamline the drug registration process by simplifying it and minimizing the types of accompanying registration documents required to be submitted.

- Mitigation of requirements for drug certificates

Based on the government Circular issued in 2022, the Certificate of Pharmaceutical Product (CPP) required of pharmaceutical manufacturers are only required to include the content specified in the WHO template, and in principle, no other additional content is required.

- Equalization of treatment for EU-based pharmaceutical companies

In Circular No. 32, the Vietnamese government classified the regulatory authorities of EU member countries into two categories: Reference Regulatory Authority (hereinafter referred to as "RRA") and Stringent Regulatory Authority (hereinafter referred to as "SRA"), and pharmaceutical companies based in EU member countries classified as RRA were given preferential treatment, including exemption from clinical trials and simplified procedures for drug registration. On the other hand, EU member states classified as SRA, which are required to have stricter regulatory processes due to this differentiation, sometimes suffered disadvantages such as reduced opportunities to participate in government procurement. To tackle this issue, the new legislation now recognizes all EU member state regulators as RRAs, making it easier for medicines from all EU member states to participate in a simpler and faster registration process and government procurement.

(2) Process from application to approval for clinical trials and local manufacturing

i. Process from application to approval for clinical trials

Clinical trials in Vietnam are regulated by the Administration of Science, Technology, and Training (hereinafter referred to as ASTT) and the Ethical Evaluation Committee in Biomedical Research ("EECBR") under the Ministry of Health. The ASTT reviews clinical trial documents, organizes meetings with the EECBR, and reviews the Investigational Brouchure (IB) portion of the application materials, The EECBR approves protocols and applications. The ASTT is also responsible for registering clinical research organizations (CROs) that support clinical research and provide other research services; the EECBR approves protocols and applications.

As shown in the chart below, these regulatory clinical trial approval processes take approximately 60 days to complete and consist of four steps: document submission to the ASTT, coordination with the investigator, committee review, and approval by the Department of Health. The entire regulatory review and approval process takes approximately 60 business days from the date the sponsor and investigator submit documents to the ASTT and EECBR.

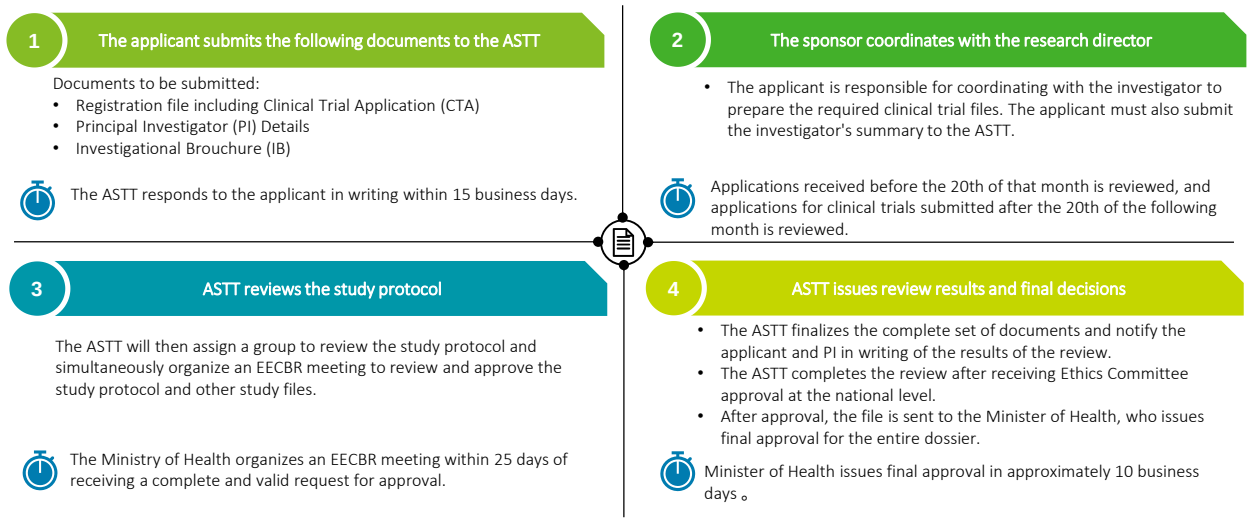


Figure 2-12 Vietnamese clinical trial approval process

The following table lists the documents required for clinical trial applications.

Table 2-3 Documents required for Clinical Trial Applications

Initial documents	Product Information	Other documents that should be submitted
• Registration files that include the clinical trial application (CTA) form • Principal investigator (PI) details • Host institution proposal • Investigator's Brochure (IB)	• Documentation of investigational product that includes general information about clinical investigational drug: ➢ Name and ingredients ➢ Physical and chemical properties ➢ Manufacturing and other relevant data	• Import license for the shipment of an investigational product used in the trial from the MOH's Drug Administration of Vietnam • After securing EECBR approval, the sponsor needs to sign a letter of agreement with the participating host institution(s) before the trial begins

In the case of Vietnam, clinical trial data conducted abroad can be used. However, insufficient clinical trial data on Asian race would necessitate conducting a phase III clinical trial in Vietnam[36].

[36] National Institute for Allegy and Infectious Diseases, "Clinical Research Regulation For Vietnam" (https://clinregs.niaid.nih.gov/country/vietnam#submission_content)

ii. Process from application to approval for local manufacturing

The DAV is the main regulatory agency that grants licenses for pharmaceutical manufacturing in Vietnam, and the main regulation on pharmaceutical manufacturing in Vietnam, Law on Pharmacy No 105/2016 QH 13, was enacted in 2017. Companies established in Vietnam may apply for a license to manufacture or trade in pharmaceutical products. After approval of the license from the DAV, companies may submit an application to manufacture or import pharmaceutical products.

To obtain a pharmaceutical manufacturing license, a pharmaceutical manufacturer must obtain the following certificates:

- Business registration certificate:
  Essential legal certificate required to establish a business in Vietnam
- Investment register:
  It provides information on registered investment projects involving foreign investors through foreign direct investment (FDI). In the case of a foreign-owned company, it must be submitted.
- Certificate of eligibility (certificate of conditions) for the terms and conditions of business of drugs:
  Since pharmaceutical manufacturing is a restricted business line in Vietnam, manufacturers are required to obtain a certificate of conditions.
- GMP certificate:
  Manufacturers operating in Vietnam are required to apply the principles and standards of Good Manufacturing Practice (GMP) issued by WHO and apply for registration in accordance with the WHO/PIC/S/EU GMP or the GMP issued by the SRA. Certification of GMP inspection need to be renewed every three years. The DAV is responsible for reviewing and approving the certificate.

The figure below also shows the normal application process for a license to manufacture drugs in Vietnam. This process usually takes 2-3 months.

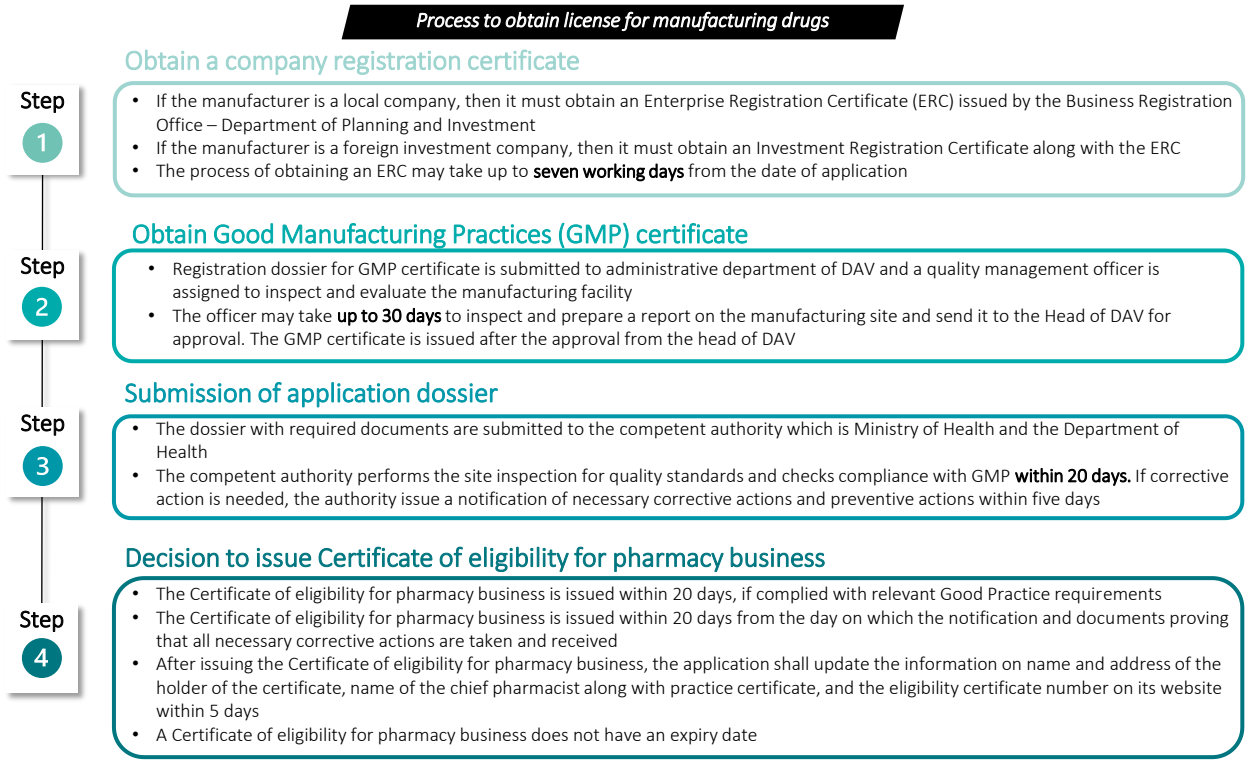


Figure 2-13 Process for obtaining drug manufacturing licenses in Vietnam

(3) Issues in target countries (Policies, regulations and legal systems for clinical trials and local manufacturing)

i. Regulations complied with international standards

The approval process for clinical trials needs to be improved to accelerate efficiency in line with international standards. Approval for clinical trials can take up to three years. In particular, the emergency regulatory measures necessary for rapid vaccine development and manufacturing during an infectious disease pandemic are incomplete and inadequately maintained for emergency situations.

In addition, prolonged regulatory processes and inconsistencies with foreign pharmaceutical regulations, including those of ASEAN countries, could undermine the entry of international joint clinical trials and the ability to compete in foreign markets[37]. For example, when a pharmaceutical product or vaccine is exported, a clinical evaluation is required for registration of the product in the destination country. In many cases, however, the results of clinical trials conducted in Vietnam are not accepted as a clinical evaluation, and the need for implementation of clinical evaluation in the exporting country is costly to Vietnamese pharmaceutical institutions and companies in terms of human and material resources, creating a barrier to exporting pharmaceutical products and vaccines.

ii. Needs for further government investment

In Vietnam, the pharmaceutical market is expanding due to an increase in the number of people with medical insurance coverage and a growing elderly population and is expected to grow to approximately US$6.2-6.4 billion per year in 2021, a growth rate of approximately 23% over the past four years. On the other hand, the country's drug development capacity is still limited to generic drugs, simplified dosage forms, and functional foods. Despite the government's commitment to further focus on upgrading the country's pharmaceutical industry, Vietnam lacks sufficient government resources to address high-priority disease issues, and pharmaceutical R&D activities are generally underfunded.

[37] JETRO "The Expanding Pharmaceutical Market and Local Needs in Vietnam" (https://www.jetro.go.jp/biz/trendreports/2023/57a586f58b0a7caf.html)

iii. Restrictions on the entry of foreign companies into the import and wholesale pharmaceutical business

Vietnam's pharmaceutical manufacturing capacity only meets 53% of domestic pharmaceutical demand, making it highly dependent on imports. However, foreign companies have been allowed to import since 2009, but have not yet been allowed to enter distribution. Article 91, paragraphs 10-12 of Decree 54/2017/ND-CP specifies the prohibition of pharmaceutical distribution activities (wholesale and retail of pharmaceutical products in Vietnam) by foreign-invested enterprises. By law, manufactured goods are to be sold to Vietnamese companies with distribution functions, such as wholesale companies. On the other hand, Article 91, Paragraph 10 of Decree 54/2017/ND-CP stipulates that the prohibition clause on pharmaceutical distribution activities by foreign-invested enterprises "excludes pharmaceutical products manufactured in Vietnam". In reality, however, the practice of drug distribution is uniformly prohibited, regardless of whether the drug is imported or manufactured domestically[38]. These strict state control practices in drug distribution have led to reduced competition in the Vietnamese drug market and higher drug prices.

2.2.2 Local implementation system for related facilities and human resources in target countries

(1) Implementation system for clinical trials and local p at related facilities, facilities, human resources, etc.

i. Local clinical trial system

A) Clinical trial institutions

There are global and regional players that provide services as contract drug development organizations (CRO), including the provision of clinical trial management services, and major areas of treatment include infectious and infectious diseases, gastrointestinal diseases, metabolic and liver diseases, respiratory and lung diseases, immune diseases, and neurology. For example, Big Leap Research provides a wide range of services, including assessing the feasibility of clinical research and negotiating with clinical trial sites. As of January 2019, more than 40 clinical studies on 12 therapeutic areas were being conducted in 36 major hospitals in Vietnam[39]. Founded in 2018 as a local subsidiary of CRU-Global, CRI Vietnam is one of the largest private clinical research centers in Vietnam. It currently provides CRO services from Phase I to Phase VI, in-patient and outpatient clinical research services, and biobanking services for clinical and basic research projects. Next, IQVIA Vietnam has been active in Vietnam for more than 10 years and provides clinical research services in disease areas with a focus on infectious diseases, diabetes, cardiovascular diseases and cancer. The company also has partnerships with health authorities and major urban hospitals and medical centers, and collaborates on clinical research. In addition, Vietstar Biomedical Research provides regulatory procedures and clinical research services for biotechnology and drug development from Phase 1 to Phase 4, including medical documentation services and data management and quality assurance of clinical trials. As a therapeutic area, it specializes in hypertension, arthritis, cancer, hepatitis, infectious diseases, etc.

B) Domestic capacity for clinical trials

Out of 1180 hospitals nationwide, approximately 60 have been allowed by the Ministry of Health to conduct clinical research. 20 hospitals have the capacity to conduct clinical research, however, only 12 hospitals, mainly Hanoi Medical University, the University of Medicine and Pharmacy and the Hospital for Tropical Diseases, are conducting them. Funding donors for long-term clinical research include the U.S. Department of Health and Human Services, the Centers for Disease Control and Prevention, the National

[38] Business Council for Trade and Investment Facilitation "Issues and Requests in Vietnam in 2022" (https://www.jmcti.org/mondai/pdf/s124.pdf)

[39] https://bigleapresearch.co/

Institutes of Health, the Wellcome Trust of the United Kingdom, the Pasteur Institute of France, the Japan International Cooperation Agency, and other organizations.

C) Examples of recent clinical trial research

In Vietnam, clinical trials, including the one shown in the table below, are being conducted in collaboration with pharmaceutical companies and universities to study various diseases, such as dengue fever and tuberculosis. For example, Janssen Pharmaceutical is studying the antiviral activity of its products in terms of dengue virus (DENV) and ribonucleic acid (RNA) reduction in dengue infection compared to placebo. It is also conducting a study to confirm the efficacy of Softgel KOVIR, used to treat colds in Vietnam, against COVID-19 symptoms.

Table 2-4 Examples of ongoing clinical trials in Vietnam

Topic of Study	Disease	Sponsor	Location	Last Update
Efficacy and Tolerability of Bedaquiline, Delamanid, Levofloxacin, Linezolid, and Clofazimine to Treat MDR-TB	TB	• Boston University	• De La Salle Health Sciences Institute (Philippines) • National Lung Hospital (Vietnam)	• 2023/6/12
Safety and Efficacy of Softgel KOVIR (TD0068) in the Combination Regimen With Background Treatment in COVID-19 Patients	COVID-19	• Sao Thai Duong Joint Stock Company	• National Hospital for Tropical Diseases (Vietnam)	• 2022/2/7
A Phase 1/2 Safety and Immunogenicity Trial of COVID-19 Vaccine COVIVAC	COVID-19		• Hanoi Medical University (Vietnam)	• 2022/11/14
The ARCT-154 Self-Amplifying RNA Vaccine Efficacy Study	COVID-19	• ARCTURUS • VinGroup	• Hanoi Medical University (Vietnam)	• 2023/10/16
A Study of S-268019 for the Prevention of COVID-19	COVID-19	• Shionogi Inc.	• Buon Ma Thuot City Medical Center (Vietnam)	• 2023/7/23

ii. Local manufacturing system

A) Pharmaceutical manufacturing base

As for associations related to the pharmaceutical industry, the Pharmaceutical Manufacturers Association of Vietnam (VNPCA) has more than 160 member pharmaceutical companies and provides support in areas such as manufacturing, trade and supply. The association aims to improve the brand of Vietnamese pharmaceuticals in the market and contribute to the development of the domestic pharmaceutical industry. It also aims to support each company's activities and benefit all member companies of the association.

Major pharmaceutical companies in Vietnam include those listed in the table below. DHG Pharma Joint Stock is the largest pharmaceutical company in Vietnam[40].

[40]DHG Pharma "Mission of Vietnamese Medicine" (https://www.dhgpharma.com.vn/images/2022/Q2/BCTN/DHG-Annual-Report-2021.pdf)

Table 2-5 List of pharmaceutical companies in Vietnam

Company	Offerings	Revenue (2021)	Year of Establishment
DHG PHARMA	The company offers pharmaceuticals in the areas of Analgesic – Antipyretic, respiratory, nutrition, musculoskeletal, gastrointestinal, nervous, cardiovascular and dermatology	USD 0.17 bn	1974
VFC	VIET NAM Fumigation JSC offers agrochemical products and is a leading enterprise in pest control and disinfection services	USD 0.09 bn	1960
PYMEPHARCO	PYMEPHARCO is a franchised manufacturer for Cephalosporin antibiotic products for pharma company like Orchid - India, SamchunDang - Korea... and especially Stada company - Germany.	USD 0.1 bn	1989
DHT HATAPHAR	The areas in which company operates in include import and export of drugs, production and trading of chemicals, medicinal materials and medical equipment	USD 0.09 bn	1965
Traphaco	The company offers pharmaceuticals (Disease prevention, antibiotics, sedatives etc.), supplements, cosmetics, medical supplies	USD 0.09 bn	1994
	Domesco Medical Import-Export specializes in pharmaceuticals derived from medicinal materials, functional foods, purified drinking water and beverages from medicinal herbs	USD 0.07 bn	1989
IMEXPHARM	The company provides pharmaceuticals for respiratory system, musculoskeletal system, central nervous system, diabetes, digestive, cardiovascular, injectable and oral antibiotics and more	USD 0.06 bn	1977
MKP MEKOPHAR	Mekophar chemicals manufactures and trades in pharmaceuticals, herbal medicines, chemicals, raw materials for pharmaceutical industry, medical devices, oriental medicines. Stem cells banking.	USD 0.05 bn	1975
NAMHA PHARMA	The company operates in four product categories, medicines, healthy food, cosmetics and medical equipment	USD 0.05 bn	1960

In addition to the capital city of Hanoi and its environs, Vietnam's major pharmaceutical companies are clustered in several southwestern provinces, including Hizeon, Ho Chi Minh, Canto and Don Tap. It also manufactures medicines in Hung Yen province, where Pymepharco and Traphaco are based, as shown in the figure below.

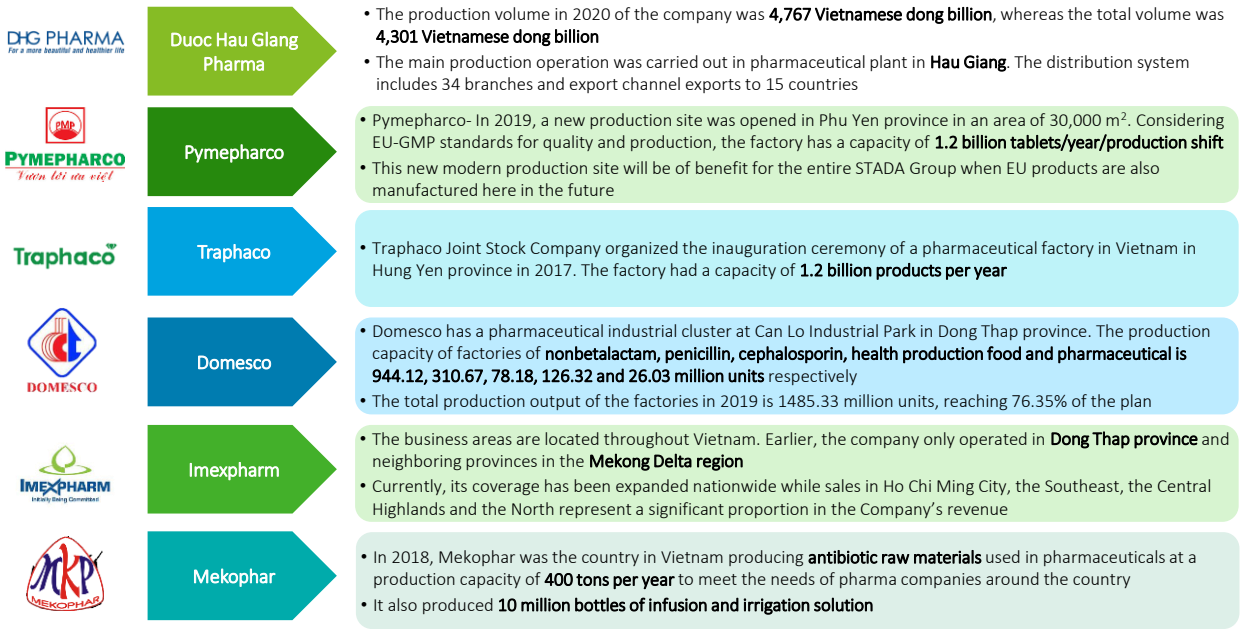


Figure 2-14 Pharmaceutical manufacturing bases of pharmaceutical companies in Vietnam

B) Types and volumes of locally manufactured drugs

The major pharmaceutical companies that produce the most drugs in Vietnam are Duoc Hau Giang Pharma, Pymepharco, Traphaco, Domesco, Imexpharm and Mekophar. The table below shows the sales of each company as of 2019. In addition, Vietnamese patients and doctors tend to prefer drugs with overseas certificates of origin, which makes it difficult to purchase drugs from local Vietnamese manufacturers even

if they have a more reasonable price. Moreover, Vietnam does not produce many types of medicines locally, thus often relying on imports.

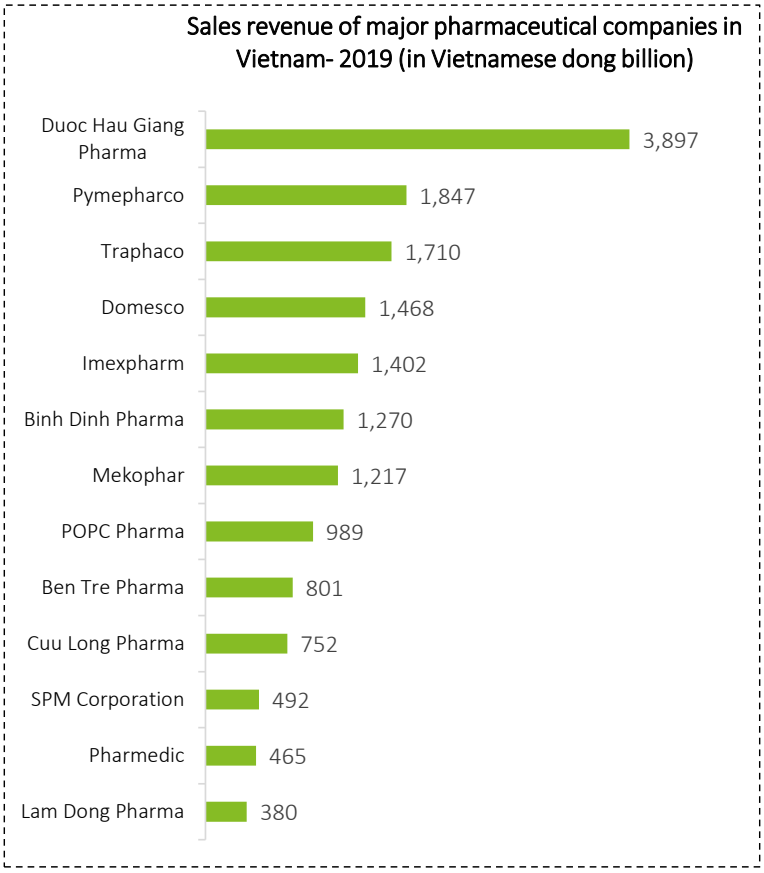


Figure 2-15 Sales of Vietnamese pharmaceutical companies (2019)

(2) Issues in target countries (regarding capacity to conduct clinical trials and local manufacturing)

i. Expansion of Phase I clinical trial sites complied with international standards

In Vietnam, Hanoi Medical University is the only facility that can conduct Phase I clinical trials. The Clinical Pharmacology Center of Hanoi Medical University is the only Phase I clinical trial laboratory in Vietnam that has obtained GCP Certificate and obtained GCP Certificate for Phase I clinical trials of botanicals and Phase I and II clinical trials of vaccines in 2021 and for Phase I clinical trials of chemicals in 2023, respectively). In the future, Vietnam needs to increase the number of clinical trial facilities that can conduct Phase I clinical trials, create clinical research centers in line with international standards, and promote international joint clinical trials.

ii. Expansion and operational maintenance of GMP-compliant manufacturing facilities

Of the first 174 Vietnamese pharmaceutical companies assessed for GMP compliance in 2014, only 42 were compliant with ASEAN GMP and only 18 with the international standard WHO GMP guidelines, but by 2021, Vietnam had approximately 180 pharmaceutical companies and 224 domestic manufacturing facilities meeting ASEAN or WHO GMP standards, a dramatic increase in GMP-compliant facilities. On the other hand, pharmaceutical companies have pointed out the complexity of GMP conformity assessment and the difficulty of assuring GMP compliance, making the maintenance of GMP standards a challenge. Therefore, it is necessary not only to strengthen inspection capacity for GMP evaluation, but also to strengthen regulation operation and monitoring for GMP compliance and its maintenance.

2.2.3 Results of a survey on initiatives taken by aid agencies, research institutes, and companies in other countries, including the target countries

(1) Overview of promotion of local manufacturing of vaccines and pharmaceuticals

i. Domestic policies and measures to promote local manufacturing

Over the past 20 years, Vietnam has made significant improvements in its pharmaceutical and bio-manufacturing industries as it seeks to produce pharmaceuticals on its own. The first law on GMP standards (No. 1516/BYT-QD) was adopted in 1996, setting out the necessary GMP principles and standards applicable to all manufacturing facilities, and many domestic companies now meet the GMP-ASEAN standards to produce high-quality medicines for domestic and export use. The original GMP-ASEAN principles and standards were based on WHO recommendations and have since been repeatedly updated to accommodate changes in international standards.

Vietnam has also developed various policies to promote homegrown manufacturing of vaccines. In Vietnam, IVAC, POLYVAC, VABIOTEC, DAVAC and 4 national vaccine manufacturing companies have been established, among them IVAC, which was established in 1978 as an indigenous unit under the Ministry of Health, which shows a high policy commitment by the government to vaccine Self Reliance from an early stage. Vietnam's National Immunization Expansion Plan (National Expanded Program on Immunization: NEPI) establishes a policy of using domestic vaccines independent of imported vaccines and always prioritizes purchasing vaccines through state suppliers as long as the domestic vaccines can meet sufficient quality standards. It plays a role in promoting domestic manufacturing of vaccines. In 2021, the Vietnamese government set up a special fund to promote a vaccination program for COVID-19. The fund will allow the company to secure materials and financial resources for manufacturing and use of the COVID-19 vaccine, and the policy will encourage domestic manufacturing. Moreover, the government is promoting a policy that expects domestic vaccines not only for domestic consumption but also for export to other countries. As for IVAC, POLYVAC and VABIOTEC, they are ambitiously aiming to obtain WHO PQ for their vaccines, and it is a national goal to increase exports as a base country for vaccine supply in the Asian region in addition to entering into UN procurement. Therefore, vaccine quality assurance is provided by the Vietnamese regulatory body, and investments are being made to ensure that domestic manufacturers undertake equipment upgrades to meet international GMP requirements as they change.

ii. Factors driving local manufacturing

WHO announced transfer of mRNA vaccine manufacturing technology to 5 countries (Besides, Bangladesh, Indonesia, Pakistan, Serbia) including Vietnam in February 2022[41]. The transfer of mRNA vaccine manufacturing technology is expected to provide favorable conditions for improving the technology of domestic vaccine manufacturers and for meeting domestic and overseas vaccine demand.

With regards to pharmaceutical manufacturing, the structural changes in the pharmaceutical industry that are now being actively carried out in Vietnam are a driving force for the development of the industry and are considered to be a major factor leading to the development of pharmaceutical manufacturing in Vietnam. Most of the leading pharmaceutical companies in Vietnam (Binh Dinh Pharmaceutical, Trafaco, Vietnam Pharmaceutical Corporation, etc.) were formerly state-owned enterprises, and many of them are still owned by government agencies representing the Ministry of Health in Vietnam. However, in recent years, the Vietnamese government has been considering selling off its large shareholdings in domestic pharmaceutical companies to large overseas pharmaceutical companies, and in fact, there have been developments such as Japan's Taisho Pharmaceutical acquiring the largest, Hauzin Pharmaceutical, and Germany's Stada acquiring a 99% stake in Pimefalco. This move has led Vietnamese pharmaceutical companies to improve their corporate management, including the transfer of technology from the acquired companies and the improvement of their performance. In fact, Pimefaco was the first company in Vietnam to obtain GMP-EU

[41] VIETJO, "WHO Transfers mRNA Vaccine Manufacturing Technology to Vietnam," (https://www.vietjo.com/news/social/220225192708.html)

certification through technology transfer from Stada[42].

(2) Donor initiatives to support clinical trials and local manufacturing of vaccines and other pharmaceutical products in target countries

i. Trends of support from the United States

The US Centers for Disease Control and Prevention (US CDC) has pledged an initial US $3.9 million to COVID-19 operations in Vietnam in 2022 to support prevention, preparedness, and response, including some community activities. These initial resources are used for laboratory testing, field research, surveillance, data analysis, infection prevention and control. In addition, it helped develop Vietnam's national guidelines and protocols with the Ministry of Health in the areas of infection control, preparing health facilities, and maintaining HIV treatment during the COVID-19. Thus, CDC has been working with the Vietnamese government since 1998 to build a high-quality, sustainable public health system leading to long-term impacts. The CDC is providing technical expertise to the Vietnamese Ministry of Health to support programs targeting priority diseases such as HIV, tuberculosis, and influenza, and is gradually scaling up.

ii. Trends of support from Europe

In the European context, in 2021, Vietnam signed a total of 60 memorandums of understanding with British and French companies, committing to fund projects in a variety of areas, including renewable energy, COVID-19 vaccine research, and education. In addition, during Prime Minister Pham Minh Chin's visit to France and the United Kingdom that same year, the Vietnamese city of Hanoi pledged $30 billion worth of commitments. In terms of the European Union (EU), Vietnam is the second largest trading partner in the Association of Southeast Asian Nations (ASEAN), and in 2020, with about 10% of EU exports to Vietnam being pharmaceuticals, Vietnam signed a new free trade agreement with the EU to increase foreign investment in medical devices and pharmaceuticals. Between 2016 and 2020, the EU also contributed 1.35 million euros to a project to scale up the Ethical Biotrade (EBT) initiative in the Vietnamese phytopharmaceutical sector. The policy and regulatory framework for biotrade enabled the sustained growth of the Vietnamese phytopharmaceutical sector.

(3) Initiatives of European and American universities, research institutes and pharmaceutical companies

On the pharmaceutical giant front, AstraZeneca said it would invest US $90 million to strengthen manufacturing in Vietnam and support technology transfer to prevent COVID-19 and other respiratory diseases. Sanofi has also invested another 5 million euros (US $5.7 million) to expand a plant that produces drugs for export. Additionally, Merck took steps to allow contract manufacturing organizations (CMO) in emerging pharmaceutical markets, including Vietnam, to produce generic versions of Merck's COVID-19 antiviral and molnupiravir.

In terms of university initiatives, Oxford University has a large clinical and public health research unit based in Vietnam, working under the Tropical Diseases Hospital in Ho Chi Minh City and the Hanoi National Tropical Hospital. For example, in 2020, the Vietnamese Ministry of Health, Ho Chi Minh City Tropical Diseases Hospital and the Clinical Research Unit (OUCRU) of Oxford University, UK, conducted a clinical trial to evaluate the safety and efficacy of chloroquine in the treatment of COVID-19. The research unit has a large clinical and scientific research program focused on Vietnam's most important infectious diseases, and the research covers aspects such as clinical research and immunology, pathogen genetics, molecular biology, and virology, and is supported by an extensive clinical trial unit and data management center. In addition, OUCRU has established formal training programs for Vietnamese and foreign clinicians and scientists.

[42] VietBiz, "Vietnam Drug Market Considerations," (https://vietbiz.jp/medicine-2022/)

2.3 Thailand

2.3.1 Legal systems and procedures in target countries

(1) Related policies and legal systems

i. National organizations and legal systems for drug regulation, including vaccines

Drug regulations in Thailand are governed by the Drug Act, B.E. 2510, with the Thai Food and Drug Administration (TFDA) under the Ministry of Health acting as the regulator. Within the TFDA, the Drug Control Division issues, registers, censors, controls, and supervises a variety of licenses for pharmaceutical companies. The law also stipulates that registration applicants for drugs must be local subsidiaries only.

As a standard for pharmaceutical products, GMP has been established in accordance with PICS[43]/GMP. As of December 2021, 151 companies[44] have received GMP certification for modern drugs and 53 companies[45] for traditional drugs. GMP certification is required for new manufacturers who have never been registered in Thailand, but PIC/GMP certification in the country of origin of the product can be accepted in Thailand.

ii. Drug approval system

Under Thailand's Pharmaceutical Affairs Law, the registration of drug manufacturing is granted for life, and no renewal is required. However, for narcotic drugs and psychotropic substances, renewal is required every five years. For imported drugs, there are exceptions, such as automatic invalidation of approval at the end of the year for products that have not been imported for two years.

Regarding the normal registration and approval system for new drugs, there are two phases: conditional approval in the first phase and unconditional approval in the second phase, after which distribution to the general market is permitted. During the conditional approval phase of the first phase, there are restrictions on sales limited to specific medical institutions only, and two years of safety monitoring under the supervision of a physician. Unconditional approval is granted after a safety report is submitted.

In addition to the standard review system, a priority review system has been established for drugs related to cancer and HIV, which are considered solutions to national health problems, public health problems, or life-threatening diseases. Furthermore, the ASEAN Common Technical Document (ACTD), an international standardization document, has been adopted as the format for submission of documents for approval.

iii. Regulations concerning clinical trials

Clinical trials in Thailand are governed by the specifications outlined in ICH-E6, with the TFDA serving as the regulatory body overseeing clinical trials in the country. Approval from both the TFDA and the ethics committee is required to initiate clinical trials in Thailand. To facilitate research and development of new drugs in Thailand, the TFDA has established a Scientific Advisory System that enables businesses to seek prior advice from the TFDA.

iv. Systems and regulations for local manufacturing

In Thailand, the FDA conducts pre-marketing control, including licensing and registration, as well as post-marketing monitoring of drug regulations. In order to produce and register the sale of a pharmaceutical-related product, individuals must possess at least one of the following licenses: a manufacturing license for modern and traditional medicines, an import license for modern and traditional medicines, a marketing license for modern and traditional medicines, and a wholesale license for modern medicines. Licenses for marketing or importing drugs are valid for one year, from January 1 to December

[43] Pharmaceutical Inspection Convention and Pharmaceutical Inspection Co-operation Scheme: An informal cooperative organization among regulatory authorities for the development, implementation and maintenance of internationally harmonized GMP standards and regulatory quality systems in the pharmaceutical sector.

[44] Thai FDA 「Tdaditional GMP」

[45] Thai FDA 「Tdaditional GMP」

31, and manufacturers must apply annually to to continue operatitions in the country.

As for the recent trend regarding the accreditation of foreign manufacturers, in response to COVID-19, a notification was issued in May 2020 with the aim of promoting the registration of approval for health products. The notification outlines criteria and procedures for the temporary marketing approval of imported drugs and hand sanitizers, including personal protective equipment (PPE) and external diagnostic kits.

v. Policy trends in clinical trials and manufacturing

In the ASEAN region, including Thailand, the ASEAN Vaccine Security and Self-Reliance (AVSSR) initiative is underway, and the Regional Strategic and Action Plan for AVSSR 2021-2025 was drafted by the National Vaccine Institute of Thailand. Thailand is playing a leading role in vaccine development in the ASEAN region, with the National Vaccine Institute of Thailand playing a central role in drafting the Regional Strategic and Action Plan for AVSSR 2021-2025.In addition, the Clinical Research Compliance Guidelines were revised in 2019, including modifications to the existing drug registration process, clinical research process, and fee schedule, In 2022, the introduction of the Personal Data Protection Act (PDPA) is also underway to ensure that personal data collected is limited to what is necessary in relation to the data controller's objectives.

The first National Drug Policy (NDP) on local manufacturing was formulated and implemented in 1981. The policy refers to the implementation of five measures: improving the supply and distribution system of drugs, improving the manufacturing of drugs, conducting research and development of modern drugs and herbal medicines, improving the knowledge of medical professionals regarding essential drugs, and strengthening the drug regulatory system. The third revision has been revised with the main objectives of improving the potential of the domestic drug industry, curbing drug expenditure, reducing imports of drugs, and promoting rational use of drugs. In 2008, the National Pharmaceutical System Development Commission (National Drug System Development Committee: NSDC) introduced the Public Procurement Standard Price to improve access to medicines and reduce expenditure on medicines, and public hospitals, especially those under the Ministry of Health (MoPH), are now required to procure medicines and medical products at below-standard prices. (However, the base price is taken as the maximum purchase price, and depending on the bargaining power of the hospital, which is the procuring entity, it is possible to procure at a price lower than the base price.) A TFDA study from 2014 to 2018 also found that 959 items in 10 treatment groups were targeted, resulting in approximately US $3.5 million in budget spending savings[46]. Recent developments include: In 2017, the TFDA developed the Priorities List (PRIMEs) listing 144 drugs to support the development of the domestic pharmaceutical industry and the promotion of domestic consumption and exports, as well as to increase access to essential drugs and strengthen the national drug system, and in 2021, the Good Distribution Practices for Drugs (GDP) were formally adopted as essential standards for drug manufacturers and importers.

In addition, a vaccine manufacturing strategy for COVID-19 was formulated, and in October 2020, the Ministry of Health, AstraZeneca K.K., Siam Bioscience and SCG agreed to produce AstraZeneca K.K.'s COVID-19 vaccine at the Siam Bioscience facility in Thailand, making Thailand one of the first countries in the world to obtain the COVID-19 vaccine, but the limited supply capacity prevented demand from being met. Initially, the Thai government declined to participate in the COVAX program and only pursued the AstraZeneca program, but since July 2021 it has been reviewing its vaccine strategy to focus on all solutions, including mRNA vaccines from other manufacturers, rather than relying on a single vaccine.

(2) Process from application to approval for clinical trials and local manufacturing

i. Process from application to approval for clinical trials

The initiation of clinical trials in Thailand requires the approval of two bodies: the TFDA and the Independent Ethics Committee/Review Committee (institutional review board/ethics committee: IRB/EC).

[46]Journal of Health Science 「National Drug Policies in Thailand: Evolution and Lessons for the Future」

The flow to clinical trials is as shown in the figure below: After approval from the IRB/EC at each medical institution, clinical trials are started with permission from the TFDA to import therapeutic drugs. There is a National IRB and a Central IRB. In addition, the format adopts the ACTD, which is the ASEAN document for international standardization, and is required to include statements regarding compliance with the GCP. The detailed process from application to approval is shown below.

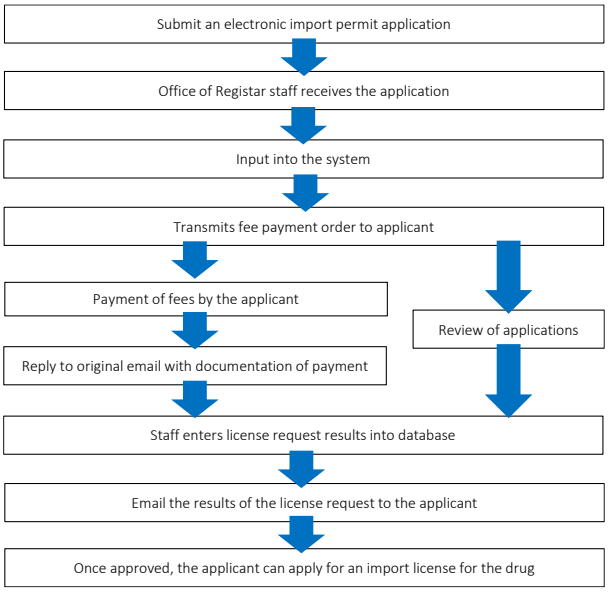


Figure 2-16 Process from application to approval of clinical trials in Thailand

ii. Process from application to approval for local manufacturing

As shown below, in order to manufacture drugs in Thailand, it is first necessary to obtain a license from the TFDA and obtain a manufacturing/import license. The license also expires for one year and must be renewed each year to continue manufacturing.

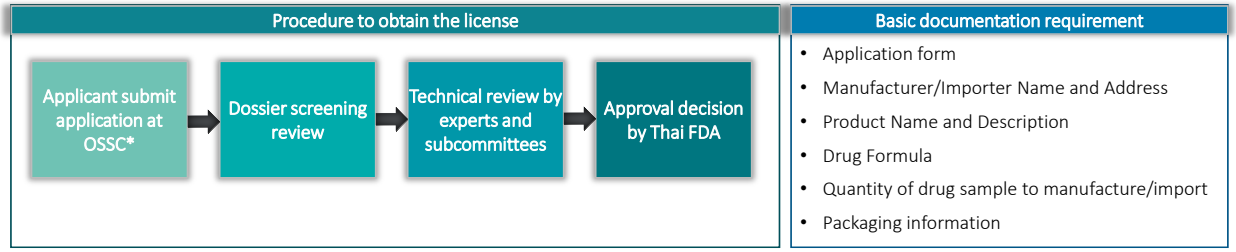


Figure 2-17 Licensing process for local manufacturing in Thailand

(3) Issues in target countries (Policies, regulations and legal systems for clinical trials and local manufacturing)

The following is a summary of the main issues related to regulatory agency (FDA) systems and approval processes that were mentioned in the desktop survey, online, and in interviews during the field survey.

i. Accelerate the regulatory process

Several stakeholders mentioned the need to speed up the FDA approval process, especially for private companies conducting clinical trials and manufacturing drugs. (The regulatory process for the Government Pharmaceutical Organization[47], which is a state-run company, is different from that for private companies.)

[47] According to the Drug Act B.E. 2510, GPO is not required to obtain FDA approval before launching a drug. According to Ministerial Regulation B.E. 2560, the Ministry of Health is required to procure at least 80% of the medicines on the national essential medicines list, and central and local government agencies other than the Ministry of Health are required to procure at least 60% of their medicines from GPO or the Thai Red Cross on a priority basis. In addition to the regulatory process, GPO also benefits from preferential treatment that private companies do not enjoy, such as the following.

In particular, the regulatory process for Phase I clinical trials tends to be delayed due to the lack of results in Thailand.

In Thailand, it is often necessary to import drugs to conduct clinical trials, and delays are also an issue, not only with regard to the usual approvals for clinical trials and drug manufacturing, but also with regard to the import process (protocol approval, package review, product import review, etc.) that is necessary when importing drugs to conduct clinical trials. Delays are also an issue.

In interviews with parties involved in international collaborations, some of them said that the speed of the Thai FDA's regulatory process lags behind that of other countries, and that they have actually had to suspend their participation in international clinical trials on several occasions because they could not start clinical trials due to delays in the FDA's approval process.

ii. Lack of regulatory guidelines that can flexibly respond to new trends

In the development of new drugs and technologies, clear regulatory guidelines have not kept pace with new trends, and there are gray areas that cannot be addressed by the existing regulatory framework. In addition, the situation changes from moment to moment during a pandemic outbreak, but there are no guidelines in place to respond to such changes.

In the case of a pandemic, it becomes difficult to find vaccine-naïve subjects in the clinical trial implementation phase, and the purpose of the clinical trial has to be changed from primary vaccine to booster vaccine. However, there are no clear guidelines for such mid-stage changes in clinical trial protocols.

In addition, while many clinical trials have been conducted for generic drugs manufactured in Thailand and the knowledge of regulatory agencies is accumulating, there are still not many clinical trials for drugs developed in Thailand, and the regulatory process and guidelines need further improvement.

iii. Lack of regulatory guidelines that can flexibly respond to new trends

The protection of personal data and intellectual property (IP) rights related to the conduct of clinical trials were also mentioned as issues to be addressed. Although measures are being taken to protect personal data, such as the introduction of the Personal Data Protection Act (PDPA) in June 2022, it is still in the early stages of implementation, and further system development is still needed. In addition, the protection of intellectual property (IP) rights has not yet been fully established, and this has caused delays in the review and approval process. In addition, the lack of protection of information and rights has hindered access to the Thai market for biopharmaceutical innovators from the U.S. and other countries.

2.3.2 Local implementation system for related facilities and human resources in target countries

(1) Implementation system for clinical trials and local manufacturing at related facilities, facilities, human resources, etc.

i. Local clinical trial system

A) Clinical trial institutions

Several clinical trial sites are located in Thailand.

① Siriraj Institute of Clinical Research (SICRES)

It is an academic and clinical research institute affiliated with the Faculty of Medicine, Sirirarj Hospital, Mahidol University. SICRES conducts cost-effective clinical research by international standards and provides clinical research design and management. The institute also serves more than 13 therapeutic areas.

② Chulalongkorn Drug Discovery and Drug Development Research Center (Chula4DR)

It is the academic and clinical research institute of Chulalongkorn University. Chula4DR was established in 2017 to promote the advancement of academic drug discovery and drug development research. It consists

of a full-time staff of 18 people, specializing primarily in 3 areas: medical chemistry, biochemistry, and drug metabolism and pharmacokinetics.

③Clinixir

A private CRO headquartered in Bangkok, providing end-to-end solutions for clinical research needs. It covers everything from clinical trial planning and design to project management and is a collaborative partner with the medical schools of Chiang Mai University and Mahidol University.

④Asia Global Research

It is a subsidiary of Bumrungrad International Hospital Public Company Limited and owns and operates the Esperance Oncology Clinic and the iConic drugstore. The company has two business segments, CRO and SMO, and provides clinical trials and staffing services from Phases 1 to 4. The CRO unit is responsible for managing clinical trials, including complete development programs or individual services required by the sponsor. The SMO division, meanwhile, is responsible for on-site surveys of pharmaceutical companies.

⑤Aclires International Limited

It is a specialized clinical research organization with GSC-certified clinical units in Thailand and Latin America. The main hub is a 30 bed unit at Mahidol University Siriraj Hospital, which mainly provides CRO services such as project management, patient recruitment and monitoring.

⑥ICON

Founded in 1990 in Dublin, Ireland, ICON is a clinical research organization with offices in 46 countries providing consulting, clinical development and commercialization services for pharmaceuticals, biotechnology, medical devices and government and public health agencies. The company has won many industry awards, including the 2022 CRO Leadership Award, and operates in biosimilars, biotechnology, medical devices, pharmaceuticals, and government offices.

⑦NOVOTECH

NOVOTECH provides clinical development services in the therapeutic area, including all clinical trial phases and feasibility assessments. It has established a clinical team in Thailand to provide quality CRO services to biotechnology companies. In the country, it also has partnerships with King Chulalongkorn Hospital and Srinagarind Hospital as part of its partner program.

B) Domestic capacity for clinical trials

There has been a lot of investment and financial cooperation in clinical trials in Thailand, especially from the United States and European countries, including Mahidol University. Thailand's major clinical research funding donors include the US Department of Health and Human Services and the National Institutes of Health, and European countries include the European Research Council (ERC), the European Commission, the Wellcome Trust and the British Medical Research Council (MRC). Thailand has the highest number of clinical trials in the ASEAN region, with the numbers per institution shown below.

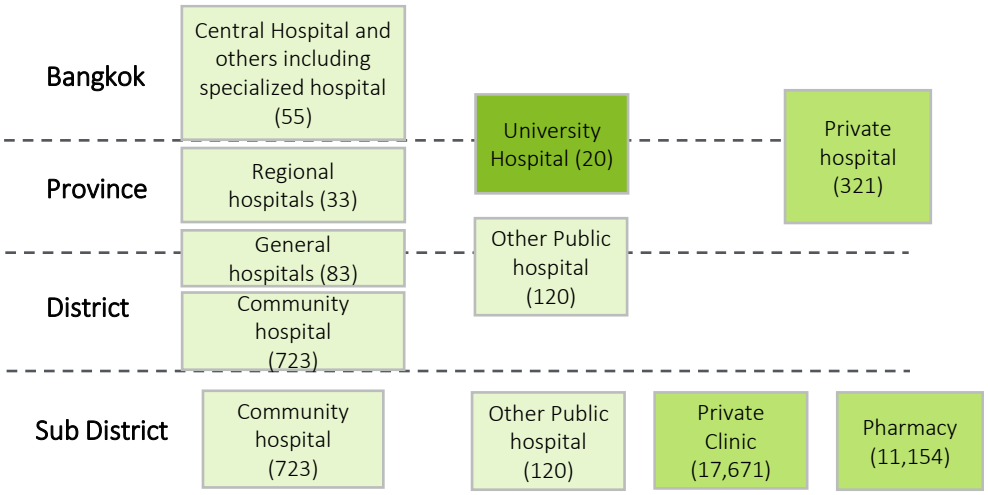


Figure 2-18 Number of clinical trials conducted by each institution in Thailand

C) Examples of recent clinical trial research

Examples of ongoing clinical trials in Thailand include the research topics listed in the table below. Many clinical trials are sponsored by federal agencies in the United States, and many tend to study HIV disease in particular.

Table 2-6 Examples of ongoing clinical trials in Thailand

Topic of Study	Phase	Disease	Sponsor	Site	Last Update
HIV Vaccine in HIV-uninfected Adults	2	HIV	U.S. Fed / HIV	• Bang Lamung District Hospital Chon Buri, Thailand • Phan Thong District Hospital Chon Buri, Thailand	• 2023/6
Study of Boosting Strategies After Vaccination With ALVAC-HIV and AIDSVAX® B/E	2	HIV	U.S. Fed / NIH	• Royal Thai Army Clinical Research Center, AFRIMS Bangkok, Thailand • Mahidol University Bangkok, Thailand • Chiang Mai University Chiang Mai, Thailand	• 2021/3
Tenofovir in Pregnancy to Prevent Mother to Child Transmission of Hepatitis B.	2	Hepatitis B Tenofovir Pregnancy	University of Oxford	• Shoklo Malaria Research unit (SMRU) clinics Mae sot, Tak, Thailand	• 2022/3
Strategic Transformation of the Market of HCV Treatments	2 & 3	Hepatitis C	• Ministry of Health, Malaysia • Ministry of Health, Thailand • National Science and Technology Development Agency, Thailand	Not Specified	• 2021/1
Plasma Immunity of Mild SARS-CoV-2 Omicron and Delta Pandemic in Thailand	-	COVID-19	Mahidol University	Mahidol University	• 2022/10
The Safety and Efficacy Test of Nutri-PEITC Jelly in Head and Neck Cancer Patients	-	Head and Neck Neoplasms Nutrition Related Cancer	• Dental Innovation Foundation Under Royal Patronage • Mahidol University • Srinakharinwirot University • Ministry of Health,Thailand	• National cancer institute Bankok • Lopburi Cancer Hospital, Thailand • Chonburi Cancer Hospital, Thailand	• 2023/2

ii. Local manufacturing system

A) Pharmaceutical manufacturing base

As of 2018, there were 194 pharmaceutical manufacturing facilities, 85 of which were located in Bangkok. Many of the major companies are based in Bangkok, making the city a hotspot for the pharmaceutical industry in Thailand.

There are both public and private pharmaceutical companies in Thailand. Among the government-owned pharmaceutical companies are the state-run Government Pharmaceutical Organization (GPO) and Defense Pharmaceutical Factory, which manufacture generic drugs as a substitute for imported drugs. The market structure is such that multinational private pharmaceutical companies manufacture original drugs, while Thai domestic companies, both government and private, manufacture generic drugs. The top three companies in terms of revenue in Thailand by 2020 are Pfizer, Novartis, and GlaxoSmithKline.

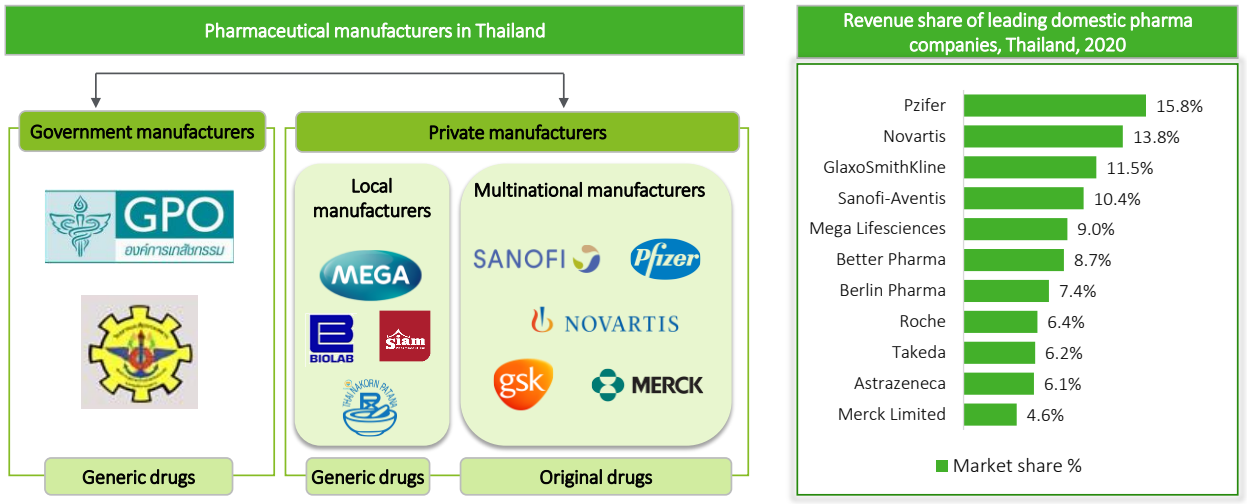


Figure 2-19 Pharmaceutical companies in Thailand

As for industry associations to which pharmaceutical companies belong, there are the Thai Pharmaceutical Manufacturers Association, the Thai Medical Association, the Pharmaceutical Research and Manufacturers Association, and the Pharmaceutical Association of Thailand (PAT) under the Royal Patronage, as shown in the figure below. For example, the Pharmaceutical Manufacturers Association of Thailand promotes and supports manufacturing of modern medicines in the country, raises the standards of the pharmaceutical manufacturing industry, and promotes education and training, thereby improving the health and welfare of the local people.

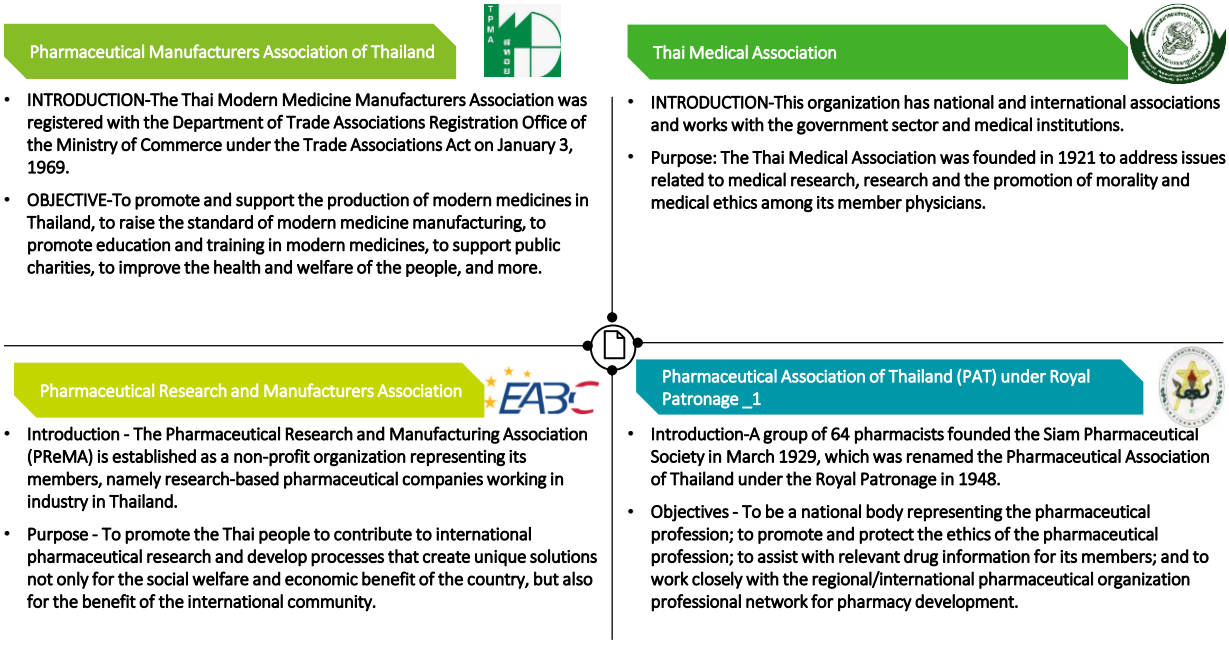


Figure 2-20 List of pharmaceutical organizations in Thailand

B) Types and volumes of locally manufactured drugs

The table below shows the share of drugs by type in Thailand. In 2021, there were about 8,400 existing pharmaceutical and medical supply manufacturers and 535 new ones[48]. In addition, as of 2020, 60% of all drugs were distributed to public hospitals, 20% to private hospitals, and another 20% were distributed over the counter[49].

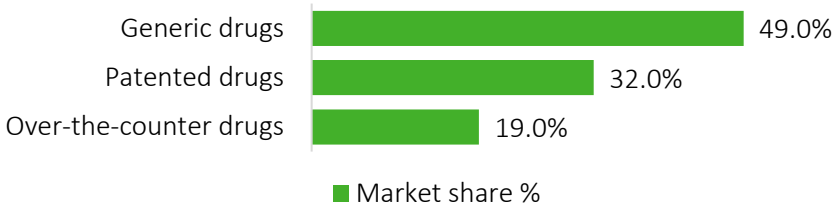


Figure 2-21 Share of drugs by type in Thailand (2021)

In terms of pharmaceutical manufacturing, tablets and liquids manufactured the most in 2021. The following figure shows the manufacturing volume for each drug dosage form[50].

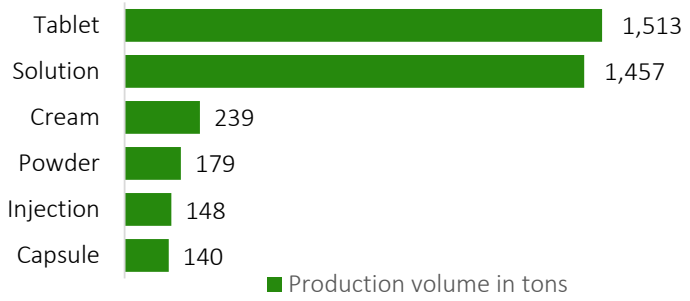


Figure 2-22 Manufacturing by pharmaceutical dosage form in Thailand (2021)

(2) Issues in target countries (regarding capacity to conduct clinical trials and local manufacturing)

i. Strengthen capacity for Phase I and Phase II clinical trials

With regard to experience in Phase I and Phase II clinical trials, it was pointed out that both the clinical trial conductors and the regulatory authorities have limited experience and that there is a need to strengthen implementation capacity and accumulate knowledge. The lack of knowledge on non-clinical trials and CMC (ChemistryManufacturing&Control: Chemistry, manufacturing and quality control, including structure determination of candidate compounds, design and research of manufacturing methods, specifications and testing methods for candidate compounds and their formulations, stability testing, etc.) was also cited as an issue. Since clinical trials of vaccines and drugs developed in Thailand are expected to be conducted in the future, there is a high need for capacity strengthening related to Phase 1 and Phase 2, non-clinical studies, and CMC.

[48] STATISTA "Number of existing pharmaceutical and medical supply businesses in Thailand as of April 2021, by type (https://www.statista.com/statistics/1197036/thailand-existing-pharmaceutical-and-medical-supply-businesses-by-type/)

[49] STATISTA "Domestic distribution of pharmaceutical products in Thailand in 2021, by channel (https://www.statista.com/statistics/666853/thailand-domestic-share-of-pharmaceutical-products-by-channel/)

[50] STATISTA "Production volume of pharmaceutical products in Thailand in May 2023, by type" (https://www.statista.com/statistics/1294691/thailand-production-of-medicaments-by-type/)

In addition, the FDA is currently relying heavily on outside experts to conduct its review of not only Phase I and Phase II clinical trials, but also clinical trials in general. It was pointed out that there is a need to expand the number of experts within the FDA and at least accumulate knowledge within the FDA to be able to understand the reviews of external experts.

ii. Expansion of laboratory facilities

With regard to research and development, there is a lack of laboratories that meet the criteria for conducting animal studies and Phase 1 clinical trials. Due to the lack of laboratories, some of the animal studies and Phase 1 clinical trials are being conducted overseas in countries such as China, Australia, and Indonesia. In addition, antibody studies can only be conducted in a few university laboratories, and there is a need to expand the number of laboratories capable of conducting antibody studies.

It was also pointed out that many of the other clinical trials currently being conducted are being conducted in large cities/large hospitals, and that one of the issues to be addressed in the future is to improve the environment and strengthen the capacity of facilities in remote areas.

iii. Utilization of digital solutions and data

In Thailand, the use of digital solutions for research and other purposes is on the rise. In terms of real-world data[51], which is a recent trend in clinical trials, Thailand's registry system is siloed[52] and has not made much progress in utilizing real-world data. It was pointed out that the recording, collection, analysis, and utilization of medical information and data are important from the perspective of building a foundation for the utilization of real-world data, and that it is necessary to establish a system that enables clinical trials to be conducted more quickly and over a wider area by utilizing more digital tools.

2.3.3 Survey results on initiatives taken by aid agencies, research institutes, and companies in other countries, including the target countries

(1) Overview of promotion of local manufacturing of vaccines and pharmaceuticals

A vaccine manufacturing strategy for COVID-19 was formulated, and in October 2020, the Ministry of Health, AstraZeneca K.K., Siam Bioscience and SCG agreed to produce AstraZeneca K.K.'s COVID-19 vaccine at the Siam Bioscience facility in Thailand, making Thailand one of the first countries in the world to obtain the COVID-19 vaccine, but the limited supply capacity prevented demands from being met. Initially, the Thai government declined to participate in the COVAX program and only pursued the AstraZeneca program, but since July 2021 it has been reviewing its vaccine strategy to focus on all solutions, including mRNA vaccines from other manufacturers, rather than relying on a single vaccine.

(2) Donor initiatives to support clinical trials and local manufacturing of vaccines and other pharmaceutical products in target countries

Major clinical research funding donors in Thailand include the National Institutes of Health (NIH), the National Science Foundation (NSF), the European Commission, the European Research Council (ERC), the Medical Research Council of the United Kingdom (Medical Research Council, MRC), the Welcome Trust and the Bill & Melinda Gates Foundation (B & MGF)[53]. The following are examples of donor assistance by country and region.

i. Trends of supports from the United States

The National Institute of Allergy and Infectious Diseases (NIAID: National Institute of Allergy and

[51] It is a type of medical big data, and refers to data collected in health care settings other than clinical trials and randomized controlled trials, such as patients' actual health status, medical information, and treatment progress.

[52] This refers to a state in which various systems, such as operational processes and applications, are isolated and information is not integrated.

[53]Clinical Research Grant (https://www2.si.mahidol.ac.th/en/news-events/sources-of-funding-for-clinical-research-grant/)

Infectious Diseases) under the NIH has a long history of cooperation in biomedical research with Thailand, funding more than 30 projects in Thailand. These projects mainly focus on HIV/AIDS, malaria, dengue fever and filariasis and include vaccine development, drug resistance and immunopathology research. As an example, NIAID funded HIV/AIDS research in Thailand through major HIV/AIDS clinical trial networks, including the International Maternal Pediatric Adolescent AIDS Clinical Trials, the International Network for Strategic Initiative in Global HIV Trials, the HIV Vaccine Trials Network, and the HIV Prevention Trials Network. NIAID also supports the Southeast Asian Influenza Clinical Research Network (SEAICRN: Southeast Asia Influenza Clinical Research Network), a multilateral cooperative partnership with WHO, Oxford University, the Welcome Trust and others[54].

The Southeast Asian Infectious Diseases Clinical Research Network (SEAICRN) is a collaborative partnership, first established in September 2005, between hospitals and research institutes in Thailand, Vietnam and Indonesia, the National Institute of Allergy and Infectious Diseases (NIAID) in the United States, and the Wellcome Trust of the United Kingdom. The network was established to develop the necessary partnerships in Southeast Asia to (i) conduct collaborative clinical research to address emerging threats, (ii) improve evidence-based scientific knowledge, and (iii) improve clinical management of patients with infectious diseases of public health importance. SEAICRN is mainly funded and supported in kind by NIAID, the Wellcome Trust and the governments of Thailand, Vietnam and Indonesia. SEAICRN strives to advance scientific knowledge and clinical management of infectious diseases in Southeast Asia through collaborative clinical research, and also focuses on enhancing the research capabilities of participating institutions and individual researchers. SEAICRN's findings provide policymakers across the region with evidence-based data to support changes in public health policies and guidelines[55].

ii. Trends of supports from Europe

A) Supports from the United Kingdom

The United Kingdom is supporting Thailand through the Better Health Programme. In March 2021, a Memorandum of Understanding was signed between the United Kingdom and Thailand, and the United Kingdom pledged to deepen cooperation with the Thai Ministry of Health through the program. The program aims to contribute to the promotion of health in Thailand through the sharing of technical and professional knowledge and expertise. Already several years ago, under the initial phase of the Better Health Programme, Thailand's Ministry of Health and the British Embassy in Thailand have been collaborating and developing partnerships in health and academia. The program aims to address non-communicable diseases by supporting behavioral change, enhance the capacity of health care workers through enhanced education and training, and develop systems that promote patient and health care worker safety in hospitals[56].

B) Supports from Germany

Germany has implemented projects in Thailand such as "Improving Occupational Health and Safety of Health Care Workers in Public Hospitals in Thailand". The program, which was implemented between February 2017 and August 2021, is a project aimed at reducing work risks for Thai healthcare workers and enhancing the safety and effectiveness of medical services. The project was funded by the German Federal Ministry for Economic Cooperation and Development (BMZ) in cooperation with Ramatibodhi Hospital's Faculty of Medicine, Mahidol University, Thailand's Healthcare Accreditation Institute, Oncology Nurse Society, Infusion Nurse Network of Thailand and GIZ (German International Cooperation). In addition to conducting training activities to enhance the safety of healthcare professionals, manuals and guidelines such as "Guidelines for Preventing Needlestick Accidents (Guidelines for Needlestick Injury Prevention)" "Guidelines and recommendations for safety in cancer treatment (Guidelines and Recommendations for Safety in Oncology Therapy)" and "Hand Hygiene Technical Reference Manual" were also prepared. These

[54] National Institute of Allegy and Infectious Diseases “Global Research in Thailand “ (https://www.niaid.nih.gov/research/niaid-research-thailand)

[55] SEAICRN Homepage (http://www.seaicrn.org/info.aspx?pageID=103)

[56] GOV.UK “UK commits to deeper collaboration with Thai MoPH “ (https://www.gov.uk/government/news/uk-commits-to-deeper-collaboration-with-thai-moph)

manuals and guidelines will be used to train health workers and distributed to hospitals across Thailand[57].

iii. Other trends

The Wellcome Trust's funding of the Mahidol Oxford Tropical Medicine Research Unit (MORU) is another example of donor support.[58] Founded in 1979 by Mahidol University in Thailand, Oxford University and the Wellcome Trust, MORU aims to combat tropical infectious diseases that primarily affect rural areas in Asia and other developing countries. MORU researchers are working to develop effective and practical tools for the diagnosis and treatment of malaria and other neglected diseases, including typhus, melioidosis and leptospirosis[59].

(3) Initiatives of European and American universities, research institutes and pharmaceutical companies

Examples of the efforts of universities, research institutes, and pharmaceutical companies in Europe and the United States include the Oxford University-sponsored study (SEACTN-HHS) to gain an overview of the disease burden in rural South and Southeast Asia, strengthening the partnership between Novotech, the CRO, and leading Thai medical institutions, and the signing of a contract between AstraZeneca and Siam Bioscience, a Thai pharmaceutical company, to manufacture the COVID-19 vaccine.

i. Examples of support by Western universities

Under a network of providers and medical facilities in South and Southeast Asia (South and Southeast Asian Community-based Trials Network: SEACTN) run by the Mahidol Oxford Tropical Medicine Research Unit (MORU), sponsored by the Wellcome Trust, a study is being conducted (Rural South and Southeast Asia Household Health Survey (SEACTN-HHS), estimated duration: June 2022 to September 2023) to outline the burden of disease in rural South and Southeast Asia.[60] The survey is designed to survey 371 randomly selected households from Thailand, Bangladesh, Cambodia and Myanmar by conducting a cross-sectional household health survey through questionnaire interviews and selected laboratory tests to understand the health status, non-communicable diseases, infectious diseases, risk factors, etc[61].

ii. Examples of CRO support

Novotech, the Asia-Pacific focused CRO, is expanding its clinical research partnership network with Thailand. For example, Novotech has signed a partnership with Maharaj Nakorn Chiang Mai Hospital (It is a 1400 bed tertiary care facility with 400 specialist physicians serving a population of about 7 million in the region and more than 1 million patients visit the hospital each year.) in Thailand. Maharaj Nakorn Chiang Mai Hospital has a dedicated Clinical Trials Unit (CTU) with its own ethics committee, and as part of the partnership, the CTU has agreed to support Novotech's research, designate appropriate lead investigators and help recruit patients.[62] Novotech has also signed MOUs with Chulalongkorn, Srinagarind and Phramongkutklao hospitals to partner with leading research sites in Thailand to facilitate high-quality and rapid feasibility studies, subject recruitment processes and more in the country[63].

iii. Examples of pharmaceutical company support

In October 2020, Thai pharmaceutical company Siam Bioscience, Siam Cement Group (SCG), AstraZeneca and Thailand's Ministry of Health signed a letter of intent to secure a joint commitment to

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[57] Thailand4 “Thailand and Germany announce the success on improving safety standard for healthcare personnel in Thailand” (https://www.thailand4.com/en/LKSR)

[58] MORU Tropical Health Network (https://wellcomeopenresearch.org/gateways/moru/about-this-gateway)

[59] MORU Tropical Health Network (https://wellcomeopenresearch.org/gateways/moru/about-this-gateway)

[60] Key objectives of the network include: (1) identifying key causes of morbidity and mortality among rural underserved populations in South and Southeast Asia, and (2) conducting scalable, high-impact intervention trials. (Website: https://www.seactn.org/)

[61] NIH National Library of Medicine (https://clinicaltrials.gov/ct2/show/NCT05389540)

[62] NOVOTEC “Novotech CRO announces several key Hospital Partnerships in India and Thailand at OCT West Coast 2019” (https://novotech-cro.com/news/novotech-cro-announces-several-key-hospital-partnerships-india-and-thailand-oct-west-coast)

[63] NOVOTEC “Novotech Signs MOU with King Chulalongkorn Memorial Hospital, Srinagarind Hospital and Phramongkutklao Hospital” (https://novotech-cro.com/news/novotech-signs-mou-king-chulalongkorn-memorial-hospital-srinagarind-hospital-and)

increase vaccine access in Southeast Asia, following a manufacturing agreement signed between AstraZeneca and Siam Bioscience. The COVID-19 vaccine manufacturing mission was supported by the Thai Ministry of Health's National Vaccine Institute with a budget of about 600 million baht, and an additional 100 million baht was budgeted by the SCG, which made it possible to prepare manufacturing equipment and processes. In return for the government's support, Siam Bioscience decided to procure the AstraZeneca vaccine at the equivalent value of the money it received and provide it to the Thai government to help the public get access to it[64]. In February 2021, the WHO allowed AstraZeneca's COVID-19 vaccine to be added to the EUL (Emergency Use List), and this EUL certification would reportedly extend to doses manufactured by Siam Bioscience[65].

iv. Other cases of support

Regarding manufacturing of the COVID-19 vaccine, a newspaper article on November 10, 2022 reported that Thailand is developing a vaccine called “Chula Cov 19” using "messenger RNA (mRNA)" technology. National Chulalongkorn University, which is the same type as Pfizer and Moderna, aims to commercialize it with the help of Drew Weissman, a professor at the University of Pennsylvania who laid the groundwork for mRNA. According to Chulalongkorn University, the second phase of the trial is expected to be as good or better than that of the Pfizer product, and the company will enter the final phase of the trial after obtaining approval from the Thai Food and Drug Administration. A vaccine for the omicron variant is also being developed, with the cost of development and manufacturing using a grant of about 2.3 billion baht (approximately 9 billion yen) from the Thai government. In addition, the Thai Pharmaceutical Corporation and others are developing inactivated vaccines, and Chulalongkorn Startup is developing plant-based vaccines[66].

2.4 Philippines

2.4.1 Legal systems and procedures in target countries

(1) Related policies and legal systems

i. National organizations and legal systems for drug regulation, including vaccines

In the Philippines, the Food and Drug Administration (Food and Drug Administration Philippines: PFDA), a subdivision of the Department of Health, is responsible for product registration of pharmaceuticals, licensing of marketing authorization, pre-marketing evaluation, post-marketing surveillance, etc. The Center for Drug Regulation and Research has been established within PFDA, under which two divisions have been established: the Licensing and Registration Division and the Product Research and Standards Development Division (Product Research and Standards Development Division)[67]. The organization and role of the PFDA are described in "Food and Drug Administration Act (RA 9711: Food and Drug Administration Act of 2009)"[68].

The Board of Food and Drug Inspection, as defined by the "Food, Drug and Cosmetic Act (Food, Drug, and Cosmetic Act)[69]," is responsible for conducting hearings and investigations into matters related to the enforcement of the law, as well as investigating and reporting to the PFDA on the manufacturing processes

[64] Bankok Post “Siam Bioscience strives to be the leading COVID-19 vaccine producer for Southeast Asia

(https://www.bangkokpost.com/thailand/pr/2056819/siam-bioscience-strives-to-be-the-leading-covid-19-vaccine-producer-for-southeast-asia)

[65] ThaiPR NET “AstraZeneca’s COVID-19 vaccine manufactured in Thailand authorised for World Health Organization Emergency Use” (https://www.thaipr.net/en/health_en/3110048)

[66] Nihon Keizai Shimbun” Southeast Asia focuses on domestically produced vaccines” (https://www.nikkei.com/article/DGKKZO65863410Q2A111C2FFJ000)

[67] Philippine FDA Homepage (https://www.fda.gov.ph/about-fda/)

[68] UN Environment Programme “Food and Drug Administration (FDA) Act of 2009 (Republic Act No. 9711” (https://leap.unep.org/countries/ph/national-legislation/food-and-drug-administration-fda-act-2009-republic-act-no-9711#:~:text=9711).,-Country&text=This%20Act%20aims%20to%20protect,Bureau%20of%20Food%20and%20Drugs.)

[69] UN FAO “Food, Drug and Cosmetic Act (Republic Act No. 3720).” (https://www.fao.org/faolex/results/details/en/c/LEX-FAOC100092/)

of foods, drugs, and cosmetics[70].

ii. Drug approval system

Product registration of drugs is regulated in the Revised Regulations and Regulations on Drug Registration (Executive Order No. 67 of 1989)[71]. After obtaining a License to Operate (LTO) from the PFDA, documents specified for each category are to be submitted to the PFDA for application. The application forms are expected to incorporate the ASEAN Common Technical Document (ACTD) and the ASEAN Common Technical Requirements (ACTR)[72].

iii. Regulations concerning clinical trials

Clinical trials of all therapeutic agents are required to follow the safety and efficacy guidelines of ICH-GCP and ICH[73].

iv. Systems and regulations for local manufacturing

To manufacture drugs in the Philippines, manufacturers are first required to obtain a License to Operate (LTO) from the PFDA. After obtaining the LTO, register each product[74]. GMP compliance is required for the acquisition of LTOs, and GMP inspections are a prerequisite for permission. The first application for an LTO will require the submission of documents: an application form, proof of company name registration, credentials for pharmacists and other qualified personnel, a risk management plan, a location plan, a site master file[75], fees and a self-assessment toolkit. The Philippines GMP complies with the PIC/S GMP[76].

v. Policy trends in clinical trials and manufacturing

1) Accelerating the review process with COVID-19 disaster

In response to the spread of COVID-19, efforts are underway to accelerate the review of clinical trials, and in May 2020, the PFDA issued a new ministerial order (Administrative Order, No. 2020-0010, Regulations on the Conduct of Clinical Trials for Investigational Products[77]). This ministerial order reduces the number of days required to obtain approval for a clinical trial from 120 to 60 days. In addition, for clinical trials that have already been approved in the reference country and are related to a public health crisis, the FDA has further reduced the review period for approval of clinical trials from 60 to 30 days by referring to reviews conducted in the reference country. Reference countries include Japan, Canada, the U.S., the EU, and Singapore, and clinical trials such as those related to COVID-19 are subject to the 30-day review period under this mechanism.

To further expedite the process, the PFDA issued a circular (FDA Circular) at the end of 2022, which allows a vaccine or drug product registered in a reference country to refer to a review conducted in the reference country if the same product is registered in the Philippines.

In this way, with limited human resources, the PFDA is moving forward with its intake of expedited reviews.

2) Establishment of SJREB

In multi-site clinical trials, the process of applying for and obtaining approval for a clinical trial from the

[70] Pharmaceuticals and Medical Devices Regulatory Information Gathering and Analysis Project for Asian Countries for FY 2020 (Additional Survey)

[71] Republic of the Philippines Department of Health OFFICE OF THE SECRETARY “Revised Rules and Regulations on Registration of Pharmaceutical Products” (https://www.wipo.int/wipolex/en/text/313066)

[72] Pharmaceuticals and Medical Devices Regulatory Information Gathering and Analysis Project for Asian Countries for FY 2020 (Additional Survey)

[73] Pharmaceuticals and Medical Devices Regulatory Information Gathering and Analysis Project for Asian Countries for FY 2020 (Additional Survey)

[74] FY 2020 Project to Collect and Analyze Regulatory Information for Drugs and Medical Devices in Asian Countries (Additional Survey)

[75] A document compiled by the drug manufacturing plant on the activities of the GMP and submitted to the authorities before GMP inspection.

[76] FY 2020 Project to Collect and Analyze Regulatory Information for Drugs and Medical Devices in Asian Countries (Additional Survey)

[77] Philippine FDA “Administrative Order No. 2020-0010 || Regulations on the Conduct of Clinical Trials for Investigational Products" (https://www.fda.gov.ph/administrative-order-no-2020-0010-regulations-on-the-conduct-of-clinical-trials-for-investigational-products/)

ethics committee of each site is required, which has caused problems with separate comments from each ethics committee. However, in 2017, the Single Joint Research Ethics Board (SJREB) was established under the Ministry of Health in order to homogenize the comments and simplify the process. Clinical trials at hospitals affiliated with the Ministry of Health are now collectively submitted to the SJREB for approval[78].

3) Other trends

The Philippines is also in the process of launching the Center for Disease Prevention and Control, which is expected to provide support for clinical trials in general.

In June 2021, the National Clinical Trials and Translation Center will be established under the umbrella of the NIH, with the main purpose of connecting individuals and sponsors of clinical trials in the Philippines and promoting standardization of clinical trials in the country.

(2) Process from application to approval for clinical trials and local manufacturing

i. Application to approval process for clinical trials

As shown below, in the Philippines, a clinical trial application must be submitted to the PFDA for technical and ethical review by the review committee (Institutional Review Board, IRB) and the ethics committee (Ethical Review Board, ERB) of each clinical trial site. The PFDA receives recommendations from the IRB and ERB and makes a final decision on approval or non-approval[79]. In 2017, the Single Joint Research Ethics Board (SJREB) was established in the Ministry of Health to simplify the application and approval process for multi-site clinical trials[80].

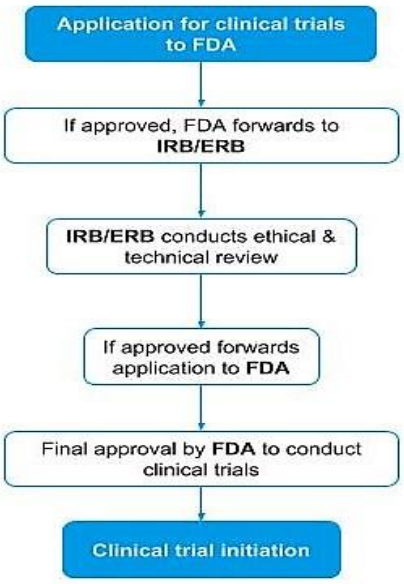

Figure 2-23 Process from application to approval of clinical trials in the Philippines

ii. Application to approval process for local manufacturing

As stated in 2.1.1, in order to manufacture pharmaceutical products in the Philippines, it is necessary to

[78] Philippine Single Research Ethics Board Homepage

[79] Philippine FDA "Clinical Trial Application Process" (https://www.fda.gov.ph/clinical-trial-application-process/)

[80] Philippine Single Research Ethics Board Homepage

first obtain a Lisence to Operate (LTO), which is a business license, from the PFDA.

(3) Issues in target countries (Policies, regulations and legal systems for clinical trials and local manufacturing)

Through the interviews, the following issues regarding regulations and legislation were indicated.

i. Simplify ethics review

Although the Single Joint Research Ethics Board (SJREB) was established in 2017 to simplify the ethical review of clinical trials, interviews with CROs and others indicated that there are practical challenges.

For example, when an application for approval is submitted to the SJREB, the same application must also be submitted to the Local IRB, requiring a double approval process. Sometimes the SJREB approval is slower than the Local IRB approval, and sometimes a document approved by the Local IRB has to be changed due to later SJREB comments.

ii. Training of personnel to conduct reviews at PFDA

Interviews with the PFDA indicated that there is a serious shortage of human resources to conduct the review. The Clinical Research Section, which is in charge of review, has only two physicians, three pharmacists, two nurses, and one molecular biologist and for the lack of expertise was voiced, leaving the Section to rely on experts from outside partner institutions (UP, St. Lukes Medical Hospital, and Philippine Heart Hospital).

It was also commented that the researchers have only gained knowledge of adaptive design and RWD through on-the-job training, but that not only the researchers but also the regulatory authorities need to gain knowledge.

iii. Improved capacity of PFDA as a regulator

In order to conduct local manufacturing, it is necessary to obtain Maturity Level 3 of the WHO Benchmark Tool, but PFDA is currently at Level 1, and obtaining Level 3 is cited as a high priority issue for the Philippines and PFDA.Not only in the interview with PFDA, but also in interviews with other government agencies and private companies, it was mentioned that improving the capacity of PFDA is an urgent issue.

2.4.2 Local implementation system for related facilities and human resources in target countries

(1) Implementation system for clinical trials and local manufacturing at related facilities, facilities, human resources, etc.

A) Clinical testing institutions

Clinical research institutes in the Philippines include the companies listed in the table below. Based in the Philippines, Pivot is a newcomer to the CRO market, with other international players including IQVIA, Parexel and SGS.

Table 2-7 List of clinical research institutes in the Philippines

CRO	Year of Establishment	Revenue (in mn USD)	Services Offered
PIVOT	2018	NA	• Clinical Trial Management • Drug and Device Trial Management • Clinical Trial Support Services • Pharmacovigilance and/or Drug Safety Surveillance (PV) • Bioavailability (BA) and Bioequivalence (BE) Studies • Post Marketing Surveillance (PMS) and Real-World Evidence (RWE)
SGS	1985	7,006.9 (2021)	• Clinical Research Services (Phase I to Phase IV Trials) • Clinical Development Consultancy • Clinical Trial Management • Biometrics Services • Pharmacovigilance and Drug Safety • Bioanalytical Services • Early Phase Clinical Research
IQVIA	1982	10,412 (2021)	• Clinical Development • Early Phase • Phase II-III, Phase IIIb-IV • Clinical Data, Supply chain management • Decentralized Clinical Trials • Biostatistics • Consulting • Pharmacovigilance
parexel	1982	2,441.5 (2017)	• Clinical Trials • Decentralized Trials • Consulting • Patient Engagement • Functional Services
Syneos Health	1999	5,213 (2021)	• Clinical Development • Early Phase • Phase II-III, Phase IIIb-IV • linical data management • Clinical Monitoring • Consulting • Biostatistics and Statistical Programming • Bioanalytical solutions

B) Domestic capacity for clinical trials

The DOST Health Research Ethics Committee (Philippines Health Research Ethics Board: PHREB) assesses the ethics levels of universities and hospitals under the National Ethics Guidelines. Level 1 institutions can conduct research only in the human and social sciences, Level 2 institutions can conduct basic research, and Level 3 institutions can conduct clinical trials. 46 institutions have achieved Level 3[81]. To achieve Level 3, an organization must have at least an ethics committee in place.

The distribution of Level 3 institutions is shown below and is concentrated in the National Capital Region.

[81] Philippine Health Research Ethics Board Homepage (https://ethics.healthresearch.ph/index.php/level-3-accredited-recs)

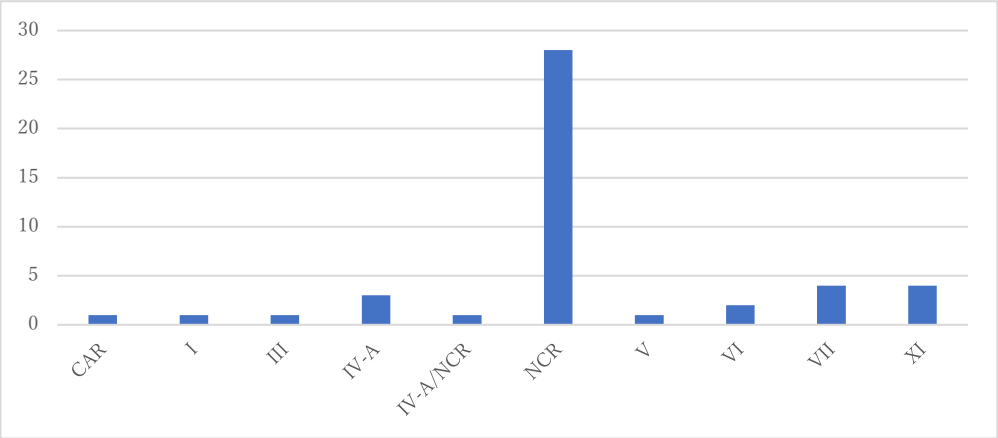

Table 2-8 Distribution of Institutions with Level 3 Ethics in the Philippines

C) Examples of recent clinical trials

Recent clinical trials in the Philippines include several COVID-19 vaccine trials, including the WHO Solidarity clinical trial for COVID-19 treatments, a clinical trial of Sanofi's dengue vaccine Dengvaxia (RITM), and a Phase I clinical trial B trial for cancer treatment (St. Luke's Medical Center).

With regard to Sanofi's dengue vaccine Dengvaxia, which was approved after a large-scale clinical trial in 2018, 27 public officials including researchers involved in clinical trials at the Ministry of Health and the RITM were impeached by the Diet due to cases in which children infected with dengue after vaccination became seriously ill and died, leading to the public's vaccine hesitancy to certain extent[82].

i. Local manufacturing system

A) Pharmaceutical manufacturing base

In terms of pharmaceutical companies, in the Philippines, the companies listed in the table below are among those with local operations. While there are many multinational companies, UNILAB is a local pharmaceutical company in the Philippines.

[82] Science “Dengue vaccine fiasco leads to criminal charges for researcher in the Philippines” (https://www.science.org/content/article/dengue-vaccine-fiasco-leads-criminal-charges-researcher-philippines)

Table 2-9 List of pharmaceutical companies in the Philippines

Company	Year of Establishment	Revenue (in mn USD)	Key Offerings	
UNILAB Trusted Quality Healthcare	1945	NA	• Prescription Drugs • Skin Care Products • Vitamins and Supplements	• Allergy Care • Specialty Medicines
GSK	2000	46,923.8 (2021)	• Prescription Medicines • Vaccines	• Consumer Healthcare Products
AstraZeneca	1999	37,417 (2021)	• Precision Medicine • Biopharmaceuticals • Vaccines	• Medicines for Oncology, Cardiovascular, Renal, Metabolism, Respiratory, Immunology
Pfizer	1849	81,288 (2021)	• **ACCUPRIL®** (quinapril HCl) • **ADENOSINE** (adenosine) • **Eliquis**	• **Comirnaty** (COVID-19 Vaccine) • **Prevnar**
NOVARTIS	1996	51,626 (2021)	• Generic Medicines • Innovative Medicines	• Radiopharmaceuticals
Roche	1896	66,747.19 (2021)	• Dermatology therapeutics • Cancer Therapeutics	• Respiratory disorders therapeutics

B) Types and volumes of locally manufactured drugs

UNILAB has a high market share in the Philippine pharmaceutical industry. It produces more than 300 prescription drugs and accounts for nearly 80% of the country's generic market. The company also exports mainly prednisolone, dexamethasone and danazol to countries and regions such as Taiwan, Singapore, Myanmar, Thailand, Pakistan, Sri Lanka, Vietnam and the UAE[83].

(2) Issues in target countries (regarding capacity to conduct clinical trials and local manufacturing)

i. Lack of facilities for clinical trials

In addition to only a limited number of hospitals having clinical trial units, many hospitals indicated that they have limited space to conduct clinical trials.

Another challenge is the lack of equipment such as refrigerators and centrifuges, and the lack of laboratories with sufficient BSL (Biosecurity Level) to handle high-risk pathogens. This is being sorted out based on the information obtained from the interviews.

ii. Existence of regional disparities

Although related to the facilities mentioned in i, many clinical trials are currently conducted on Luzon Island, especially in Manila, and there is a regional disparity in the number of clinical trials conducted. In addition to the uneven distribution of facilities in the metropolitan area, skilled personnel to conduct clinical trials are also unevenly distributed in the metropolitan area.

iii. Lack of local manufacturing facilities

There are currently no facilities in the Philippines to produce vaccines. Facilities to produce pharmaceuticals are also limited. There are local producers such as Unilab and Pascual, but they only produce synthetic products and do not produce biological products such as growth hormones or antibodies. Because antibodies cannot be manufactured, the country is dependent on imports for pregnancy test kits (St. Luke's) because local manufacturing capacity for vaccines and medicines is limited, the country is not self-sufficient, and there are concerns about the availability of vaccines and medicines in the event of a pandemic.Japanese clinical trial system.

[83] Volza "Exports from Philippines Overvuiew" (https://www.volza.com/p/pharmaceutical/export/export-from-philippines/)

2.4.3 Results of a survey on initiatives taken by aid agencies, research institutes, and companies in other countries, including the target countries

(1) Overview of promotion of Local manufacturing of vaccines and pharmaceuticals

i. Domestic policies and measures to promote local manufacturing

The Philippines has policies to promote local manufacturing in order to increase self-sufficiency of medicines. For example, the Department of Science and Technology (DOST) of the Philippines funds research through TOKLAS LUNAS, a program to search for and develop new drugs from local resources. 26 research institutes have participated in the program over the past 20 years, and some of the drugs have reached clinical trials in the last three years.

TOKLAS LUNAS has been a pre-Corona initiative, but according to interviews with Philippine government officials, the Philippine government is further emphasizing self-sufficiency in vaccines and other medicines, especially in the wake of COVID-19. A related bill to establish the Virology and Vaccine Institute (VVI) is being debated in Congress and is expected to pass Congress in 2023; the VVI is expected to become the center of R&D in the Philippines, with plans to start with R&D and eventually move to manufacturing, and to establish a self-sufficiency system for vaccines in the Philippines. The VVI will take a one-health approach and will conduct viral research not only in humans, but also in animals and plants. A roadmap has also been developed for the VVI with short, medium, and long term goals.

In addition, as for the virologists who will conduct research at the VVI, Filipino researchers who are studying abroad are being considered. It is planned to recruit them through the Balik Program, which encourages researchers studying and conducting research abroad to return to the Philippines.

(2) Donor initiatives to support clinical trials and local manufacturing of vaccines and other pharmaceutical products in target countries

i. Donor movements to support the Philippine health care system and related research activities

Through its Medicines, Technologies, and Pharmaceutical Services (MTaPS) program, USAID has been providing technical assistance to the Philippine Department of Health to help the Philippines achieve its goals set out in the National Objectives for Health (2017 - 2022), Sustainable Development Goal 2030, and the Universal Health Coverage Act. The key objectives of technical assistance are (1) to establish an integrated and effective health supply chain management system, (2) to implement a fully functional pharmacovigilance (PV) system, and (3) to improve pharmaceutical services. The overall goal is also to: (1) strengthen and institutionalize systems to ensure sustainable access to safe, effective, quality assured and affordable tuberculosis, family planning and other essential health products; (2) protect patients from harm; and (3) promote rational access to health care[84]. Again. In May 2022, the US Centers for Disease Control and Prevention (CDC) formally opened its new country office in Manila as part of a commitment to strengthen and expand existing collaborations with the Philippine Department of Health to advance a range of common health priorities, including strengthening health security in Asia. The Department of Health of the Philippines and the U.S. Department of Health and Human Services (HHS) also signed a Memorandum of Understanding on Health and Medical Sciences, focusing on strengthening cooperation on public health emergency preparedness and response, prevention and control of vaccine-preventable communicable diseases, prevention and control of non-communicable diseases, etc[85].

The UK is also actively supporting the Philippines, for example the Newton Agham Fund under the UK's Official Development Assistance Program (ODA) to provide 3 million pounds from 2016 to develop

[84] MTaPS Program" Philippines " (https://www.mtapsprogram.org/where-we-work/philippines/)

[85] US Embassy in the Philippines "CDC OPENS NEW COUNTRY OFFICE IN THE PHILIPPINES" (https://ph.usembassy.gov/cdc-opens-new-country-office-in-the-philippines/)

science and innovation partnerships that promote economic development and social welfare in the Philippines. The British Council in the Philippines is working with the Philippine government to implement a program that will benefit Filipino researchers[86]. The Health Research and Development Council of the Philippines (Philippine Council for Health Research and Development, PCHRD), one of the three divisional councils of the Department of Science and Technology (DOST), has a partnership with the Medical Research Council of the United Kingdom (UK Medical Research Council, MRC) where six research collaborations have been approved for the surveillance, diagnosis and characterization of infectious diseases such as malaria, HIV, schistosomiasis, dengue fever, antimicrobial resistance and tuberculosis with research grants from the Newton Agham Fund[87]. The MRC and the Department of Science and Technology of the Philippines (DOST) also held a joint United Kingdom-Philippines Health Research Council (UK-Philippines Joint Health Research Call), which discussed ways to further strengthen the research base of both countries on infectious and non-infectious diseases, and to provide related funding[88].

In addition, the Marcos administration in the Philippines has been trying to strengthen its domestic manufacturing capacity for generic drugs, and has indicated its willingness to work with India to support the development of the local pharmaceutical industry, and has agreed with India to strengthen relations on manufacturing of generic drugs[89].

ii. Donor assistance to enhance securing of COVID-19 vaccine

The World Bank, the Asian Development Bank and the Australian government had provided financial assistance to the country to help it secure more COVID-19 vaccines. For example, in April 2020, the World Bank approved a loan of US $100 million for the Philippine COVID-19 Emergency Response Project to meet post-pandemic emergency health care needs and enhance public health preparedness in target countries[90]. In February 2021, the Asian Development Bank (ADB) allocated $25 million to support the Philippine government in purchasing COVID-19 vaccines[91]. Also in March of the same year, the Philippines received a $400 million loan from ADB's Asia Pacific Vaccine Access Facility (APVAX) to help procure vaccines[92].

Australia also actively supported the Philippine government's vaccine procurement, providing US $820,000 in assistance to UNICEF Philippines, with funds provided for the procurement of cold-chain equipment and components[93]. In April of that year, to support the Philippine Department of Health's rollout of the COVID-19 vaccination, the U.S. government, through USAID, provided the country with $3.5 million to help strengthen supply chains and monitor vaccine safety, among other things. It is assumed that the total support of the US government as of April 2021 will be about $27 million and that these funds will be used to strengthen the health system and vaccine supply efforts in the Philippines[94].

As for the clinical trials of the COVID-19 vaccine, the Philippine government's Inter-Agency Task Force on the Response to the Novel coronavirus (IATF-EID) conducted clinical trials of the COVID-19 vaccine in collaboration with five Chinese and Taiwanese pharmaceutical companies. In China, three companies

[86] British Couincil "Newton Agham Programme" (https://www.britishcouncil.ph/programmes/education/newton-agham-programme)

[87] Department of Science and Technology Philippine"PCHRD, MRC award Php 262M in grants to 6 UK-Filipino health research collaborations "(https://www.pchrd.dost.gov.ph/news_and_updates/pchrd-mrc-award-php-262m-in-grants-to-6-uk-filipino-health-research-collaborations/)

[88] Region 2 Research and Development Consortiuam Homepage (https://region2.healthresearch.ph/index.php/8-news/173-call-for-concept-proposals-uk-philippines-joint-health-research-initiative)

[89] INQUIRER.NET "PH, India boost ties, eye generic drugs production" (https://globalnation.inquirer.net/205891/ph-india-boost-ties-eye-generic-drugs-production)

[90] World Bank "Philippines: World Bank Approves US$100M to Support COVID-19 Emergency Response" (https://www.worldbank.org/en/news/press-release/2020/04/23/philippines-world-bank-approves-usd100m-to-support-covid-19-emergency-response)

[91] ADB "ADB Provides $25 Million to Help Philippines Procure COVID-19 Vaccines" (https://www.adb.org/news/adb-provides-25-million-help-philippines-procure-covid-19-vaccines)

[92] ADB "ADB Provides $25 Million to Help Philippines Procure COVID-19 Vaccines" (https://www.adb.org/news/adb-provides-25-million-help-philippines-procure-covid-19-vaccines)

[93] Unicef "Australia, UNICEF partner to strengthen PH vaccine supply chain " (https://www.unicef.org/philippines/press-releases/australia-unicef-partner-strengthen-ph-vaccine-supply-chain)

[94] USAID "US provides php170-million support-covid-19 vaccine deployment in the Philippines" (https//www.usaid.gov/philippines/press-releases/apr-15-2021-us-provides-php170-million-support-covid-19-vaccine-deployment-in-the-philippines)

participated: the Guangzhou Institute of Biomedicine and Health Research of the Chinese Academy of Sciences, Sinopharm (the COVID-19 vaccine developed by the Beijing Institute of Biological Products and the Wuhan Institute of Biological Products), and Sinovac Biotech Limited[95].

(3) Initiatives of European and American universities, research institutes and pharmaceutical companies

The Philippine Council for Health Research and Development (PCHRD), one of the departmental councils of the Philippine Department of Science and Technology (DOST), is actively partnering with universities, institutions and research networks overseas to build collaborations in clinical research, including vaccine discovery and development, liver diseases and molecular medicine.

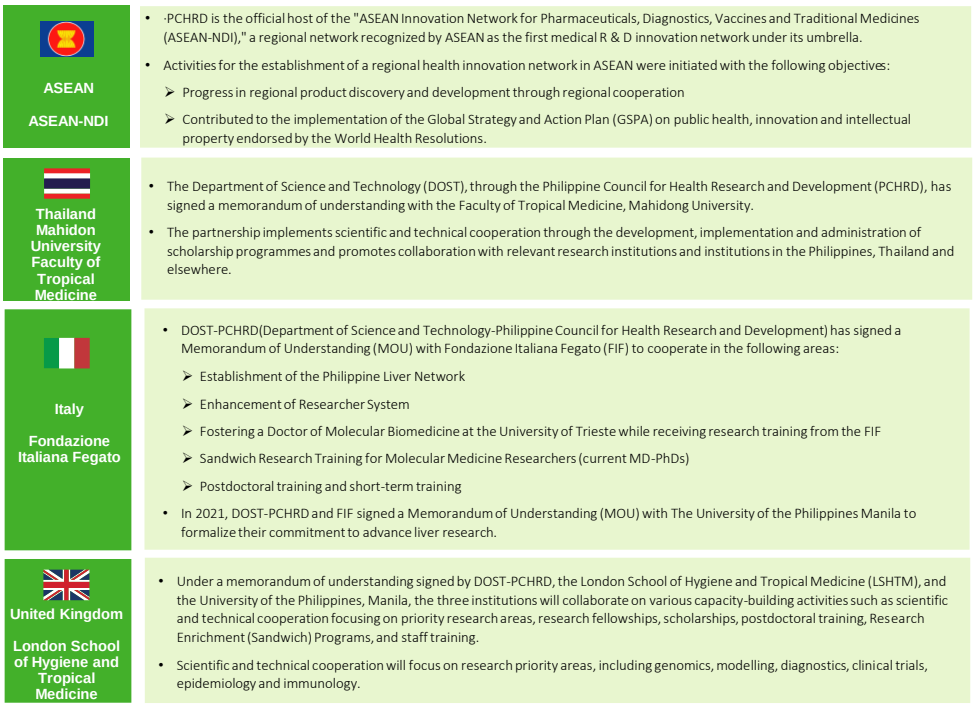

Figure 2-24 Cooperation between the PCHRD and overseas universities, institutions, and research networks

PCHRD is the official host of the ASEAN Innovation Network on Drugs, Diagnostics, Vaccines and Traditional Drugs (ASEAN-NDI). Established in 2009, the ASEAN-NDI is a regional innovation network comprised of ASEAN member states, with the aim of building sustainable partnerships to rapidly build the human resources, technology and financial resources needed for health development and security in member states. It aims to promote research and development, develop North-South and South-South cooperation to support capacity building, and establish a strategic research network to facilitate coordination among stakeholders[96].

The PCHRD has signed a Memorandum of Cooperation with the Department of Tropical Medicine, Mahidong University, Thailand and the London School of Hygiene and Tropical Medicine (LSHTM), UK to promote scientific and technological cooperation in the field of health care. The Memorandum of Understanding with Mahidong University covers the direction of cooperation aimed by both sides,

[95] SunStar Philippines "Philippines ties up with 5 firms for Covid-19 vaccine trials" (https://www.sunstar.com.ph/article/1862975/Manila/Local-News/Philippines-ties-up-with-5-firms-for-Covid-19-vaccine-trials)

[96] National Library of Medicine 「A look at the ASEAN-NDI: building a regional health R&D innovation network (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4021759/)

including the provision of scholarships for master's and doctoral degrees, the realization of joint use of research and training facilities, the promotion of knowledge exchange, and the promotion of cooperation between related scientific institutions in the other two countries. Through this partnership, it has been agreed that support will be provided in the areas of epidemiological studies of tropical diseases, endemic and emerging diseases associated with environmental changes, diagnosis of tropical infectious diseases through immunological and molecular biological methods, and tropical medicine and public health.[97] As for the partnership with LSHTM, under the Memorandum of Understanding, PCHRD, LSHTM and the University of the Philippines (UP Manila) have agreed to collaborate on various collaborations focusing on priority research areas including genomics, modeling, diagnostics, clinical trials, epidemiology and immunology. The partnership will also involve an exchange of scientists, faculty and experts interested in science and technology cooperation in health. The PCHRD agreed to fund various capacity building activities, including research fellowships, scholarships, postdoctoral training, research enrichment programs, and staff training[98].

The PCHRD has also signed a Memorandum of Understanding (MOU) with the University of the Philippines and the Italian Fegat Foundation (FIF) to facilitate collaborative research efforts and liver research capacity building initiatives for both Filipino and Italian researchers. The directions for cooperation include enhancing the fellowship system, sharing expertise to establish a liver disease research program, and promoting cutting-edge care and clinical trials for liver diseases[99].

2.5 Indonesia

2.5.1 Legal systems and procedures in target countries

(1) Related policies and legal systems

i. National organizations and legal systems for drug regulation, including vaccines

The Ministry of Health is responsible for the overall health and medical policy in Indonesia, but when it comes to pharmaceuticals, Division I (Deputy I: Therapeutic Product, Narcotics, Psychotropic and Addictive Substance Control) of the National Agency for the Supervision of Food and Drug Administration (National Agency of Food and Drug Control, Badan Pengawas Obat & Makanan: BPOM) is in charge of the review, specification and GMP certification of pharmaceuticals[100].

The BPOM was a subdivision of the Ministry of Health until 2000, when it became an independent agency in 2001. When reviewing new drugs, the committee is supposed to hear the opinion of the Pharmaceutical Affairs Council (Committee on Drug Evaluation, a panel of outside experts)[101].

Regarding the legal system, there are related laws and regulations as shown in the table below[102].

[97] PCHRD "PCHRD signs MOU with Thailands's Mahidol university to implement capacity-building activities for health researchers" (https://www.pchrd.dost.gov.ph/news_and_updates/dost-pchrd-signs-mou-with-thailands-mahidol-university-to-implement-capacity-building-activities-for-health-researchers/

[98] Region 2 Health Research and Development Consortium "Philippines and UK strengthen S&T cooperation in health" (https://region2.healthresearch.ph/index.php/8-news/454-philippines-and-uk-strengthen-s-t-cooperation-in-health)

[99] Region 2 Health Research and Development Consortium "DOST-PCHRD, FIF, and UPM sign partnership advancing PH liver research" (https://region2.healthresearch.ph/index.php/8-news/513-herdinphrrnotice-of-bid-and-notice-of-award-dost-pchrd-fif-and-upm-sign-partnership-advancing-ph-liver-research)

[100] FY 2020 Project to Collect and Analyze Regulatory Information for Drugs and Medical Devices in Asian Countries (Additional Survey)

[101] FY 2020 Project to Collect and Analyze Regulatory Information for Drugs and Medical Devices in Asian Countries (Additional Survey)

[102] FY 2020 Project to Collect and Analyze Regulatory Information for Drugs and Medical Devices in Asian Countries (Additional Survey)

Table 2-10 Relevant Laws and Regulations Concerning Drug Regulation in Indonesia

Acts	Years of Issue	Overview
Health Law No. 36/2009	2009	・The law also mentions restrictions on advertising of adverse reactions, licensing and advertising. (Article 106) ・The government is responsible for the safe management and supply of medicines (Article 99). ・The quality assurance and transport of medicines, and approval of suppliers are mandatory. (Article 105, 106) ・The government's authority over the supply and recall of pharmaceuticals and medical devices and medical equipment (Article 106). ・The storage, supply, and storage of medicines, and the provision of medical services or medical information based on a physician's prescription shall be performed by medical personnel. (Article 108)
Laws and Regulations Concerning the Registration of Medical Products		
Minister of Health Regulation No. 1010/MENKES/PER/XI/2008 on Drug Registration (Regulation 1010)	2008	Registration of drugs (Article 14), Fees (Article 15), Council (Article 19), Reconsideration (Article 22), Distribution license (Article 21), Sanctions (Article 23)
Indonesian FDA Regulation No.24 of 2017 on Criteria and Drug Registration Procedure (Regulation 24)	2017	・Registration of pharmaceutical products is a requirement for pharmaceutical products to guarantee the quality standards of the manufacturing process based on GMP certification (Cara Pembuatan Obat yang Baik-""CPOB""). ・The obligation to register the product before marketing authorization (Izin Edar). ・Registration of new drugs, generic drugs, biotech drugs, etc. are newly added.
Laws and Regulations Concerning Post-Marketing Safety Surveillance		
MOH Regulation No.1799/Menkes/Per/XII/2010 on Pharmaceutical Industry	2010	・Regulations on Adverse Reaction Reporting
Indonesian FDA Regulation No. HK. 03. 1. 23. 12. 11. 10690 TAHUN 2011 on Implementation of Pharmacovigilance for Pharmaceutical Manufacturers	2011	・ Regulations pertaining to post-marketing safety surveillance ・Reporting obligations of pharmaceutical companies regarding adverse events of pharmaceutical products
Laws and Regulations Concerning Domestic Supply and Demand Rates for Pharmaceutical Raw Materials and Manufacturing		
Presidential Directive No.6 of 2016 on the Acceleration of the Development of the Pharmaceutical and Medical Equipment Industry	2016	・Notice to strengthen domestic pharmaceutical companies and reduce imported raw materials.
Ministry of Industry (MOI) Regulation No.16 of 2020 on Provisions and Procedures for the Calculation of Domestic Component Levels for Pharmaceutical Products (MOI Reg. 16/2020)	2020	・The minimum domestic supply-demand ratio for medicinal products and their raw materials. ・The procedures for obtaining local content certificates for pharmaceutical products and their raw materials that meet the criteria for domestic demand.
Laws and Regulations Concerning Clinical Trials		
Indonesian FDA Regulation No.21 of 2015 on the Procedures for Clinical Trial Approval (Regulation 21)	2015	・Rules for Clinical Trials

ii. Drug approval system

Drug registrations are classified into seven categories: (1) new registration ("Class 1: New drugs/biopharmaceuticals including biosimilars" "Class 2: Imitation drugs/generic drugs" "Class 3: Other"), (2) change registration ("Type 4 Major change" "Type 5 Minor change with approval" "Type 6 Minor change with notification"), and (3) re-registration/renewal (Type 7)[103].

Applications for registration are to be made using the ASEAN Common Technical Document (ACTD), which consists of "Administrative documents, product information and markings" quality documents, non-clinical documents and clinical documents[104].

The review period will be shortened if the assessment report is available in the United States or the EU and approved in another reference country, or approved in three reference countries. Japan is also regarded as a country with an established evaluation system, and it is possible to conduct an abbreviated examination using the Japanese examination report[105].

[103] FY 2020 Project to Collect and Analyze Regulatory Information for Drugs and Medical Devices in Asian Countries (Additional Survey)

[104] FY 2020 Project to Collect and Analyze Regulatory Information for Drugs and Medical Devices in Asian Countries (Additional Survey)

[105] FY 2020 Project to Collect and Analyze Regulatory Information for Drugs and Medical Devices in Asian Countries (Additional Survey)

Another characteristic is that because Indonesia is a Muslim country, there are halal regulations on medicines and, in principle, does not approve medicines made from specific ingredients such as pigs[106].

iii. Regulations concerning clinical trials

When conducting Phase 1 to Phase 3 studies in Indonesia, it is mandated that the GCP stipulated by the BPOM must be observed[107]. The GCP guidelines set out by the BPOM have a two-part GCP, with the first part providing for items not covered by the regulations or ICH-GCP, and the second part complying with ICH-GCP. Clinical trial procedures are defined in the "Decree of the Head of National Agency of Drug and Food Control Republic of Indonesia No. 02002/SK/KBPOM REGARDING CLINICAL TRIAL PROCEDURE"[108].

In Indonesia, there are two types of IRBs for ethics review of clinical trials: the Central IRB, such as the National Ethical Committee, and the Local IRB, which is owned by the institution conducting the clinical trial, such as a hospital or university, but the choice of which IRB to use is voluntary. Observational studies usually apply to the Local IRB for ethics review, but if the clinical trial process is complex or there are multiple study sites (e.g., studies of COVID-19 therapeutics), the Central IRB is often used for review. (INA-RESPOND)

iv. Systems and regulations for local manufacturing

Drugs sold in Indonesia must be registered, but for registration approval, a manufacturing facility in the country is required, and an Indonesian manufacturer is required to be the applicant[109].

According to Ministerial Ordinance No. 1010, a marketing license is issued by the Minister of Health as soon as a drug is registered (Article 21). The manufacture or import of drugs must begin within 1 year of registration (Article 21). The marketing period is 5 years (Article 20), after which an application for re-registration must be submitted[110].

As for manufacturing and quality control, Indonesia is a member of PIC/S and must comply with the GMP. GMP accreditation/inspection/quality control is governed by BPOM[111].

v. Policy trends in clinical trials and manufacturing

1) Development of domestic vaccines

Indonesia is focusing on the development of domestically manufactured vaccines. With the government's support, the state-owned pharmaceutical company Bio-Pharma began development of a vaccine for COVID-19, Indovac, in November 2021, which was urgently approved by BPOM, and the first vaccination was administered in October 2022 under the watchful eye of President Joko. The background to this is the international battle for the vaccine due to the coronary disaster. In addition, the fact that the vaccine manufactured by the British company AstraZeneca uses ingredients derived from pigs, which are forbidden by Islam, in its manufacturing process, caused concern in Indonesia, which has a large Muslim population. Exports are being considered not only to Indonesia but also to other countries with large Muslim populations and to Africa, where vaccinations have been delayed[112].

2) Halal Compliance

The Indonesian Parliament has passed the Halal Products Law, which requires producers to label their products as halal or non-halal. The domestically manufactured COVID-19 vaccine "Indowak" is also halal

[106] FY 2020 Project to Collect and Analyze Regulatory Information for Drugs and Medical Devices in Asian Countries (Additional Survey)

[107] FY 2020 Project to Collect and Analyze Regulatory Information for Drugs and Medical Devices in Asian Countries (Additional Survey)

[108] FY 2020 Project to Collect and Analyze Regulatory Information for Drugs and Medical Devices in Asian Countries (Additional Survey)

[109] FY 2020 Project to Collect and Analyze Regulatory Information for Drugs and Medical Devices in Asian Countries (Additional Survey)

[110] FY 2020 Project to Collect and Analyze Regulatory Information for Drugs and Medical Devices in Asian Countries (Additional Survey)

[111] FY 2020 Project to Collect and Analyze Regulatory Information for Drugs and Medical Devices in Asian Countries (Additional Survey)

[112] Nihon Keizai Shimbun"Southeast Asia rushes halal-compliant corona vaccine" (https://www.nikkei.com/article/DGXZQOGS319N80R31C22A0000000/)

compliant, and since Muslims account for approximately 87% of the population in Indonesia, halal compliance is becoming more and more important[113].

(2) Process from application to approval for clinical trials and local manufacturing

i. Process from application to approval for clinical trials

The figure below shows the application to approval process for a clinical trial in Indonesia. The sponsor must obtain approval from the ethics committee before applying to BPOM for permission to start a trial. After approval by the ethics committee, BPOM evaluates the clinical trial documents in consultation with the Pharmaceutical Affairs Council and decides on approval or rejection within 20 days of submission. If a clinical trial is approved, a letter of approval valid for two years is issued[114].

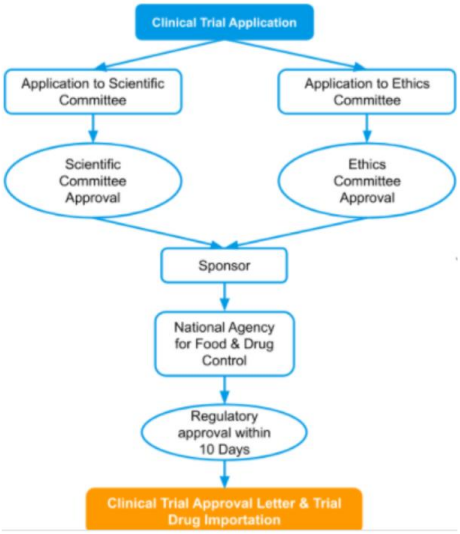

Figure 2-25 Application to approval process for clinical trials in Indonesia

ii. Process from application to approval for local manufacturing

In order to produce pharmaceutical products for sale in Indonesia, it is necessary to obtain a PIBL (Pharmaceutical Insutry Business License) from the Ministry of Health. The PIBL can be applied for through an online portal, and once obtained, it is valid for an unlimited period of time. A manufacturing license is also required to demonstrate compliance with PIBL regulations. The process from application to approval usually takes 2 to 3 months[115].

(3) Issues in target countries (Policies, regulations and legal systems for clinical trials and local manufacturing)

i. Simplify the process for reviewing clinical trials

Simplifying the clinical trial review process was cited as an issue by several interviewees. Specifically, they mentioned the lack of an integrated ethics committee and the need to obtain approval from each site's ethics committee one by one. In addition, INA-RESPOND, which is under the jurisdiction of the Ministry of Health, has a National Ethical Committee separate from the BPOM, and clinical trials conducted under INA-RESPOND must be submitted to that committee, therefore, some said that it is a challenge that clinical trials conducted under INA-RESPOND are not integrated with the ethical review by BPOM (an

[113] RECOVERY "Taking RECOVERY to Indonesia" (https://www.recoverytrial.net/case_studies/taking-recovery-to-indonesia)

[114] Baker McKenzie "CLINICAL TRIALS HANDBOOK Asia Pacific Indonesia"(https://www.bakermckenzie.com/-/media/files/insight/publications/2019/healthcare/ap/dsc125067_clinical-trials-handbook-indonesia.pdf?sc_lang=en&hash=14071A1C6B480E41D89E454A6B31BDA8)

[115]"REGULATION OF THE MINISTER OF HEALTH NUMBER 1799/MENKES/PER/XII/2010" (http://www.flevin.com/id/lgso/translations/JICA%20Mirror/english/4883_1799_MENKES_PER_XII_2010_e.html)

organization independent from the Ministry of Health).

ii. Balance between protection of domestic industry and entry of companies from abroad

As mentioned in 2.1.1(5)v, Indonesia has policies such as requiring foreign pharmaceutical companies to cooperate with Indonesian companies for manufacturing in Indonesia and to indicate whether or not their products are halal compliant. While these policies may be desirable from the perspective of developing the Indonesian industry, they may also create barriers to entry for foreign pharmaceutical companies, therefore balance must be taken into account[116].

2.5.2 Local implementation system for related facilities and human resources in target countries

(1) Implementation system for clinical trials and local manufacturing at related facilities, facilities, human resources, etc.

i. Local clinical trial system

A) Clinical trial sites

Indonesia is home to international and local clinical research institutions, which provide services such as feasibility studies, clinical trial consulting, and bioanalysis to institutions such as Prodia and SGS. The main agencies are listed in the table below.

Table 2-11 List of clinical research institutes in Indonesia

CRO	Year of Establishment	Revenue (in mn USD)	Services Offered		
Prodia the CRO	2008	1.17 (2018)	• Feasibility Study • Trial Sites and Investigator Selections • Subject Recruitment	• Investigational Product Management • Bioavailability and Bioequivalence Study • Clinical Trial Consulting	• Data Management
SGS	1985	7,006.9 (2021)	• Clinical Research Services (Phase I to Phase IV Trials) • Clinical Development Consultancy • Early Phase Clinical Research	• Clinical Trial Management • Biometrics Services • Pharmacovigilance and Drug Safety	• Bioanalytical Services
IQVIA	1982	10,412 (2021)	• Clinical Development • Early Phase • Phase II-III, Phase IIIb-IV	• Clinical Data, Supply chain management • Decentralized Clinical Trials • Pharmacovigilance	• Biostatistics • Consulting
parexel	1982	2,441.5 (2017)	• Clinical Trials • Decentralized Trials • Functional Services	• Consulting • Patient Engagement	
Syneos Health	1999	5,213 (2021)	• Clinical Development • Early Phase • Phase II-III, Phase IIIb-IV	• Clinical data management • Clinical Monitoring • Consulting	• Biostatistics and Statistical Programming • Bioanalytical solutions

B) Domestic capacity for clinical trials

Indonesia's national capacity for clinical trials is concentrated in West Java, the province with the most hospitals. Local CROs such as Hayya Life Science and Prodia the CRO conduct clinical trials and provide SMO services.

[116]ERIA "Indonesia's Local Content Requirements: Assessment with WTO Rules" (https://www.eria.org/uploads/media/discussion-papers/FY21/Indonesias-Local-Content-Requirement-WTO-Rules.pdf)

C) Examples of recent clinical trials

Currently, there are around 190 clinical trials underway in the country, many of which relate to the efficacy of the COVID-19 vaccine[117]. Examples of clinical trials from 2021 to 2023 are as follows.

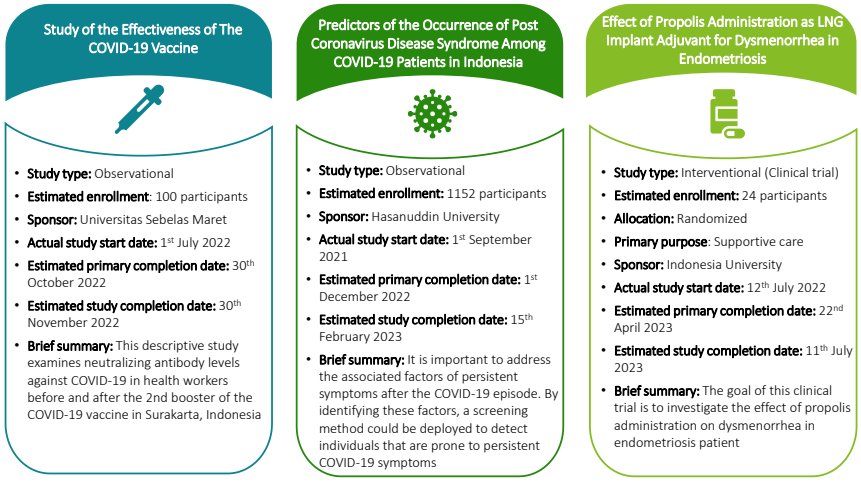

Figure 2-26 Recent clinical trial case studies in Indonesia

ii. Local manufacturing system

A) Pharmaceutical manufacturing base

As for pharmaceutical companies, international pharmaceutical companies such as GSK, AstraZeneca, Astellas, and Meiji Group have been expanding their operations in the country, partly because the revision of the Alien Ownership Law has made it easier for foreigners to own real estate. In addition, Pt Kalbe Farma Tbk., the largest domestic pharmaceutical company in Indonesia, has a significant market share.

State-owned Bio Pharma partnered with the Baylor College of Medicine to develop COVID-19's halal vaccine, which has been available since October 2022[118].

[117] National Library of Medicine “Post Coronavirus Disease (COVID-19) Syndrome Indonesian Population” (https://clinicaltrials.gov/ct2/show/NCT05060562)

[118]Nihon Keizai Shimbun”Southeast Asia rushes halal-compliant corona vaccine” (https://www.nikkei.com/article/DGXZQOGS319N80R31C22A0000000/)

Table 2-12 International pharmaceutical companies based in Indonesia

Company	Year of Establishment	Revenue (in mn USD)	Key Offerings
GSK	2000	46,923.8 (2021)	• Prescription Medicines • Vaccines • Consumer Healthcare Products
AstraZeneca	1999	37,417 (2021)	• Precision Medicine • Biopharmaceuticals • Vaccines • Medicines for Oncology, Cardiovascular, Renal, Metabolism, Respiratory, Immunology
astellas	2005	11,786 (2021)	• Enzalutamide • Gilteritinib • Enfortumab vedotin • Roxadustat • Mirabegron • Tacrolimus
meiji	1974	7,291 (2021-22)	• Vaccines • CNS Disorders Pharmaceuticals • Blood Plasma Products • Animal Healthcare • Infectious Diseases Drugs, Vaccines
MENARINI group	1886	3,800 (2020)	• Anti-Infectives • Cardiometabolic Therapeutics • Gastrointestinal Therapeutics • Urology Therapeutics • Respiratory and Allergology Therapeutics
MERCK	1891	48,704 (2021)	• Prescription Pharmaceuticals • Vaccines • Animal Health
Mitsubishi Tanabe Pharma	2001	3,830.2 (2019)	• Cardiovascular Drugs • Health Supplements • Prescription Pharmaceuticals • Animal Healthcare • TENELIA® OD Tablets
Pfizer	1849	81,288 (2021)	• Quinapril HCl • Adenosine • Apixaban • COVID-19 Vaccine • Pneumococcus vaccine
NOVARTIS	1996	51,626 (2021)	• Generic Medicines • Innovative Medicines • Radiopharmaceuticals
Roche	1896	66,747.1 (2021)	• Dermatology therapeutics • Cancer Therapeutics • Respiratory disorders therapeutics • Medicines for Infectious diseases
Dexa Medica	1969	932 (2021)	• Branded Generic Pharmaceuticals • Advanced Herbal Medicines
KALBE	1966	1836.3 (2021)	• Prescription Drugs • Consumer Healthcare • Animal Health • Nutritional • Biopharma
kimia farma	1971	899.1 (2021)	• Generic Pharmaceuticals • Radiopharmaceuticals • Skin care • OTC Drugs
combiphar	1971	689 (2021)	• Pharmaceuticals • Consumer Healthcare • Wellness
TEMPO SCAN	1953	785.6 (2021)	• Consumer Healthcare • Generic, Branded Generic Drugs
NOVELL PHARMACEUTICAL LABORATORIES	1982	582 (2021)	• Health Supplements • Antibiotics • CNS Drugs • Antihistamine
bioFarma	1890	149 (2021)	• Combination Vaccines • Viral Vaccines • Bacterial Vaccines • Diagnostic Vaccines

B) Types and volumes of locally manufactured drugs

Indonesian companies account for a large share of the pharmaceutical market in Indonesia, with Biofarma having the largest share (8.2%). The main destinations for exports of pharmaceuticals from Indonesia are the Philippines, India, Malaysia and Singapore[119].

For example, Dexa Medica produces more than 1 billion pills, vials and ampoules (all generic) each year[120].

Biofarma also exports vaccines for polio, measles, tuberculosis, and triplex to countries such as India, Egypt, South Africa, Thailand, Turkey, and Mexico. It has a capacity of 2 billion doses each year, of which 60% are for domestic use and 40% for export[121].

In 2020, Kalbe Farma manufactured 15.4 million tablets, 1409.7 million capsules and 113 million ampoules for prescription drugs. Of these, 95% were for domestic use and 5% for export[122].

(2) Issues in target countries (Capacity to conduct clinical trials and local manufacturing)

i. Expansion of laboratory facilities

Indonesia has few labs for BSL-3, which can handle at-risk pathogens, and limited facilities for analysis. Because the Indonesian government prohibits the removal of domestically collected biological specimens from the country, analysis using domestic specimens cannot be conducted outside the country and must be financed domestically, requiring a sufficient level of laboratory in the country.

ii. Recruitment of clinical trial subjects

Recruitment for clinical trials was considered a challenge in several interviews. Some of the reasons that were given include fear of adverse events and lack of awareness of clinical trials.

2.5.3 Results of a survey on initiatives taken by aid agencies, research institutes, and companies in other countries, including the target countries

(1) Overview of promotion of local manufacturing of vaccines and pharmaceuticals

i. National policies and measures to promote local manufacturing

In 2016, the Indonesian government issued Executive Order No. 6 of 2016 on accelerating the development of the pharmaceutical and medical device industries in order to strengthen domestic medical product manufacturers and reduce their dependence on imported raw materials. In response to the Presidential Decree, in 2020, the Ministry of Industry (MOI) introduced Regulation No. 16 of 2020 on "Provisions and procedures for the calculation of national component proportions of pharmaceuticals" to support local manufacturing of pharmaceuticals. It specifies the method for calculating the national component percentage of the final product and raw material of a drug and the procedure for obtaining a certificate showing it[123].

In addition, Indonesia is promoting the transfer of technology to the country in manufacturing of pharmaceuticals. Foreign pharmaceutical companies are allowed to import medicines into Indonesia only

[119] Pharma Industry "Top 10 Largest Pharmaceutical Companies in Indonesia" (https://farmasiindustri.com/industri/largest-pharmaceutical-companies.html)

[120] Dexa Medica Home Page (https://www.dexagroup.com/dexa-medica)

[121] Pharma Industry "Top 10 Largest Pharmaceutical Companies in Indonesia" (https://farmasiindustri.com/industri/largest-pharmaceutical-companies.html)

[122] KALBE "Sustainability Report 2020" (https://www.kalbe.co.id/api-content/File/GetFile/2021-06-07%20KalbeFarma%20SR%202020%20Design%20Layout-ENG-LoRes_FINAL%20after%20RUPS.pdf)

[123] ERIA "Indonesia Local Content Requirements: Assessment with WTO Rules" (https://www.eria.org/uploads/media/discussion-papers/FY21/Indonesias-Local-Content-Requirement-WTO-Rules.pdf)

if they can produce them domestically within five years after forming a partnership with an Indonesian company and transferring manufacturing technology[124].

(2) Donor initiatives to support clinical trials and local manufacturing of vaccines and other pharmaceutical products in target countries

i. Donors move to support infectious disease research in Indonesia

The United States is actively supporting infectious disease research in Indonesia. A representative example of a joint initiative between American and Indonesian government agencies is the Indonesian Partnership for Infectious Disease Research (INA-RESPOND: Indonesia Research Partnership on Infectious Disease). INA-RESPOND was established to promote and conduct high-quality clinical research on infectious diseases in Indonesia, with the primary objective of conducting basic and clinical research in line with the priority issues of the Indonesian Ministry of Health to promote a better understanding of disease pathogenesis and to prevent and treat infectious diseases, and has been conducting clinical research since 2011. Malaria, avian influenza, dengue fever, AIDS (HIV), tuberculosis and neglected infectious diseases are among the infectious diseases that have been prioritized by the Indonesian Ministry of Health[125]. Examples of recent research studies include the International Observational Cohort Study of Adult Patients with SARS-CoV-2 Infection/COVID-19 (ICOS Study), a study to identify cases of respiratory infections in COVID-19 and elsewhere, describe the course of COVID-19's disease and case management, evaluate the accuracy of diagnostic tests, understand hospitals, evaluate treatments and short-term outcomes, generate epidemiological data to inform disease control and prevention efforts (ORCHID Study), and compare the virological efficacy of regimens for treating patients with HIV -1 infection (HIV) (D2 EFT Study)[126]. Partners of INA-RESPOND include the University of Indonesia, the Centers for Disease Control and Prevention (CDC), the National Institutes of Health and the National Institute of Allergy and Infectious Diseases (NIH-NIAID)[127].

[124] PhRMA「PHARMACEUTICAL RESEARCH AND MANUFACTURERS OF AMERICA (PhRMA)」(https://phrma.org/-/media/Project/PhRMA/PhRMA-Org/PhRMA-Org/PDF/P-R/PhRMA_2021-Special-301_Review_Comment-1.pdf)

[125] INA-RESPOND Homepage (https://ina-respond.net/about/)

[126] INA-RESPOND Homepage (https://ina-respond.net/our-studies/)

[127] INA-RESPOND Homepage (https://ina-respond.net/ourpartners/#)

INA RESPOND

- **INA Respond is a collaborative between the US and Indonesia to promote and conduct clinical research in Indonesia**
- **INA Respond has been conducting clinical research since 2011**
- **It is a multi center clinical research network operating at 9 hospitals and 7 academic institutes and 4 major collaborators**

- **The network hospitals include**
  - Pusat Infeksi Nasional RSPI Sulianti Saroso, Jakarta
  - RSUD Dr. Soetomo, Surabaya
  - RSUP Dr. Hasan Sadikin, Bandung
  - RSUP Dr. Kariadi, Semarang
  - RSUP Dr. Sardjito, Yogyakarta
  - RSUP Dr. Wahidin Sudirohusodo, Makassar
  - RSUP Persahabatan, Jakarta
  - RSUP Sanglah, Denpasar, Bali
  - RSUPN Dr. Cipto Mangunkusumo, Jakarta
- **The academic institutes includes:**
  - Universitas Airlangga
  - Universitas Diponegoro
  - Universitas Gadjah Mada
  - Universitas Hassanudin
  - Universitas Indonesia
  - Universitas Padjadjaran
  - Universitas Udayana
- **The major collaborators includes:**
  - Eijkman Institute for Molecular Biology, Jakarta
  - National Institute of Health Research and Development (NIHRD)
  - United States Centers for Disease Control and Prevention (CDC)
  - United States National Institutes of Health, National Institute of Allergy and Infectious Diseases (NIH-NIAID)

Examples of studies being conducted in Indonesia by INA-RESPOND and NIAID

- INA-PROACTIVE is a multicenter, prospective, observational cohort study of HIV positive antiretroviral-naïve and treatment-experienced individuals
- Study name: "A Prospective Observational Cohort Study on HIV Infection and Risk Related Coinfections/Comorbidities in Indonesia"
- Study period: 2018 to 2023
- Collaborator: NIAID US
- Overview: The observational study has an active involvement with 19 hospitals. In July 2020, the total number of participants in the study were 4,336. As of February 2021, out of 4,336 enrolled participants, 209 ended the study, 21 withdrew, 161 died, 22 relocated to a different city, and 5 subjects reported negative HIV results.

Figure 2-27 Examples of joint research with INA-RESPOND partner institutions and NIAID[128]

ii. Donor movement to support health and medical sectors

The United Kingdom is strengthening its cooperation with the Indonesian government in health. At the 3rd Indonesia-UK Partnership Forum held on April 7, 2021, a wide range of topics were discussed with COVID-19, including vaccine diplomacy, economic partnership and trade, security, and climate change. In the area of health and vaccine cooperation, commitments were made to (1) strengthen cooperation for health recovery after COVID-19 infections, including the distribution of the COVID-19 vaccine, and (2) ensure fair, affordable and equitable distribution of the COVID-19 vaccine. Both countries welcomed the cooperation between the University of Oxford and AstraZeneca and the state-owned pharmaceutical company, Biopharma, and the conclusion of an MOU by both countries' ministries of health on cooperation in the health sector, and stressed the importance of cooperation under the GAVI COVAX facility[129]. Both countries' MOUs focus on areas of cooperation such as health services, disease prevention and control, health technology and medical equipment, human resources for health development, and research and development in health, and the cooperative activities agreed under this MOU include digital health services and community-based telemedicine cooperation, and information sharing on infectious diseases in hospitals (such as COVID-19). In addition, the two countries also signed a grant agreement worth 4.8 million pounds for the Fleming Fund partnership for AMR surveillance targeting human health in Indonesia. The Fleming Fund grant program aims to help partner countries create, share and use data on AMR to increase understanding and encourage action on drug resistance at the national and international levels. In Indonesia, the Fleming Fund is focused on building capacity in laboratories and will support up to 10 Indonesian scientists, researchers and clinicians as part of a fellowship scheme[130].

[128] National Library of Medicine "HIV Infection and Risk Related Coinfections/Comorbidities in Indonesia (INAPROACTIVE)" (https://clinicaltrials.gov/ct2/show/record/NCT03663920?recrs=cd&type=Obsr&cntry=ID&fund=02&draw=2&view=record)

[129] GOV.UK "Indonesia-United Kingdom Partnership Forum 2021: joint statement " (https://www.gov.uk/government/publications/indonesia-united-kingdom-partnership-forum-2021-joint-statement/indonesia-united-kingdom-partnership-forum-2021-joint-statement)t

[130] Embassy of the Republic of Indonesia to the United Kingdom, Ireland, and IMO "The UK and Indonesia announces MoU on Health Cooperation and a Grant Agreement on Anti-Microbial Resistance Surveillance"

(https://kemlu.go.id/london/en/news/7288/the-uk-and-indonesia-announces-mou-on-health-cooperation-and-a-grant-agreement-on-anti-microbial-resistance-surveillance)

(3) Initiatives of European and American universities, research institutes and pharmaceutical companies

Examples of supporting clinical trials and vaccine and drug manufacturing in Indonesia include the programs shown below.

The National Institute of Allergy and Infectious Diseases (NIAID) supports Indonesia in such areas as HIV/AIDS, malaria and influenza research, including avian influenza. In the area of HIV/AIDS, Indonesia participates in the International Epidemiologic Database to Evaluate AIDS, which is supported by NIAID. NIAID also supports extramural research projects on anti-AIDS drugs of marine origin, including collaborations between universities in the United States and Indonesia. In addition, NIAID is also supporting malaria-related research on severe malaria in Indonesia. In Indonesia, three hospitals - Persahabatan, Sulianti Saroso and Hasan Sadikin - are part of the NIAID-supported Southeast Asian Infectious Diseases Clinical Research Network (SEAICRN) and are conducting clinical trials for severe influenza and avian influenza[131].

The Indonesian Ministry of Health and the Korean Ministry of Health are supporting practical cooperation between the two governments and the health industry. Daewoong Pharmaceutical, a global health care company in South Korea, is focused on developing its biopharmaceutical business in Indonesia, bringing its advanced technologies to the country and working with local pharmaceutical companies there[132]. Daewoong Pharmaceutical partnered with Indonesian pharmaceutical company Infion to establish a joint venture Daewoong Infion in 2012. The Indonesian Ministry of Health's National Institute of Health Research and Development (NIHRD) and Daewoong Infion Korea are collaborating, for example, on a clinical trial of stem cell therapy for COVID-19 patients with acute respiratory distress syndrome (ARDS).

The Indonesian state-owned pharmaceutical company Biopharma, in collaboration with the Baylor College of Medicine, a private independent medical service center in the US state of Texas, developed the IndoVac COVID-19 vaccine, which is a halal (It was approved by a national certification body for eliminating ingredients from pigs, alcohol and other substances banned by Islam) vaccine in line with Islamic precepts and began inoculating people in October this year[133] [134]. Biopharma teamed up with Baylor College of Medicine to use a technology called "recombinant proteins," and the company says its trials "confirmed efficacy over a comparable vaccine with more than 80% efficacy." The final-stage trial involved about 4000 people. Development began in November 21[135].

[131] National Institute of Allegy and Infectious Diseases “Global Research in Indonesia” (https://www.niaid.nih.gov/research/niaid-research-indonesia)

[132] Independent Observer “Daewoong Infion, Daewoong Pharmaceutical’s Bio-Pharmaceutical Business Center In Indonesia” (https://observerid.com/daewoong-infion-daewoong-pharmaceuticals-bio-pharmaceutical-business-center-in-indonesia/)

[133] Asia One “Indonesian pharmaceutical Bio Farma ready to produce IndoVac Covid-19 vaccines” (https://www.asiaone.com/business/indonesian-pharmaceutical-bio-farma-ready-produce-indovac-covid-19-vaccines)

[134] Nihon Keizai Shimbun” Southeast Asia focuses on domestically produced vaccines” (https://www.nikkei.com/article/DGKKZO65863410Q2A111C2FFJ000/)

[135] Ibid.

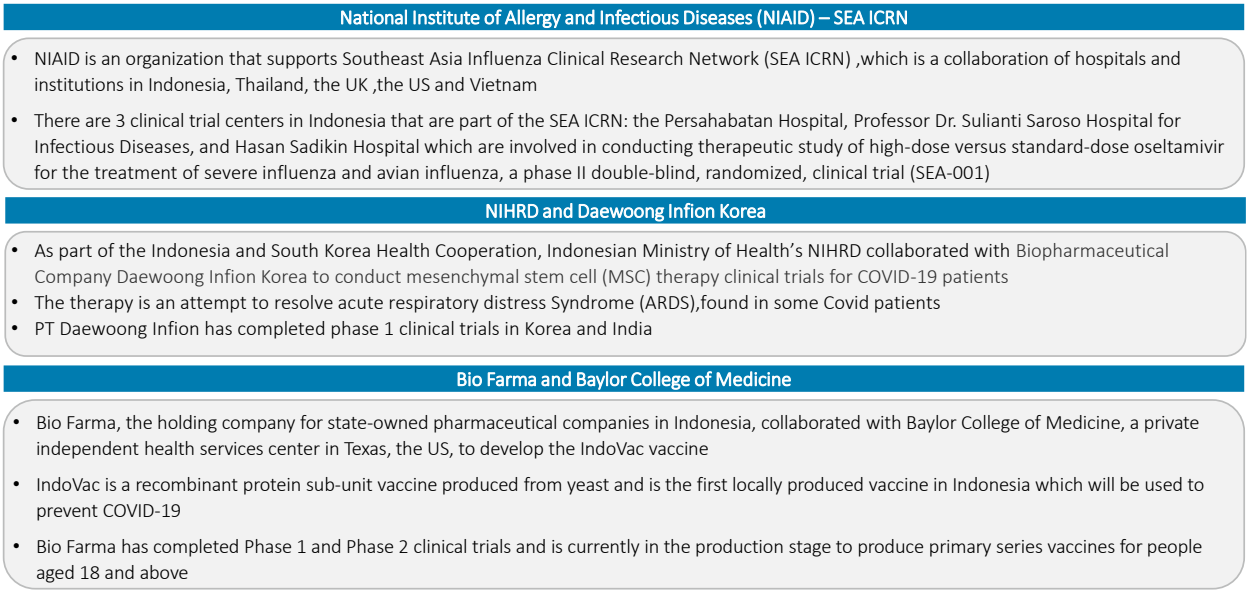

Figure 2-28 Key programs supporting clinical trials, drug and vaccine manufacturing in Indonesia

Another example of donor support is infection-related work at the Eijkman-Oxford Clinical Research Unit (EOCRU), a joint research institute between the UK and Indonesia. The EOCRU is a joint research institute of the University of Oxford and Indonesia, which was established in 2008 as one of the units of the EIMB through a memorandum of understanding between the Eijkman Institute for Molecular Biology (EIMB) and the University of Oxford to conduct joint research on infectious diseases affecting the health of residents of Indonesia and other Southeast Asian countries. These institutions are currently collaborating on clinical, laboratory and field research on infectious diseases of public health importance in Indonesia. Focused areas include tuberculosis, malaria, other emerging and neglected infectious diseases. The EOCRU is also part of the Oxford Tropical Network, which has research units in Africa, Asia and the UK, and is run under the auspices of the Oxford University Clinical Research Unit (Oxford University Clinical Research Unit: OUCRU) in Vietnam[136]. In 2017, the EOCRU and the University of Indonesia Medical School (Faculty of Medicine University of Indonesia: FMUI) jointly established the University of Indonesia - Oxford Clinical Research Institute (Universities of Indonesia and Oxford Clinical Research Laboratory: IOCRL) within the Department of Parasitology at FUMI with the aim of expanding clinical research activities. New areas of challenge include central nervous system infections, tuberculosis, HIV and antimicrobial resistance.

2.6 Kenya

2.6.1 Legal systems and procedures in target countries

(1) Related policies and legal systems

i. National organizations and legal systems for drug regulation, including vaccines

Medicines, hazardous substances and other drug-related products in Kenya are regulated by the Pharmacy and Poisons Board (PPB) established under Chapter 244 of the Medicines and Poisons Act, Kenya Law. The PPB has a Biologics Unit with expertise in vaccines and aims to implement appropriate regulatory measures to achieve the highest standards of safety, efficacy and quality for all drugs, chemicals and medical devices.

[136] Life at Social "[Eijkman-Oxford Clinical Research Unit] : Assistant Researcher" (https://lifeatsosial.wixsite.com/my-site/post/eijkman-oxford-clinical-research-unit-assistant-researcher)

In addition, as a standard for pharmaceutical products, a GMP roadmap document covering basic principles in line with WHO's Good Manufacturing Practices (GMP) is established and required to be followed.

ii. Drug approval system

Drug registration in Kenya is valid for five years. According to PPB guidelines, the application process takes 12 months.

iii. Regulations Concerning Clinical Trials

The PPB serves as the regulatory agency for approvals, inspections, and monitoring related to clinical trials. The PPB has an Expert Committee on Clinical Trials (ECCT) that assesses all matters related to clinical trials[137], with the PPB and ECCT responsible for reviewing, evaluating and approving applications for clinical trials with registered and unregistered investigational products (IPs). The ECCT provides guidelines and includes information on the requirements for conducting clinical trials involving investigational drugs, medical devices, and herbal medicines[138]. In addition to approval from the PPB, a research license from the National Commission for Science, Technology and Innovation (NACOSTI) must also be obtained in order to conduct clinical research in Kenya.

iv. Systems and regulations for local manufacturing

To manufacture a drug, a manufacturer is required to obtain a manufacturing license valid for one year from PPB. (Each manufacturing license expires on December 31 of each year) In addition, staff belonging to the National Drug Quality Control Laboratory are authorized to conduct on-site inspections at all manufacturing facilities to collect pharmaceutical substances during manufacturing and certify that the drugs are manufactured in accordance with approved manufacturing methods. The PPB has also established good manufacturing practices (GMP) guidelines, which require pharmaceutical manufacturers in Kenya to follow GMP.

v. Policy trends in Clinical trials and manufacturing

Recent trends in clinical trial-related policies have included updates to guidelines for conducting clinical trials and moves to improve the safety of trial participants and the ethical review process.

In terms of local manufacturing, promoting domestic manufacturing (including pharmaceuticals) was listed as one of the four objectives of the Big Four Development Agenda in 2017, and in the same year, the Ministry of Industry, Trade and Enterprise Development issued the Buy Kenya Build Kenya Strategy, which aims to promote domestic manufacturing and enhance domestic market access for domestically manufactured products and services[139]. Under the Department of Health's National COVID-19 Vaccine Deployment Plan, the company is establishing a vaccine factory to produce not only corona but also polio vaccines, with the aim of being fully operational by 2024. In addition, in March 2022, the Kenyan government signed an MoU with Moderna, Inc. of the United States to build an mRNA manufacturing facility, and the Kenyan Parliament amended the law in 2022 to grant tax incentives to local vaccine producers with capital investments exceeding US $82 million.

In Africa, under the leadership of the African Centers for Disease Control and Prevention (CDC), the African Union established the Partnerships for African Vaccine Manufacturing (PAVM) in 2021. The goal is to develop, produce, and supply more than 60% of the necessary vaccine doses in Africa by 2040. In addition, six African countries (Egypt, Senegal, Kenya, South Africa, Tunisia, and Nigeria) have been the first recipients of mRNA technology transfer under the WHO's mRNA Technology Transfer Hub initiative, with Kenya also benefiting from the technology transfer.

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[137] Kenya PPB 「Guidelines for the Conduct of Clinical Trials in Kenya」(https://africacheck.org/sites/default/files/media/documents/2021-03/Guidelines%20for%20Conduct%20of%20Clinical%20Trials%20in%20Kenya%202nd%20Revision.pdf)

[138] Kenya PPB 「Guidelines for the Conduct of Clinical Trials in Kenya」(https://africacheck.org/sites/default/files/media/documents/2021-03/Guidelines%20for%20Conduct%20of%20Clinical%20Trials%20in%20Kenya%202nd%20Revision.pdf)

[139] President Uhuru Kenyatta has set forth four key economic policies (Big Four Development Agenda): food security, improved access to affordable housing, promotion of manufacturing and universal health care.

(2) Process from application to approval for clinical trials and local manufacturing

i. Application to approval process for clinical trials

Clinical trial investigators are required to obtain clinical trial approval from the Clinical Trials Expert Committee (ECCT) of the Pharmacy and Poisons Board (PPB). The detailed process from application to approval is shown below.

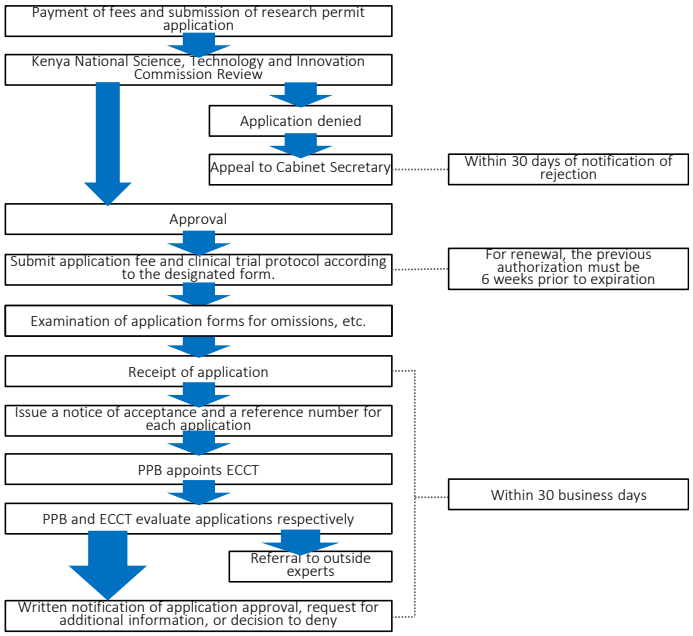


Figure 2-29 Application to approval process for clinical trials in Kenya

ii. Application to approval process for local manufacturing

To manufacture drugs for sale in Kenya, it is mandatory to obtain a valid manufacturing license from PPB. The entire licensing process usually takes 30 days to complete, and licenses are supposed to be valid for one year. It is also necessary to confirm that the products have been certified under Good Manufacturing Practices (GMP) and Good Distribution Practices (GDP) before they are registered.

(3) Issues in target countries (Policies, regulations and legal systems for clinical trials and local manufacturing)

The following are some of the regulatory process and policy issues that were mentioned in the online interviews and during the interviews during the field survey.

1) Accelerate the regulatory process

Several stakeholders have raised the issue of speeding up the regulatory process when conducting clinical trials. In addition to the PPB, the National Commission for Science, Technology and Innovation (NACOSTI) and the counties where clinical trials are conducted need to go through the approval process before a clinical trial can be conducted in Kenya. However, delays in the regulatory process are particularly serious, according to the report. One of the reasons for the delay in the regulatory process is that the number of personnel at the National Quality Control Laboratory (NQCL), which is the technical division of the PPB, as well as the PPB, has been decreasing year by year, and the shortage of personnel has led to delays in the regulatory process. (According to interviews with the PPB, one of the major challenges to achieving WHO's Maturity Level 3 is the expansion of staffing.) In addition, many of the reviewers of application documents sent to the PPB rely on external personnel who belong to other research institutes or private facilities. The need for external personnel to coordinate with their core business is also a factor causing delays, so it is necessary to consider reducing reliance on external personnel and expanding PPB's internal

review staff.

In other situations, there is no effective mechanism for efficiently handling large volumes of data (such as electronic platforms with automated processes, as in Europe and the U.S.) and no effective linkage between systems, and the situation is not conducive to processing the enormous volume of data submitted in the course of conducting clinical trials. Given the limited human resources of regulatory agencies, automation of processes and implementation of data management systems would help to efficiently expedite the process.

2) Clinical trial guidelines

As for guidelines for clinical trials, it was mentioned as an issue that they are mainly based on experiences in the field of infectious diseases such as malaria, tuberculosis, HIV, etc., and are not guidelines that can support products utilizing the latest technologies or the movements of innovator companies and multinationals.

2.6.2 Local implementation system for related facilities and human resources in target countries

(1) Implementation system for clinical trials and local manufacturing at related facilities, facilities, human resources, etc.

i. Clinical trial system

A) Clinical trial agency

The main clinical trial institutions in Kenya and their summary are as follows:

① Kenya Medical Research Institute (KEMRI)

KEMRI is a national research institute established in 1979 under the Ministry of Health. It plays an important role in the fight against infectious diseases and health crisis preparedness in Kenya and abroad, and many of the clinical trials in Kenya are being led by the institute. In addition to its close cooperation with JICA in both soft and hard aspects for about 40 years, KEMRI has a strong relationship with Japan, as evidenced by the establishment of the Kenya Project Center for Research on Infectious Diseases in Asia and Africa at the Institute of Tropical Medicine, Nagasaki University, in 2005. Amongst KEMRI's 15 research centers, the Center for Clinical Research (CCR) serves as a clinical trial unit, supporting the development of medicines and vaccines focusing on priority diseases in Kenya.

② KAVI Institute of Clinical Research

The Kenya AIDS Vaccine Initiative (KAVI) was established in 1998 as a research unit within the Department of Microbiology, Faculty of Health Sciences, University of Nairobi, to conduct basic research in HIV epidemiology and clinical trials of HIV/AIDS vaccines. It is currently conducting general clinical research in the area of developing drugs and vaccines related to infectious diseases, beyond HIV-related research. By 2013, 8 HIV vaccine trials, 2 drug trials, and 13 epidemiology and basic research projects had been conducted, and research is underway on the development of mucosal sampling and the standardization of mucosal immunoassays. It also makes a significant contribution to human resource development in the East African region by training various ethics committees and clinical trial personnel on research ethics, standards for conducting clinical trials (GCP) and standards for conducting clinical trials (GCLP) in the East African region.

③ Clinwin Research Services

It is a local CRO based in Nairobi, Kenya, with regional offices in Kampala, Uganda, and Kigali, Rwanda. It provides a variety of services, including clinical trials, pharmacovigilance monitoring, facility and study management, ICH GCP training, pharmaceutical supply chain management, handling and shipping of biological samples, and the design and conduct of epidemiological studies. It also offers data

science and technology-related services such as Clinical Trials Management Systems (CTMS).

Clinical Trial Facility	Description
Kenya Medical Research Institute	The most prominent CT facility with international (WHO, JICA, Global Research Unit) collaborations and local partnerships (Ministry of Health, University of Nairobi etc.), it reviews at least 25 clinical trials every month, while also collaborating with US agencies and universities
Moi Teaching & Referral Hospital CT unit	Located in Eldoret Kenya, MTRH is a public hospital that has conducted CTs in areas such as HIV, Oncology and other chronic diseases by working with the Moi University College of Health Sciences and other collaborators
Kenyatta National Hospital CT Unit	Established in 1987, as the largest referral and teaching hospital in the country. Research is one of the four core mandate of the 2,400 bedded facility having collaborations with institutions like KEMRI, University of Nairobi, and African Medical and Research Foundation
Jaramogi Oginga Odinga CT Unit	This tier 4 health facility, established in the early 1900s, has long-term collaborations with major international research agencies such as CDC and WRP from the USA, Mildmay International from the UK, and local NGOs
University of Nairobi	It is a research-intensive university with 48 collaborations and partnerships for research including universities for science and technologies and other technical universities
Kombewa Clinical Research Center	A KEMRI satellite clinic in Kisumu County, participates in HIV prevention and treatment research. They are currently working with the Kenya Defense Force on research related to HIV-positive children and adolescents
Maseno University CT Unit	The university has sponsored (Till date) 4 clinical trial studies related to pregnancy, neonatal care, stunting, anemia, zinc deficiency and environmental enteric dysfunction
KAVI institute of Clinical Research	Established in 1998 as a research unit within the Department of Medical Microbiology, has conducted 8 HIV vaccine trials, 2 drug trials, & 13 research projects. It also pioneered the development of mucosal sampling & standardization of mucosal immune assays by 2013
Kericho Clinical Research Centre	Since its establishment in 2012, the KEMRI Walter Reed Project Clinical Research Center in Kericho has carried out over 52 studies, encompassing clinical trials of vaccines and therapeutics as well as cohort studies, all of which have been successful

Figure 2-30 List of Major Public Institutions for Clinical Trials

B) Domestic capacity for clinical trials

Most clinical trials are conducted by public research institutions, including universities in Kenya, primarily through partnerships with U.S. institutions and research organizations such as KEMRI. In addition, funding is often provided by donors. Most clinical trial sites in Kenya are public or private facilities associated with foreign pharmaceutical companies or international research institutions, and the number of clinical trial sites in the local private sector in Kenya tends to be limited.

C) Examples of recent clinical trial research

According to the National Institutes of Health , 54 clinical trials were underway in Kenya as of October 2022. Of these, 9 are under way in Phase 1, 11 in Phase 2 and 12 in Phase 3. (Of the above 54 cases, in addition to Phases 1 through 3, clinical studies, such as post-marketing surveillance, are ongoing.) KEMRI is the largest sponsor of the ongoing clinical trials in Kenya, followed by the University of Washington and the National Institute of Allergy and Infectious Diseases (NIAID). In terms of diseases, many of them are related to HIV, malaria, and COVID-19.

ii. Domestic local manufacturing system

A) Pharmaceutical manufacturing base

Kenya is considered one of the largest producers of pharmaceuticals in East and Southern Africa, producing approximately US$140 million worth of pharmaceuticals each year. According to a 2020 Pharmaceutical Industry Report, there are 33 pharmaceutical manufacturers in Kenya. These are local companies, subsidiaries of large multinational corporations, joint ventures, etc., most of which are based in or near Nairobi. Major local companies include Cosmos Limited (established 1978), Beta Healthcare (established 2003), Dawa Life Science (established 1993), Elys Chemical Industries Ltd (established 1991), Laboratory and Allied Ltd (established in 1968). More than 95% of local pharmaceutical manufacturers cannot bid for international donor-funded programmes for essential drugs (such as HIV and AIDS, malaria, or tuberculosis) due to non-compliance with Good Manufacturing Practice pre-qualification requirements.

B) Types and volumes of local manufactured drugs

In terms of local manufactruing of pharmaceuticals in Kenya, many companies in Kenya produce simple non-patented products, relying on technology transfer agreements from multinational manufacturers

outside the country. Although some domestic companies manufacture raw materials for manufacturing of APIs, they are only producing them for export due to the lack of development of API manufacturing technology in Kenya. In terms of quality and cost, large pharmaceutical companies import about 60% of packaging materials, while small and medium-sized pharmaceutical companies import 35%.

Kenya's 10 largest pharmaceutical companies account for much of the domestic manufacturing of generic drugs largely using imported ingredients. Domestic manufacturers meet about 30% of domestic pharmaceutical demand, and the top five export about 40% to 85% of their manufacturing to other East African countries. (Kenya is the largest producer of pharmaceuticals in the COMESA region, supplying about 50% of the region's market.) More than half of Kenyan companies produce medicines related to infectious diseases, and the market for medicines related to areas such as immunology and cardiovascular diseases remains underdeveloped.

(2) Issues in target countries (regarding capacity to conduct clinical trials and local manufactruing)

i. Strengthening the capacity of regulatory agency personnel

In line with the fact that many of the issues raised in Kenya were to speed up the regulatory process, there were also references to strengthening the capacity of the PPB as a regulatory body. In the interviews with the PPB, it was mentioned that the PPB recognizes the need to strengthen the capacity of inspectors, particularly regarding GCP and GMP audits for vaccines.

ii. Expansion of pharmacy-related curricula at universities and other institutions of higher education

From the viewpoint of future human resource development, there was a reference to curriculum revision at universities. Current pharmacy-related courses focus only on clinical and theoretical knowledge and do not cover practical knowledge, creating a large skills gap in the pharmaceutical industry. Industry pointed out the need to establish a curriculum that includes content related to drug manufacturing and that directly relates to practical work. In addition, training in clinical research is not provided, and training must be obtained after graduation from medical school, according to industry.

In addition, most of the equipment used in Kenya is imported from overseas, but the high cost of hiring overseas engineers makes it difficult to maintain the equipment in Kenya. Therefore, it was pointed out that there is a need for engineering courses at universities and other institutions of higher learning to provide the engineering skills needed in the pharmaceutical industry.

iii. Strengthen data management

In Kenya, not only clinical trials, but also information on patients during an infectious disease pandemic and various other necessary healthcare information is not organized in an appropriate manner at the hospital level, and the overall picture has not yet been grasped. In addition, although a certain amount of data exists at government-related organizations, government agencies mentioned the need to strengthen the analysis of accumulated data as "information" and the use of data to determine various directions.

In addition, many clinical trials are decentralized clinical trials [140]. It was also pointed out that it is necessary to utilize technologies that enable data to be collected remotely, and that it will be necessary to strengthen data collection, data analysis, and other technical aspects of clinical trials in order to conduct them more efficiently.

[140] DCT: Decentralized Clinical Trial, a clinical trial that does not depend on visits to medical institutions by utilizing IOT such as online medical care, visiting nurses, and wearable devices.

2.6.3 Results of a survey on initiatives taken by aid agencies, research institutes, and companies in other countries, including the target countries

(1) Overview of promotion of local manufacturing of Vaccines and Pharmaceuticals

In Africa, under the leadership of the African Centers for Disease Control and Prevention (CDC), the African Union established the Partnerships for African Vaccine Manufacturing (PAVM) in 2021. The goal is to develop, produce, and supply more than 60% of the necessary vaccine doses in Africa by 2040. In addition, six African countries (Egypt, Senegal, Kenya, South Africa, Tunisia, and Nigeria) have been the first recipients of mRNA technology transfer under the WHO's mRNA Technology Transfer Hub initiative, with Kenya also benefiting from the technology transfer.

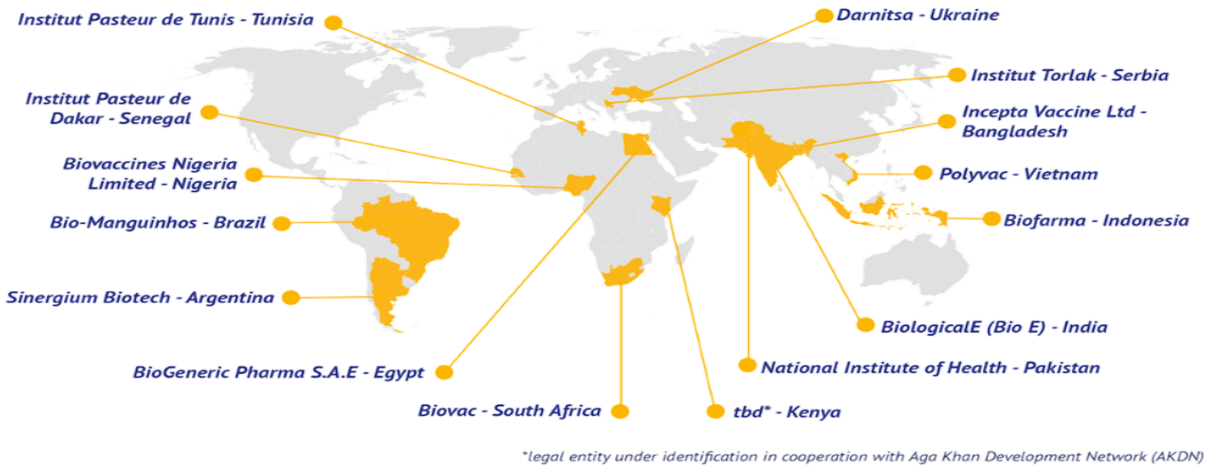


Figure 2-31 Countries receiving technology transfer under the WHO mRNA Technology Transfer Hub

(2) Donor initiatives to support clinical trials and local manufacturing of vaccines and other pharmaceutical products in target countries

i. Trends of supports from the United States

The US Military HIV Research Program (MHRP) entered into a partnership with the Kenya Medical Research Institute (KEMRI) in 1999 to provide expertise, technology and infrastructure support in HIV vaccine, treatment and other infectious disease research. All MRHP activities in Kenya are conducted under the African Army Medical Research Directorate (USAMRD-A), which is located on the premises of the Kenya Medical Research Institute (KEMRI) in Nairobi. The institute is also conducting vaccine trials for Ebola and polio. In addition, one Shigella vaccine trial is being reviewed at the site, two other trials are in development, and yellow fever vaccine trials and COVID-19 vaccine trials are planned.

For more than 40 years, the U.S. Centers for Disease Control and Prevention (CDC) has also helped Kenya strengthen its public health and testing systems and operate an integrated research center. It is also working with stakeholders such as the National Institutes of Health to conduct clinical trials and evaluate new vaccines, diagnostics, and prevention strategies. CDC Kenya, which supports approximately 25 outbreak investigations per year nationwide, provided on-site epidemiological and laboratory support and provided nearly $2.5 million in funding to support the Ministry of Health's rollout of COVID-19 vaccinations in 14 countries from March 2021 to July 2022.

ii. Trends of support from the United Kingdom

Key institutions of the Kenya-British Health Alliance, which began in 2022, include the University of Manchester, Christie's Hospital, Xie University and the University of Kenyatta's Teaching, Referral and Research Hospital (KUTRRH). The alliance will promote initiatives centered on a comprehensive cancer medical services network, as well as enhance medical education and training. To develop solutions to non-

communicable diseases starting with cancer, the initiative brings together clinicians, researchers and trainees from the UK and Kenya to engage in the clinical research needed to address diseases affecting East Africans. This initiative will help tackle the surging number of cancers and other non-communicable diseases in sub-Saharan Africa.

In 2020, KEMRI conducted a clinical trial of a coronavirus vaccine in collaboration with Oxford University and the Welcome Trust. The partnership of the 3 institutions led to the establishment of the KEMRI-Wellcome Trust Research Program (KWTRP), which has grown from a small group to a facility that hosts more than 100 research scientists and 700 support staff working in regions such as Kenya and Uganda. Serving as a center where promising African researchers can work in a strong environment, KWTRP has developed a unique connection with the international scientific community, and has conducted many groundbreaking and life-threatening studies, including mosquito net trials for malaria prevention, pneumonia vaccine trials, and Ebola vaccine trials.

iii. Trends of supports from France

On May 5, 2015, France and Kenya signed a Hubert Curian "PAMOJA" partnership covering 2021 to 2026, and this French-Kenyan research grant program invites applications every 2 years. It is implemented in the Kenyan Ministry of Education through the National Research Fund (NRF) and in France by the European and the Ministry of Foreign Affairs (MEAE) and the Ministry of Higher Education, Research and Innovation (MESRI). The program aims to support and promote science and technology cooperation between French and Kenyan researchers within public institutions, with a funding cap of 23,000 euros per project, 5,000 euros per year for French researchers and 6,500 euros per year for Kenyan researchers.

(3) Initiatives of European and American universities, research institutes and pharmaceutical companies

i. Initiatives by American universities and pharmaceutical companies

The University of Washington in the United States has been conducting research and training in Kenya for nearly 30 years and its faculty, staff and students work closely with their Kenyan colleagues and institutions to promote improved public health and health care in Kenya through research, education and services. Against the backdrop of higher rates of cervical cancer in African countries compared to the rest of the world, the university conducted a randomized controlled trial in Kenya and led the study on the efficacy of a single-dose HPV vaccine. Also, clinical stage biopharmaceutical company based in the United States, Tonix Pharmaceuticals Holding Corp will conduct Phase 1 clinical trials in Kenya to develop TNX -8011 as a vaccine to prevent monkeypox and smallpox in collaboration with the Kenya Medical Research Institute (KEMRI) for research beginning in the first half of 2023.

ii. Initiatives by British universities

The University of Oxford in the United Kingdom has conducted human trials of a DNA/modified vaccinia virus prime-boost HIV vaccine developed in collaboration with the University of Nairobi in Kenya. The KEMRI-Welcome Trust Research program conducted clinical trials of ChAdOx1 nCoV -19, a vaccine developed by the university in collaboration with the pharmaceutical company AstraZeneca, and about 40 volunteers, health care workers, participated in the COVID-19 vaccine trials. In addition, the university has partnered with the Serum Institute of India in manufacturing of the malaria vaccine R 21/Matrix-M and has conducted phase 3 trials at 5 sites in Burkina Faso, Kenya, Mali and Tanzania.

2.7 Interview results of each target country

2.7.1 India

A total of 15 interviews were conducted with relevant organizations in India, including 1 international organization, 8 medical research institutions and academia, and 6 industry associations and private companies. Interview results were compiled for each category of interviewees, and issues related to the implementation and promotion of clinical trials, research and development and local manufactruing of vaccines and drugs, and requests for pilot activities were extracted.

(1) International organizations

In interviews with international organizations, process management of clinical trials was cited as the main issue. For example, there was an opinion that it was necessary to clarify the roles of the relevant organizations in the clinical trial process and to visualize the progress. It was also desirable to have a mechanism that could provide centralized input of information such as the overall flow, necessary tools, and regulatory mechanisms.

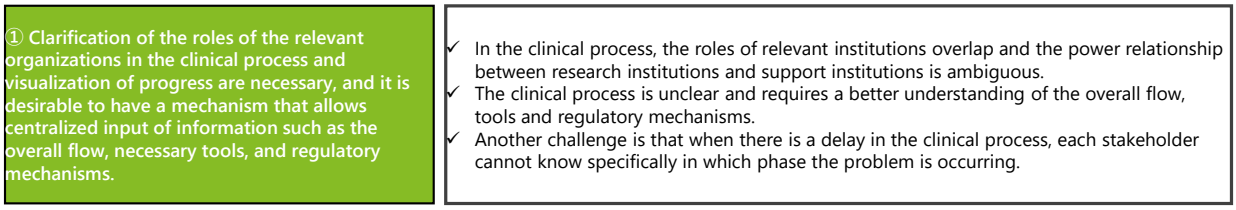


Figure 2-32 Interview results of international organizations (India)

As for pilot activities, it is important to focus on areas that are highly relevant to existing support areas and activities to India, or that can be tied to the initiatives of the Government of India. It is also desirable to have an information platform that can comprehensively show the process and framework of clinical trials and the basic information and position of relevant institutions.

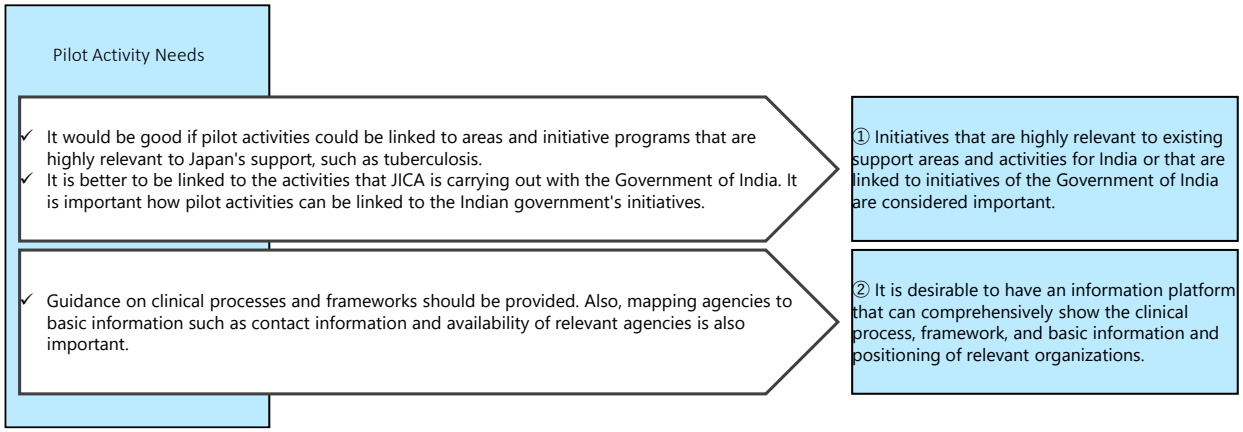


Figure 2-33 Pilot activity needs of international organizations (India)

(2) Medical research institutions and hospitals

Interviews with medical research institutions and academia revealed four main challenges in clinical trials and vaccine and drug manufacturing systems. Regarding clinical trials, there were opinions that (1) the processes and procedures related to registration, review, and approval of clinical trials need to be improved, and that guidelines focusing on biopharmaceuticals need to be developed, and (2) the availability of human resources to conduct clinical trials is insufficient. With regard to vaccine and pharmaceutical manufacturing systems, it is necessary to (3) establish a more rapid and smooth vaccine development and manufacturing system in the event of a pandemic, as well as establish a pharmaceutical manufacturing and supply system independent of other countries, and (4) strengthen cooperation between academia and industry and promote technology transfer.

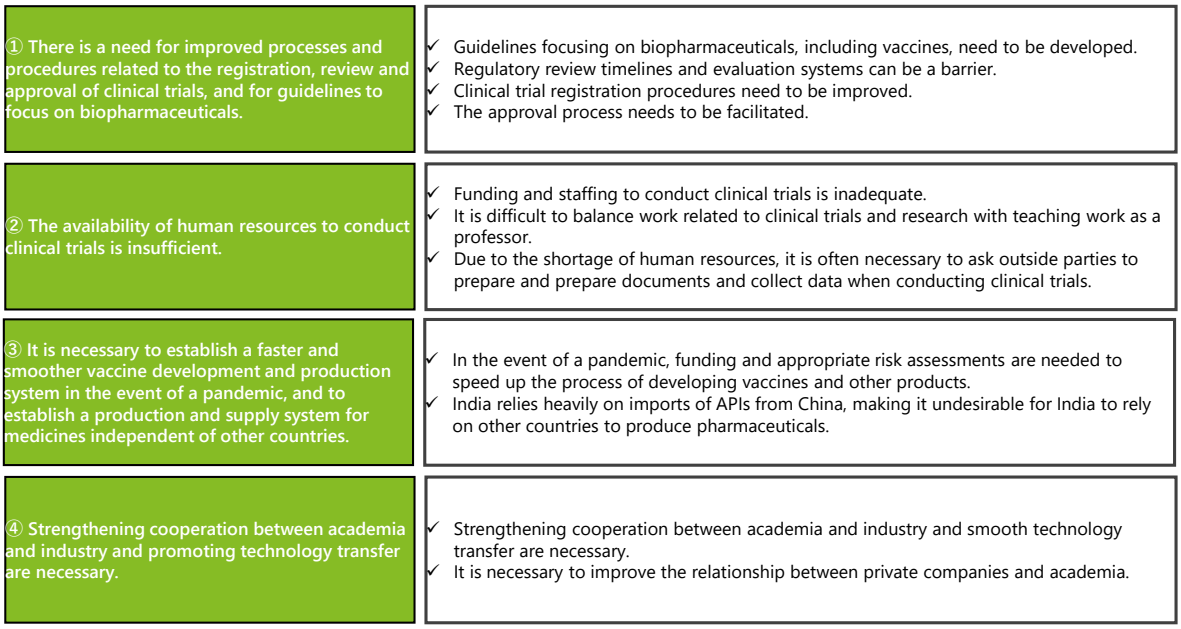


Figure 2-34 Interview results of medical research institutions and hospitals (India)

There are four main needs and requests for pilot activities. (1) There are requests for training, seminars, etc. that will lead to human resource development for both clinical trial institutions and regulatory agencies. (2) There is a need to strengthen the infrastructure (both hard and soft) necessary to strengthen capacity for clinical trials and research and vaccine research and development, and to improve data management capabilities. (3) Networking and business matching activities that promote collaboration among pharmaceutical companies, joint research among related organizations, and global collaboration between Japan and India are desirable. (4) Support activities focusing on specific themes such as promotion of local manufactruing of pharmaceuticals including APIs, prevention of disease spread and disease control, AMR, and Point of Care Testing are expected.

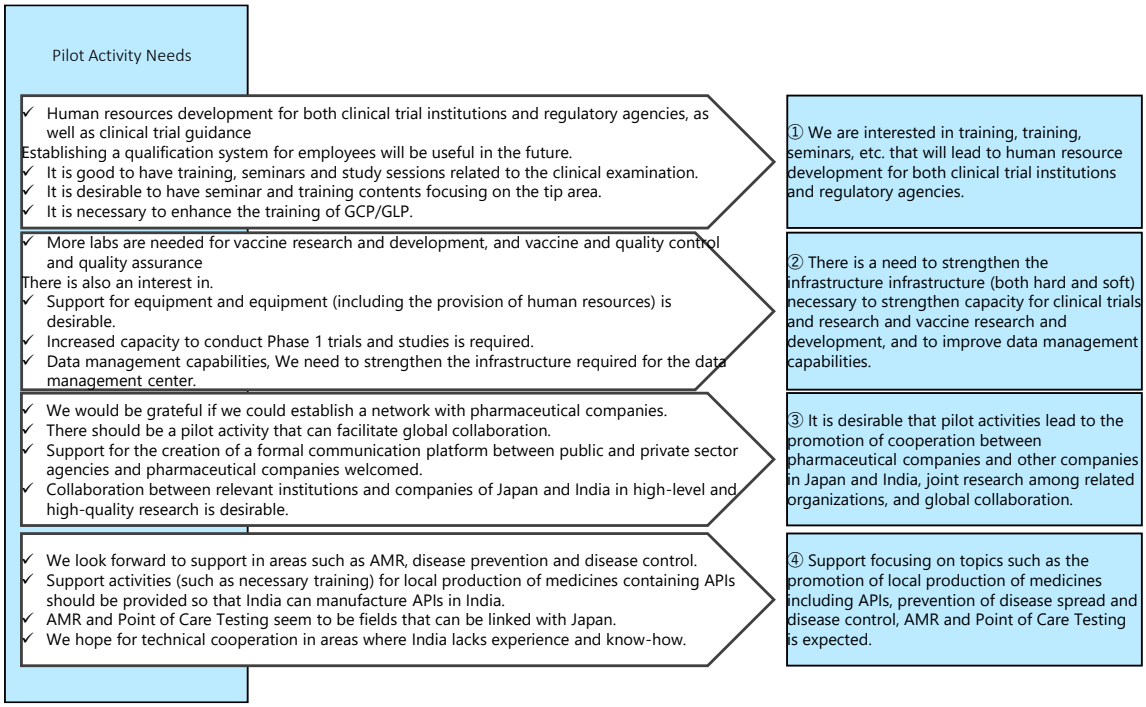


Figure 2-35 Pilot activity needs of medical research institutions and hospitals (India)

(3) Industry associations and academia

According to interviews with industry groups and private companies, there are three major challenges in clinical trials and vaccine and drug manufacturing systems. (1) With regard to clinical trials, there are problems in terms of human resources and capacity of CRO, such as uneven distribution of knowledge and inconsistencies in information of personnel in charge, lack of understanding of application methods of protocols, lack of human resources in cutting-edge technology fields, and lack of ability to develop new technologies for CRO. (2) Issues in local manufacturing of vaccines and pharmaceuticals include a shortage of raw materials and difficulty in procurement (dependence on imports). (3) The creation of a framework for drug discovery and the development of drugs for new diseases, the promotion of regulatory harmonization, and the creation of a regulation-related system are insufficient.

① With regard to clinical trials, there are problems in terms of human resources and capacity of CRO, such as uneven distribution of knowledge and inconsistencies in information of personnel in charge, lack of understanding of application methods of protocols, lack of human resources in cutting-edge technology fields, and lack of ability to develop new technologies for CROs.	✓ As for clinical trials, one of the bottlenecks is the uneven distribution of knowledge and inconsistencies in information among those in charge. Although protocols exist, many people do not understand how to apply them in clinical trials. ✓ The shortage of human resources in the cutting-edge technology sector is also a problem, and with advanced technology platforms, efficient quality control is necessary. However, the infrastructure involved is quite weak and human resources are lacking. ✓ The lack of knowledge and technology in the clinical trial field is one of the challenges, and many CROs do not have the capacity or capacity to develop new technologies.
② The shortage of raw materials and the difficulty of procuring (dependence of imports) for local production of vaccines and medicines are cited as problems.	✓ During the pandemic, there was a problem of not being able to import the raw materials needed to make vaccines and medicines. ✓ With regard to local production, the shortage of raw materials and the difficulty of procurement are cited as challenges.
③ The creation of a framework for drug discovery and the development of drugs for new diseases, the promotion of regulatory harmonization, and the creation of a regulatory system are insufficient.	✓ Harmonization of regulations, especially after reviewing the framework for drug development for new diseases, is necessary to respond to emergencies such as pandemics. ✓ There is no regulatory system in place to support drug discovery for diseases for which no cure has been found.

Figure 2-36 Interview results of industry associations and academia (India)

As a result of the interview on the request for the pilot activity, there is a high interest in exchange and cooperation with Japanese pharmaceutical companies, holding workshops as a forum for exchange and discussion between experts of both countries under a specific topic, and participating in the international clinical trial network. In addition, it is desirable to provide technical, equipment, infrastructure, and human resources support to CROs in cutting-edge technology fields.

Pilot Activity Needs	
✓ Establishing an international clinical trial network would help. ✓ Japanese pharmaceutical companies (e.g., providing dengue and monkeypox vaccines companies). ✓ One-on-one meetings with Japanese companies and opportunitues to speak with Japanese researchers would be desirable. ✓ Networking is effective because it encourages Indian and Japanese companies to get to know each other and form partnerships by presenting each other's capacity and business. ✓ There seems to be value in holding focused workshops that bring together experts from both Japan and India to focus on specific topics. ✓ Specifically, we would like to collaborate with Japanese companies in the fields of oncology, endocrine diseases, vaccines, transplantation, nutritional support, food, medical devices, and gene and cell therapeutics.	① There is a strong interest in exchanges and cooperation with Japanese pharmaceutical companies, holding workshops as a forum for exchanges and discussions between experts from both countries, and participating in international clinical trial networks.
✓ Many Indian CROs do not have the most advanced technologies or the latest technology platforms, so they need not only technology and equipment support, but also infrastructure and human resource development.	② It is desirable to have technical, equipment, infrastructure, and human resources support for CROs in cutting-edge technology fields.

Figure 2-37 Pilot activity needs of industry associations and academia (India)

2.7.2 Vietnam

A total of 10 interviews were conducted with relevant institutions in Vietnam, including 2 interviews with government agencies and regulatory authorities, 5 interviews with medical research institutions, 1 interview with vaccine corporation, 1 interview with state-owned company, and 1 interview with hospital. Results of those interview results were complied for each category of interviewees, and challenges related to the implementation and promotion of clinical trials, research and development, and local manufacturing of vaccines and drugs, and requests for pilot activities were extracted.

(1) Government agencies and regulatory authorities

Interviews with government agencies and regulatory authorities revealed that the challenges in clinical trials are mainly concentrated in two areas: (1) human resources and (2) infrastructure. Specifically, the main challenges cited were (1) a lack of human resources capable of handling and conducting clinical trials and gap in the knowledge and skills of human resources at different institutions, and (2) a lack of or difficulty in finding institutions, equipment, funds, and capacity of subjects to conduct clinical trials in Vietnam.

① There is a shortage of human resources capable of conducting clinical trials and analysis, resulting in differences in human resources' knowledge and skills.	✓ There is a shortage of well-trained human resources who can handle and conduct clinical trials, and there are differences in the level of human resources among relevant institutions. ✓ Data analysis requires technology, but there are not enough people to handle it.
② There is a lack of facilities, equipment and financial capacity to conduct clinical trials in Vietnam.	✓ Few institutions are equipped to handle the entire process of conducting clinical trials of developed vaccines. ✓ In particular, it takes time to complete the entire process due to the lack of facilities and systems for animal testing and the need to rely on overseas facilities ✓ There is a need to improve the quality and standards of clinical trial databases and facilities. ✓ There is a funding shortage in clinical trials. ✓ Large differences in national income between regions make it difficult to select subjects when monitoring and evaluation are considered.

Figure 2-38 Interview results of government agencies and regulatory authorities (Vietnam)

There are three major requests for pilot activities: (1) interactive activities such as discussions, networking, and matching with related organizations and experts, (2) training for physicians, clinical trial managers, and researchers since training on the skill and technical aspects of clinical trials are desired, and (3) support for improving the hardware capacity of clinical trial facilities and soft support for harmonization with overseas regulations are also desirable.

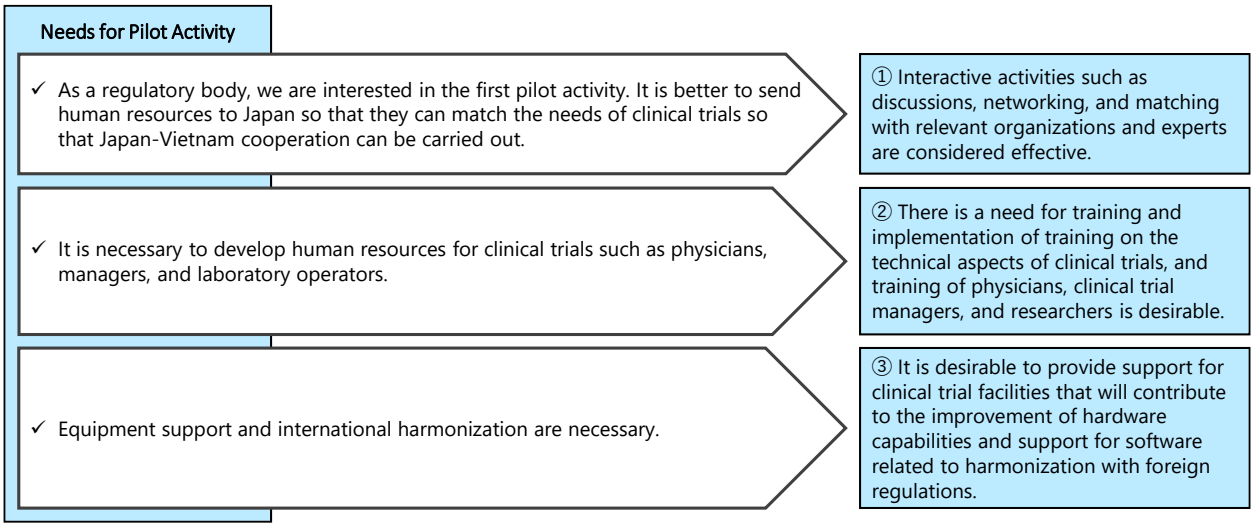


Figure 2-39 Pilot activity needs of government agencies and regulatory authorities (Vietnam)

(2) Medical research institutions and hospitals

Interviews with medical research institution and hospital revealed that the challenges in clinical trials and manufacturing systems of vaccine and drug mainly concentrated in two areas: (1) human resources and human resource development, and (2) infrastructure. Specifically, one of the main challenges cited was (1) a lack of educational system to train experts and physicians capable of conducting clinical trials and manufacturing of vaccine and drug. Another main challenge cited was (2) shortage of facilities, bases, human subject, laws, and funds to conduct clinical trials. A lack of laws and funds is a challenge not only in clinical trials but also in manufacturing.

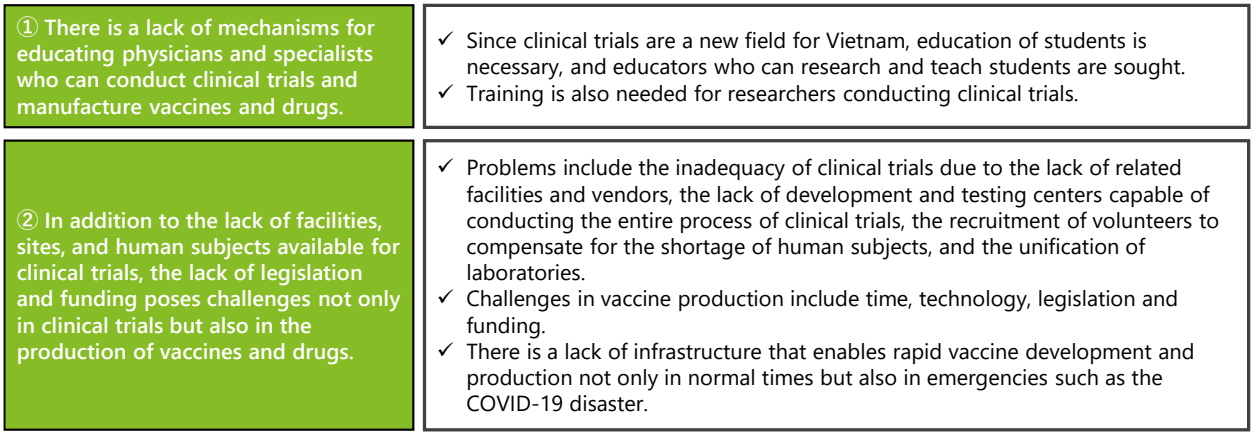


Figure 2-40 Interview results of medical research institutions and hospitals (Vietnam)

There are three major requests for pilot activities: (1) opportunity for discussion where information exchange and networking in both software and gardware can be conducted interactively, (2) training or short-term training for youth, doctor, researchers, and others to learn about the techniques and equipment of clinical trials in Japan , and (3) advice and support on how to aseemble projects, build system, adopt to change, and update regulations for internaltial harmonization for technology transfer.

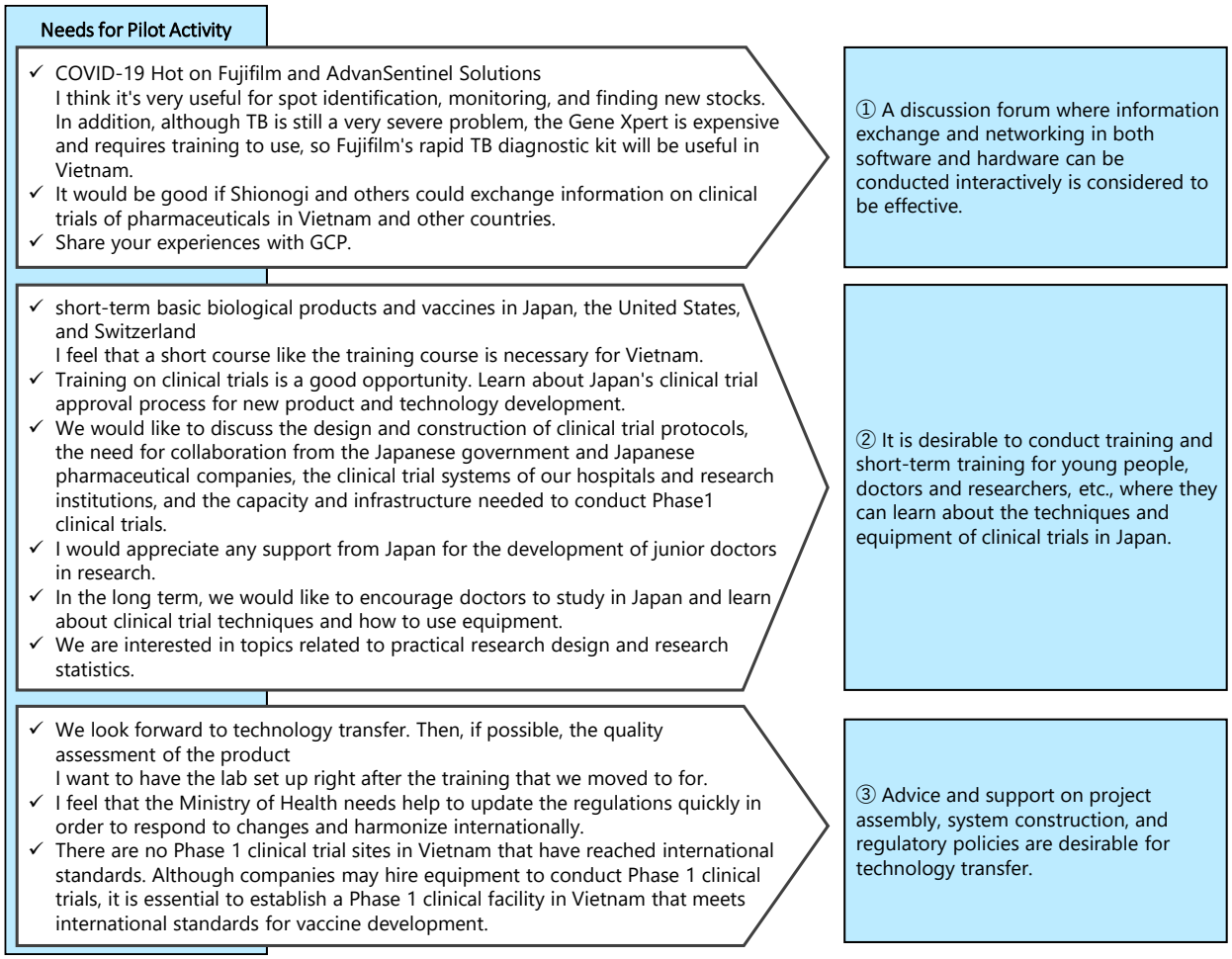


Figure 2-41 Pilot activity needs of medical research institutions and hospitals (Vietnam)

(3) Public corporations and state-owned companies

Interviews with public vaccine corporations and state-owned company revealed that there are two challenges: (1) human resources and (2) infrastructure. Regarding (1) human resources, clinical trial is a new technologu for Vietman; therefore, there is a shortage of human resources capable of handling clinical trials. There is also challenge in (2) infrastructure such as a lack of institutions, equipment, standards, and funds for the new technologies.

① There is a shortage of people who can handle new technologies.	✓ Human resource development with access to new technologies is necessary.
② There is a lack of institutions, equipment and standards capable of responding to new technologies, as well as the funding required for implementation.	✓ Capital investment in the utilization of new technologies is necessary. ✓ Vietnam has fewer clinical trial institutions overall, lacks clinical trial units and data, and the cost of conducting clinical trials is very high. ✓ Part of this is due to difficulties in accessing financing, and in addition, the lack of international cooperation from abroad makes it difficult to access and implement new and advanced technologies. ✓ The clinical trial sites must be in accordance with international standards. ✓ It is necessary to develop regulations to cope with emergencies. ✓ The need for clinical evaluation at the destination has become a human and material resource cost for Vietnamese vaccine manufacturers and a barrier to vaccine exports.

Figure 2-42 Interview results of public corporations and state-owned companies (Vietnam)

There are two major requests for pilot activities: (1) training program to build capacity of human resources and institutions for the clinical trial, and (2) support for development of infrastructure (equipment, facilities, systems, processes, regulations, etc.) necessary to conduct development, clinical trials, and manufacturing.

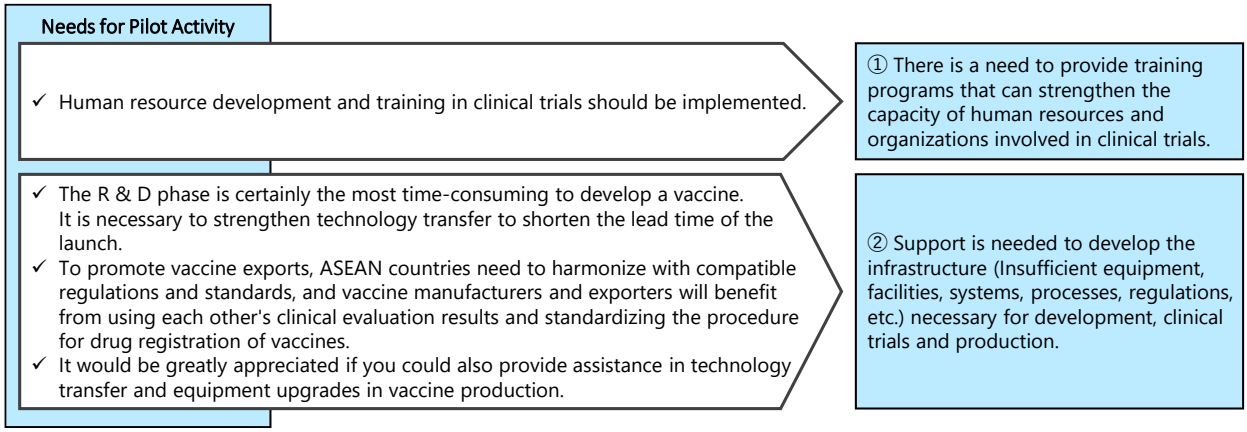


Figure 2-43 Pilot activity needs of public corporations and state-owned companies (Vietnam)

2.7.3 Thailand

A total of 12 interviews were conducted with relevant institutions in Thailand, including 5 interviews with government agencies and regulatory authorities, 4 interviews with medical research institutions and hospitals, and 3 interviews with industry associations and private companies.

(1) Government agencies and regulatory authorities

Interviews with government agencies and regulatory agencies revealed that challenges in clinical trials and vaccine and drug manufacturing systems are mainly focused on four areas: (1) human resources and skills, (2) quality control, (3) law, regulation and policy, and (4) regulatory capacity and policy. Specifically, the following issues are raised: (1) lack of human resources capable of handling and conducting clinical trials, lack of knowledge and skills; (2) difficulty in maintaining quality safety in a tropical environment such as Thailand; (3) insufficient legal and policy efforts in pharmaceutical R&D and local manufactruing; and (4) inefficient regulatory review and approval processes for clinical trials, and lack of knowledgeable reviewers.

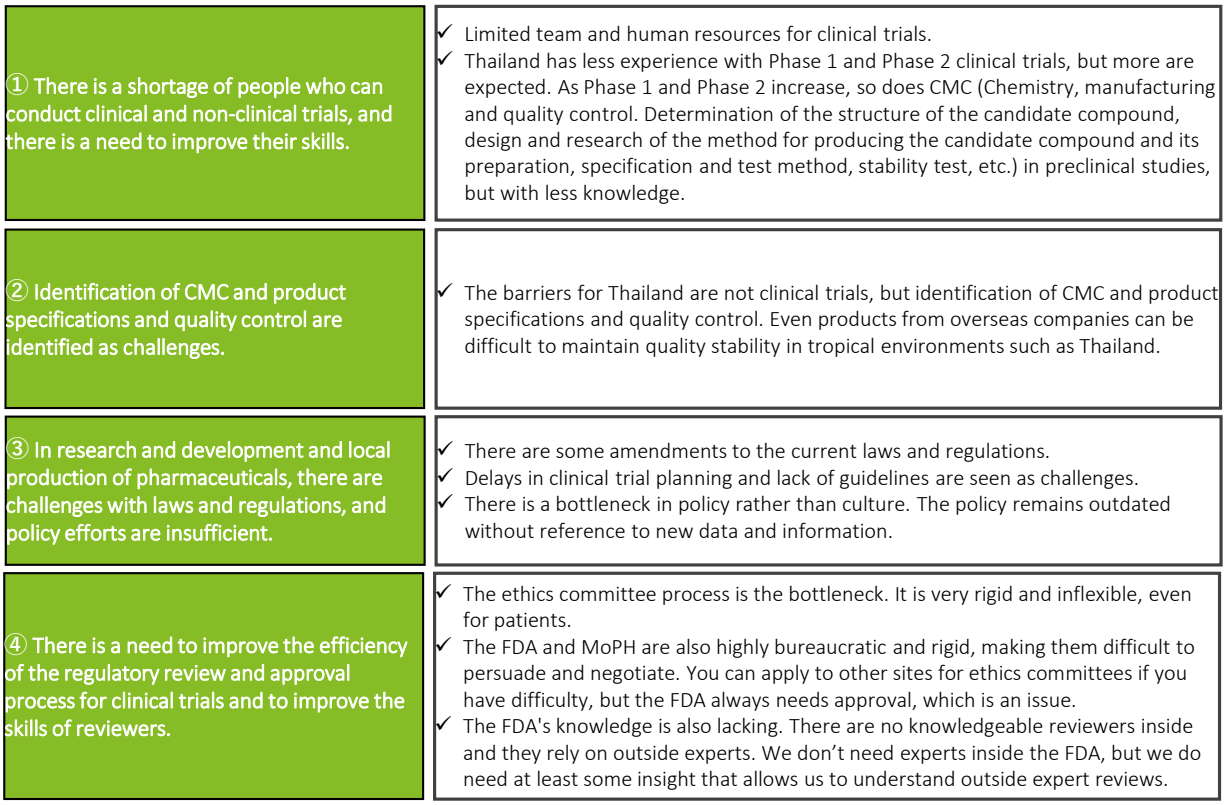


Figure 2-44 Interview results of government agencies and regulatory authorities (Thailand)

There are four main requests for pilot activities. Specifically, (1) training on drug development and clinical trials, such as ICH-GMP and adaptive design; (2) workshops for protocol development teams and consultation and training for clinical trial teams; (3) interactive collaboration activities, such as networking and matching between stakeholders; and (4) opportunities to learn from experts directly during FDA reviews and GMP inspections.

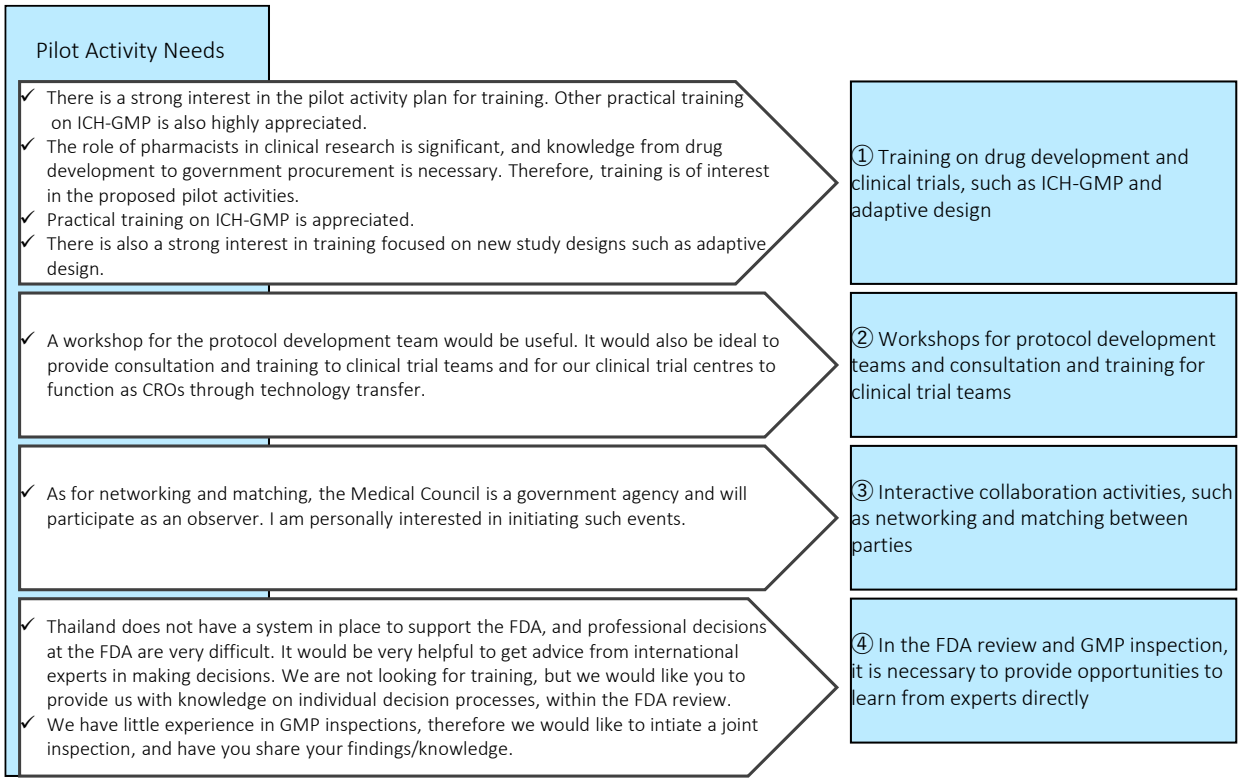


Figure 2-45 Pilot activity needs of government agencies and regulatory authorities (Thailand)

(2) Medical research institutions and hospitals

Interviews with medical research institutions and hospitals revealed that challenges in clinical trials and vaccine and drug manufacturing systems are mainly focused on three areas: (1) regulatory capacity and policy; (2) infrastructure development; and (3) development of the entire industry in clinical trials and local manufactruing. Regarding (1), the regulatory process for phase I clinical trials has not yet been fully established, and the time required for the regulatory import and licensing processes is very long. Regarding (2), the lack of sites for conducting clinical trials and lack of laboratories for conducting research and development were stated as challenges. Regarding (3), it was mentioned that development of the entire industry in clinical trials and local manufactruing is required, and various issues such as quality control, data management, and inter-organizational cooperation are also required to be addressed.

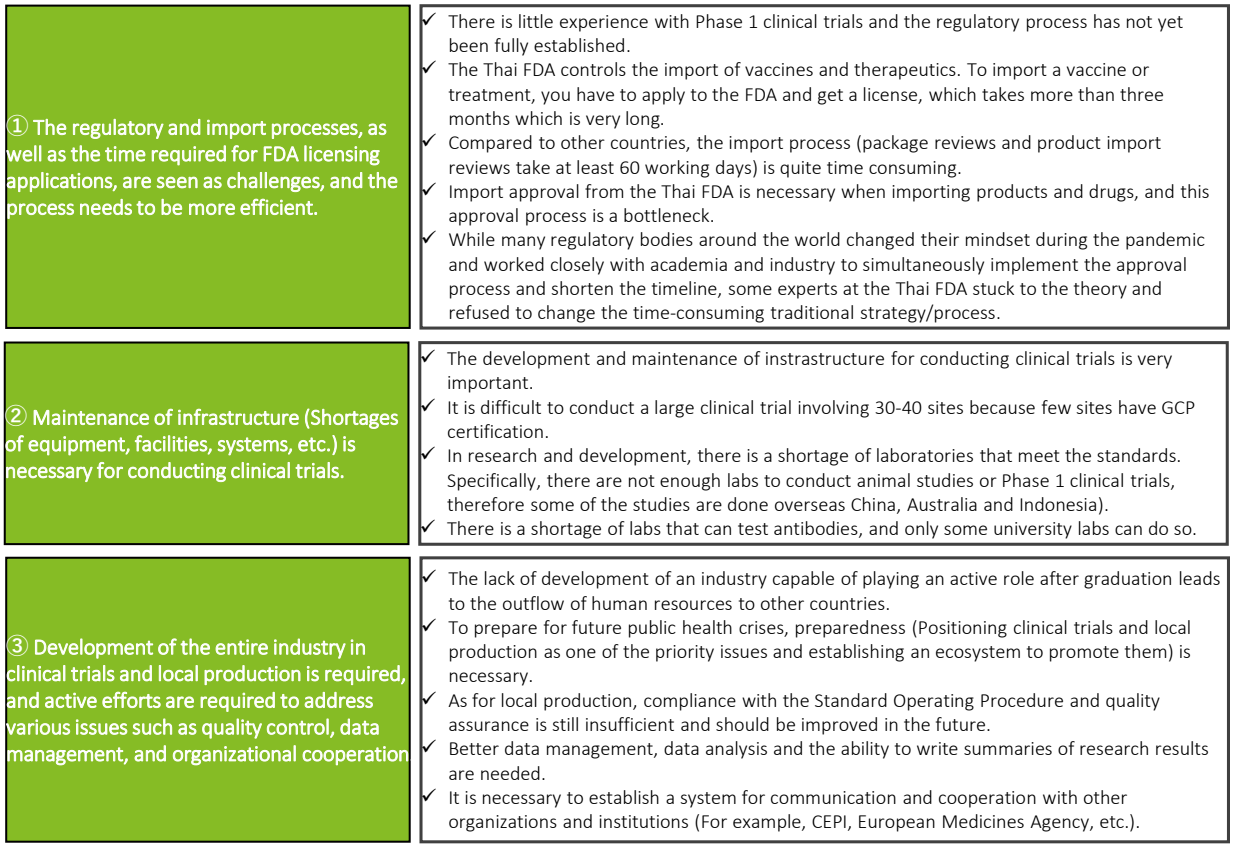


Figure 2-46 Interview results of medical research institutions and hospitals (Thailand)

There are four main requests for pilot activities. (1) provide training programs and build the infrastructure and capacity of clinical trial facilities that can strengthen the capacity of human resources involved in clinical trials; (2) engage in interactive collaboration and exchange activities, such as networking between regulatory authorities and organizations in other countries and holding joint seminars; (3) implement PoC; and (4) collaborate with Japanese pharmaceutical companies, including technology transfer.

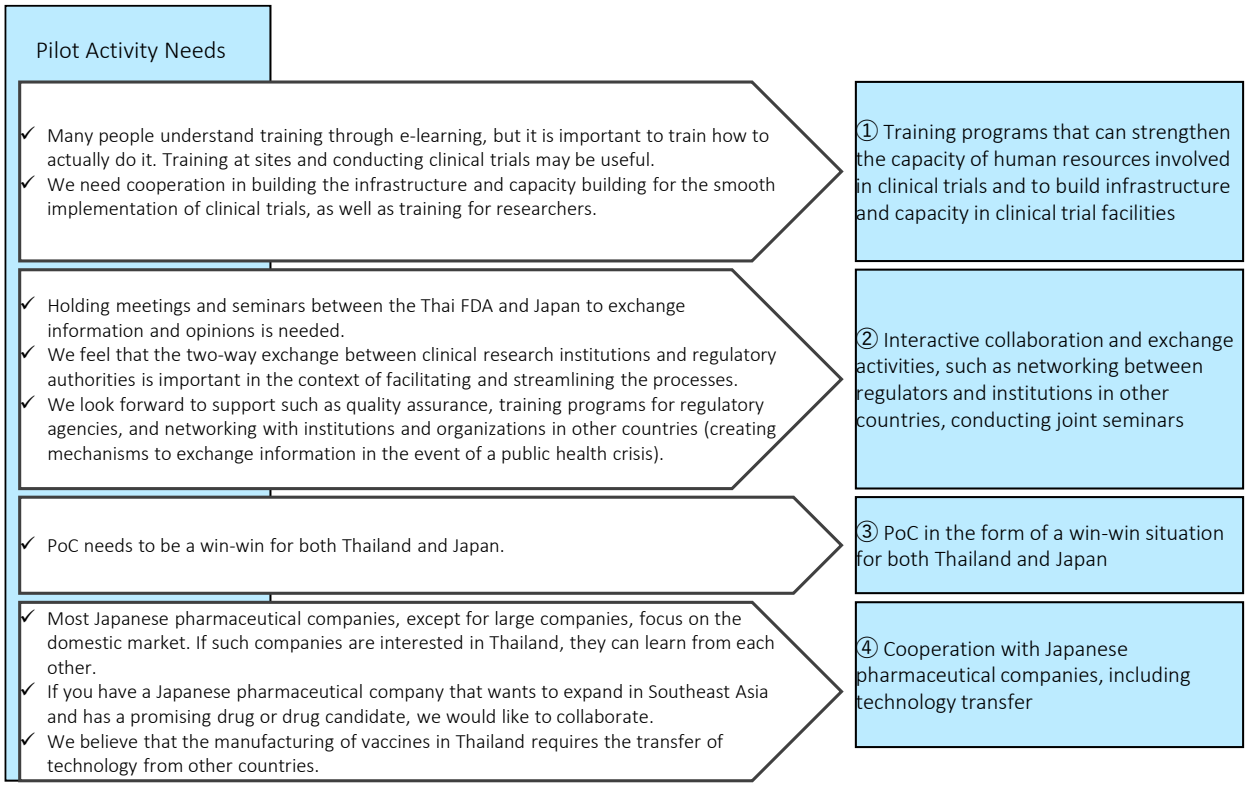


Figure 2-47 Pilot activity needs of medical research institutions and hospitals (Thailand)

(3) Industry associations and private companies

Interviews with industry associations and private companies revealed that the challenges in clinical trials and vaccine and drug manufacturing systems are mainly focused on three areas: (1) a shortage of human resources in drug development, (2) a shortage of skills in conducting clinical trials, and (3) improvements in the approval process and database development. Few companies are working on new drug development, and the lack of human resources with regulatory or drug approval knowledge to handle the development of new drugs is stated as an issue. Improving the skills of healthcare professionals conducting clinical trials has also been identified as a challenge, and knowledge transfer and training are required. In addition, a database is required to accelerate the approval process and enabling fast-track review is also necessary.

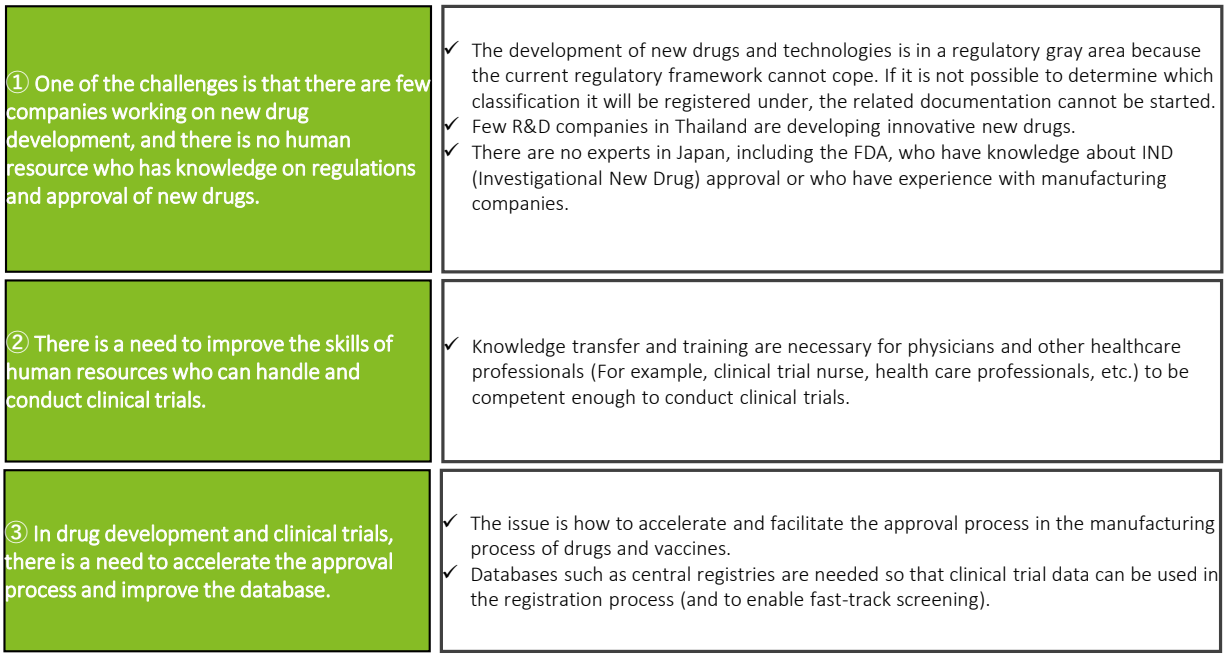


Figure 2-48 Interview results of industry associations and private companies (Thailand)

There are four main requests for pilot activities. (1) support for facility and capacity building in vaccine manufacturing; (2) sharing and technology transfer of Japanese technologies and knowledge; (3) networking with relevant organizations and business matching with investors; and (4) opportunities to learn about solutions to existing problems and conduct case studies that lead to real impact through training.

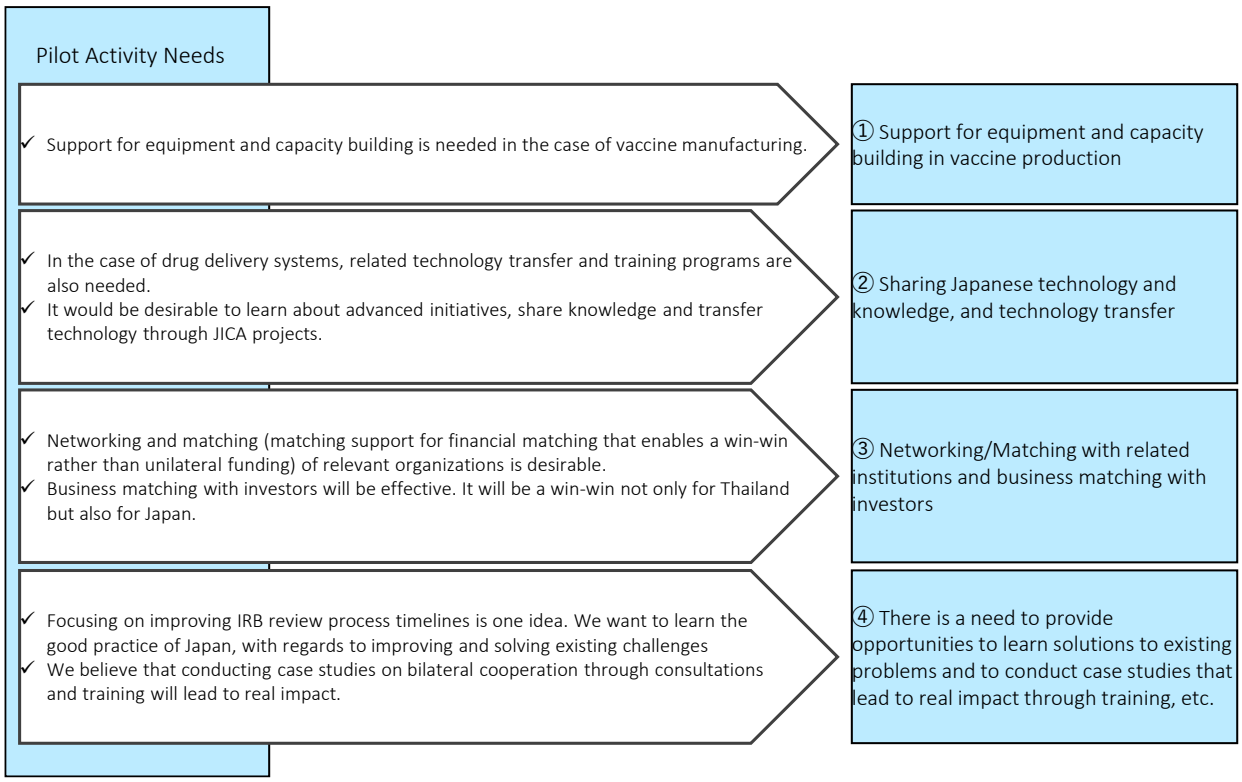


Figure 2-49 Pilot activity needs of industry associations and private companies (Thailand)

2.7.4 Philippines

A total of 17 interviews were conducted with relevant institutions in the Philippines, including 7 government agencies/regulators, 7 medical research institutions and hospitals, 2 CROs, and 1 trade association/private company. Interview results were compiled for each category of interviewees, and issues related to the implementation and promotion of clinical trials, research and development and local manufactruing of vaccines and drugs, and requests for pilot activities were extracted.

(1) Government agencies and regulatory authorities

Interviews with government agencies and regulatory authorities revealed that challenges in clinical trials and vaccine and drug manufacturing systems are mainly focused on three aspects: (1) human resources, (2) regulatory capabilities and policies, and (3) infrastructure. Specifically, (1) there is a shortage of human resources and experts on the regulatory side who can handle and conduct clinical trials, as well as a lack of knowledge and skills; (2) there are insufficient efforts to strengthen the capacity of regulatory authorities and to coordinate policies to promote research and development and local manufacturing of pharmaceuticals; and (3) there are insufficient facilities to conduct clinical trials and limited facilities to produce pharmaceuticals.

① There is a shortage of human resources and regulatory experts who can handle and conduct clinical trials, and there is a need to improve their skills.	✓ There are few people who can handle and conduct clinical trials, such as specialists and research-oriented doctors, and there is a shortage of talented research assistants. ✓ On the regulatory side, there is always the problem of a shortage of human resources. There is a shortage of experts and too much workload for the number of people, affecting the technical capacity of the Clinical Research Section (in some cases relying on experts from external partner agencies). ✓ Overall, technical knowledge is lacking, and information technology skills are also required. ✓ Rural areas need more people with the skills to conduct clinical trials. ✓ Efforts should be made at the Center for Drug Regulation and Research (CDRR) to develop evaluators and examiners in clinical trials.
② Efforts to strengthen the capacity of regulatory authorities to promote research and development and local production of pharmaceuticals, and policy coordination are insufficient.	✓ For local production, the main challenge is the low level in the FDA's WHO Benchmarking Tool. Maturity level 3 must be obtained before a vaccine manufacturing facility can be granted. ✓ In terms of policy, there is a problem of lack of coordination among different government agencies.
③ There is a lack of facilities to conduct clinical trials and limited facilities to produce drugs.	✓ There is a gap in facilities in the capital and rural areas. Research and manufacturing in rural areas are very weak, and there is a lack of research and data to be conducted in the field. ✓ Researchers say they don't have the equipment or skills to conduct Phase 1 clinical trials, and equipment development has become an issue. ✓ There are no facilities capable of producing vaccines, and there are still limited facilities capable of producing drugs. Most depend on imports.

Figure 2-50 Interview results of government agencies and regulatory authorities (Philippines)

There are four main requests for pilot activities. (1) there is a need for the implementation of training on the regulatory, skill, and technical aspects of clinical trials, and it is desirable that regulatory officials and medical practitioners involved in clinical trials visit Japan for training. (2) support for the establishment of infrastructure conducive to clinical trials and new drug development is required, and sharing of methods for utilizing advanced technologies is also desirable as content. (3) support that will contribute to the enhancement of the hard and soft capabilities of regulatory authorities is desirable. (4) interactive collaboration activities such as technical and research cooperation, networking among parties who understand the field, and matching are considered to be effective.

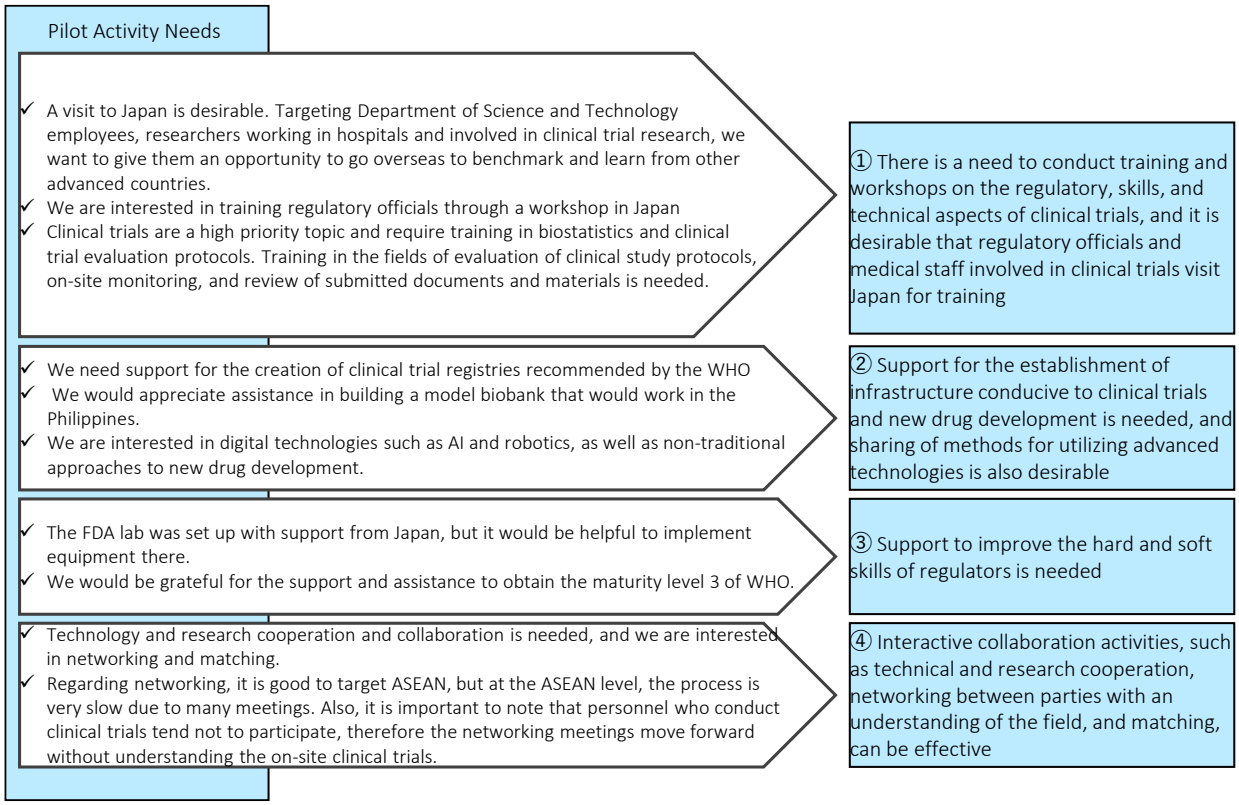


Figure 2-51 Pilot activity needs of government agencies and regulatory authorities (Philippines)

(2) Medical Research Institutions/Hospitals

Interviews with medical research institutions and hospitals revealed that challenges in clinical trials and vaccine and drug manufacturing systems are mainly focused on three areas: (1) infrastructure, (2) human resources, and (3) regional disparities. The lack of facilities and medical institutions capable of conducting clinical research and clinical trials, as well as the lack of facilities and bases capable of producing vaccines, are stated as major infrastructure challenges. In terms of human resources, insufficient availability of human resources and experts who are knowledgeable about drug R&D and vaccine manufacturing has been identified as a problem. In addition to infrastructure and human resources, there is also mention of regional disparities, noting that more clinical trials are being conducted in Manila compared to other regions, and that clinical trial experts are also unevenly distributed in Manila.

① There is a lack of facilities and medical institutions capable of conducting clinical research and clinical trials, and there are no facilities capable of producing vaccines.	✓ There is a lack of facilities to conduct clinical research. ✓ There is a shortage of hospitals and institutions with clinical trial units. ✓ The lack of facilities capable of producing vaccines is a major challenge.
② The availability of human resources and experts who are familiar with drug R&D and vaccine manufacturing is insufficient.	✓ It is difficult to retain people who are familiar with drug development research and vaccine production, and there are many cases where people go abroad to conduct research or move to other professional positions.
③ Regional disparities in clinical trials and related specialists (between Manila and rural areas) are a challenge.	✓ There is a disparity between Manila and rural areas, with more clinical trials being conducted in Manila compared to other regions, and clinical trial experts are also unevenly distributed (Manila has more than other regions).

Figure 2-52 Interview results of medical research institutions and hospitals (Philippines)

There are two main requests for pilot activities. (1) it is desirable to identify the needs and priority areas of medical institutions and sites, and to provide necessary equipment and technology according to the needs. It is necessary to prepare facilities and related equipment for clinical trials, and to support the provision of laboratory equipment and equipment. (2) human resource development for clinical trials is important. Seminars/workshops to strengthen the management and technical aspects of clinical trials and training for investigators are required.

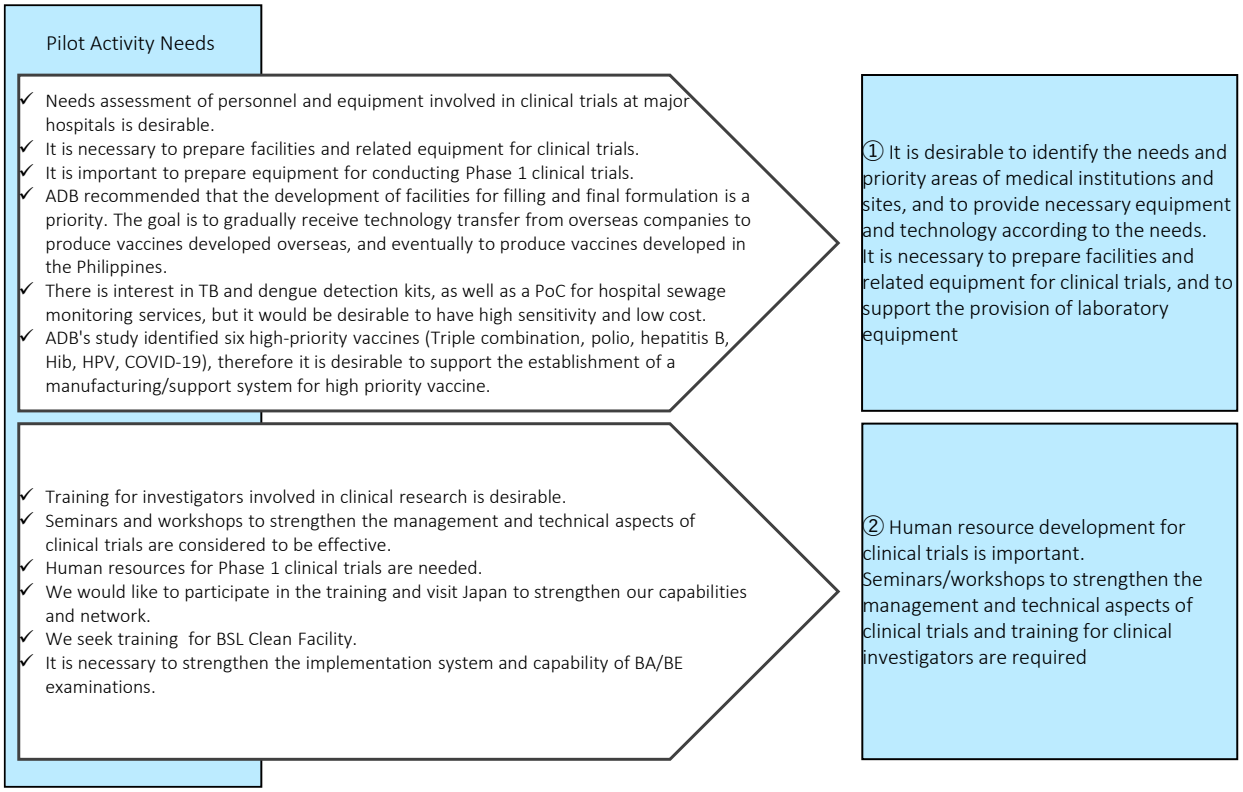


Figure 2-53 Pilot activity needs of medical research institutions and hospitals (Philippines)

(3) CROs

From the perspective of CROs, the following are key issues: (1) inefficient regulatory review and approval processes for clinical trials; (2) insufficient funding for researchers involved in clinical research and insufficient efforts to maintain job security for researchers; and (3) insufficient training to strengthen the capacity of those involved in the conduct of clinical trials.

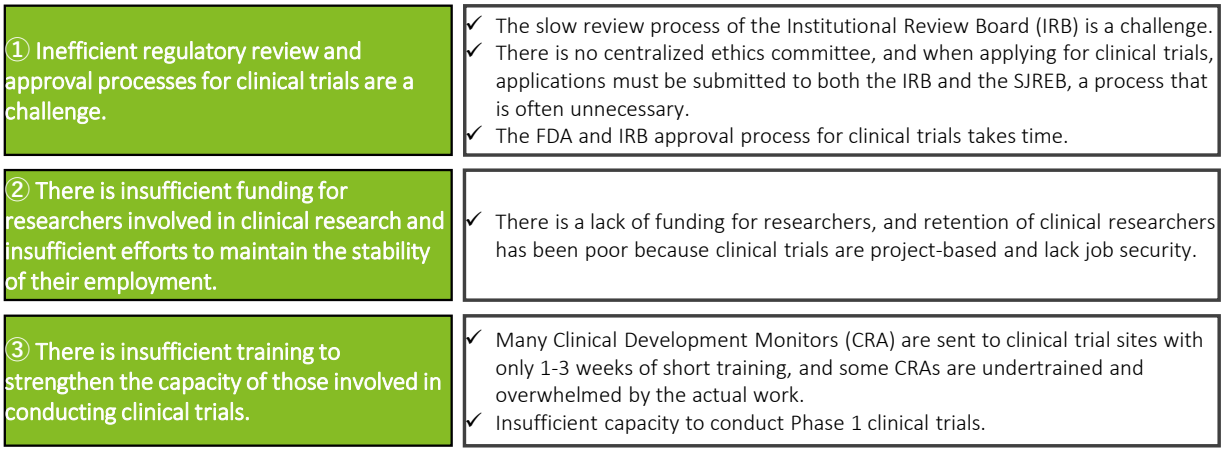


Figure 2-54 Interview results of CROs (Philippines)

There are three main requests for pilot activities. (1) support activities are needed to promote improved and more efficient regulatory review and approval processes for clinical trials. (2) there is a need to provide training programs that can strengthen the capacity of human resources and organizations involved in clinical trials and to provide opportunities to learn good practices face-to-face. (3) support for the development of the infrastructure necessary for conducting clinical trials (shortages of equipment, facilities, systems, etc.) is required.

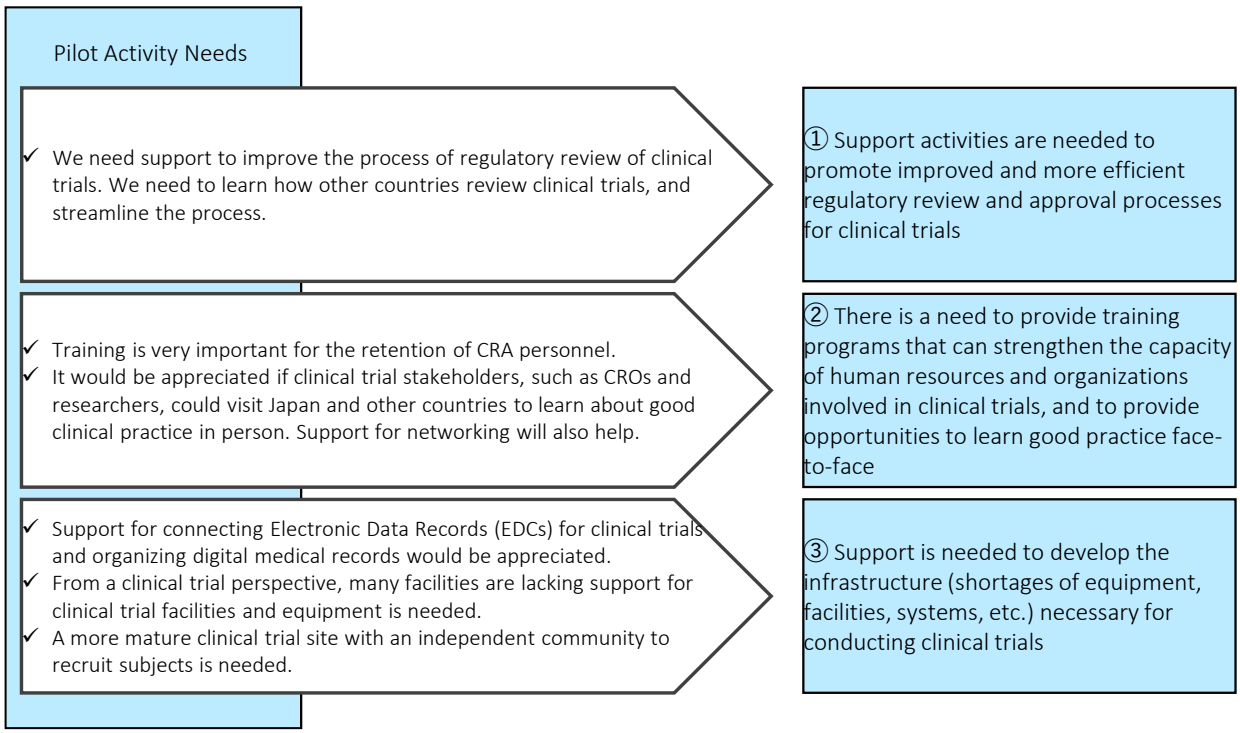


Figure 2-55 Pilot activity needs of CROs (Philippines)

(4) Industry associations and private companies

In interviews with industry groups/private companies, the main challenges stated were a lack of simplification of the review process for clinical trials, a lack of capacity by private institutions to develop vaccines, and a lack of human resource development and educational environment for vaccine research and development.

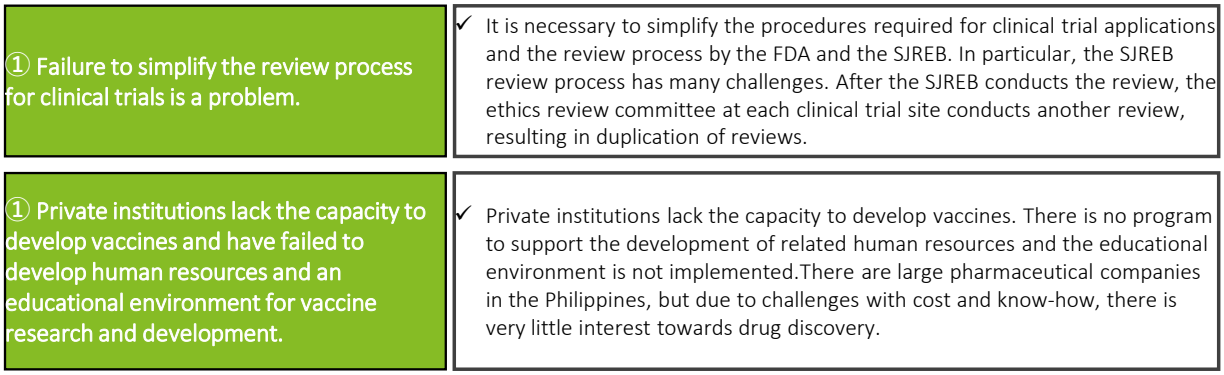


Figure 2-56 Interview results of industry associations and private companies (Philippines)

Requests for pilot activities include training to strengthen the capacity to conduct clinical trials, and support activities to promote regulatory harmonization and facilitate conversations and information sharing among regulators.

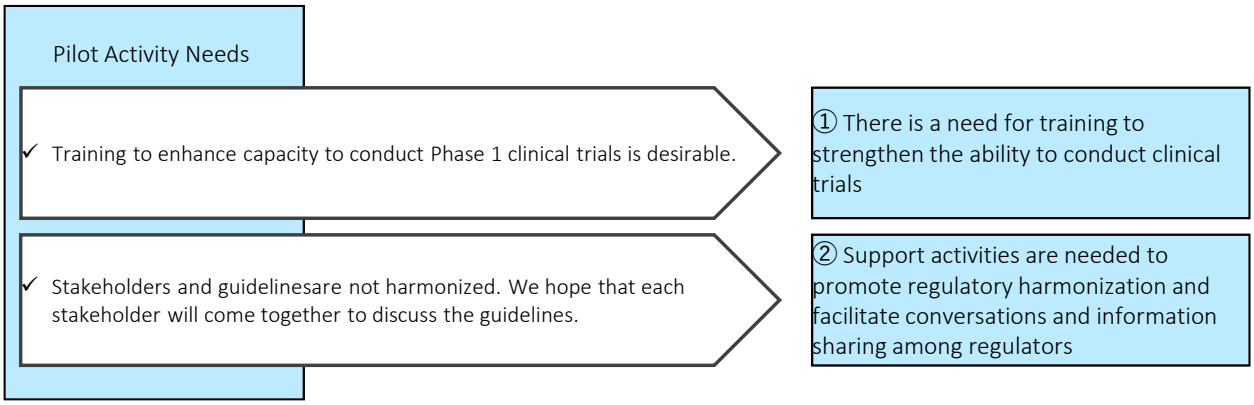


Figure 2-57 Pilot activity needs of industry associations and private companies (Philippines)

2.7.5 Indonesia

A total of 16 interviews were conducted with relevant institutions in Indonesia: 6 government agencies and regulatory authorities, 6 medical research institutions and hospitals, 1 CRO, 2 industry organizations and private enterprises, and 1 donor.

(1) Government agencies and regulatory authorities

Government agencies and regulatory authorities gave four main challenges in clinical trials and vaccine and drug manufacturing systems: (1) review processes, (2) human resources, (3) lack of collaboration among stakeholders related to clinical trials, and (4) research and development capabilities. Specifically, improvements are required in the following areas: (1) the process of approval review and ethics review takes time; (2) there is a shortage of human resources capable of handling and conducting clinical trials, and there are few opportunities to nurture these human resources; and (3) there is a lack of communication between stakeholders such as clinical research institutions and pharmaceutical companies.

① Because the process of approval review and ethics review takes time, it is necessary to review the process to speed up the review.	✓ The review process for conducting clinical trials of drugs derived from natural materials is time-consuming. ✓ The ethical review of the National Ethical Committee of INA Respond is not integrated with that of BPOM.
② There is a shortage of human resources who can handle and conduct clinical trials, and there are few opportunities to nurture these human resources.	✓ It is necessary to build the skills and infrastructure necessary to carry out standard research practices based on GCP, GCLP, etc., and to have the ability to compile papers and recommendations from research results in a timely manner. ✓ There is no training facility for clinical trial personnel.
③ There is a lack of cooperation among clinical trial-related stakeholders such as clinical research institutions and pharmaceutical companies.	✓ There is a lack of cooperation among clinical research organizations. ✓ Few pharmaceutical companies in Indonesia sponsor drug development and research. ✓ There is a lack of leadership, coordination and communication to enhance mutual understanding of research among stakeholders and stakeholders.
④ Although there are research institutions capable of conducting clinical trials, they lack research and development capacity relative to global standards.	✓ There is a lack of lab capacity. In Indonesia, there are many laboratories that provide clinical trial services, but many do not meet the required international standards. ✓ In Indonesia, the number of clinical trials is small, necessitating the promotion or advocacy of clinical research as a national or regional priority.

Figure 2-58 Interview results of government agencies and regulatory authorities (Indonesia)

As a request for pilot activities, (1) in addition to the training content that will strengthen the capacity of human resources for clinical trials, the content of training on how to conduct clinical research is required. Also, (2) it is desirable to provide a platform where researchers and manufacturers in Japan and Indonesia can share their knowledge and concerns with each other. Finally, (3) there is a need for management

methods related to clinical trials, such as managing funding and data, and it would be effective to conduct training to cover cases in Japan.

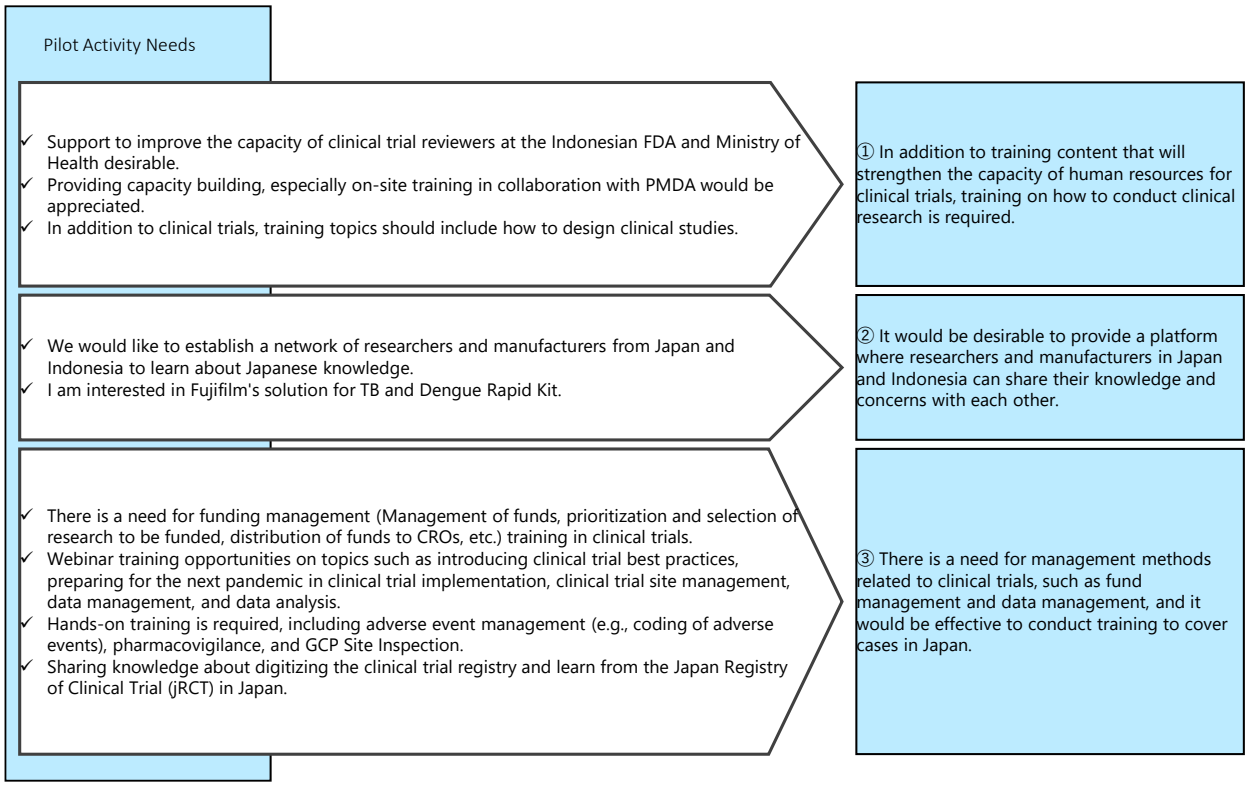


Figure 2-59 Pilot activity needs of government agencies and regulatory authorities (Indonesia)

(2) Medical research institutions and hospitals

After holding interviews with medical research institutions and hospitals, the four main challenges that were given in clinical trials and vaccine/drug manufacturing systems were (1) approval process, (2) shortage of human resources, (3) human resources, and (4) equipment and funding. (1) With regard to the approval process, the approval process within the administration and affiliated organizations is time-consuming and needs to be expedited. In addition, (2) the importance of clinical trials has not been recognized, and it is difficult to collect a sufficient number of subjects. (3) In terms of human resources, there is a lack of opportunities for human resources development for clinical trials on topics such as GCP training and protocol design. (4) In regards to equipment and financial issues, there is a lack of basic strength in each institution to conduct more research and development, and it is necessary to strengthen equipment and financial capacity.

① The administrative and institutional approval process for conducting clinical trials takes time and must be expedited.	✓ Before the pandemic, the administrative process, or the time it took to approve clinical trials at the Indonesian FDA, was an issue. The COVID-19 pandemic has accelerated the process for coronavirus-related medicines to about half the time. ✓ Even if ethical approval is obtained, it takes time to obtain approval from hospital management. ✓ The Ethics Review Committee has also been supportive, but feels that there are areas of the review process that need improvement.
② Because the importance of clinical trials has not been widely recognized, it is difficult to collect a sufficient sample size.	✓ Recruitment of subjects was also a problem. It is difficult to have people understand the importance of clinical trials, and it's hard to receive informed consent from people and their families. ✓ The bottleneck regarding clinical trials is that recruitment is quite difficult. Many people are reluctant to participate in clinical trials, especially for new vaccine or drug trials, where there is a lack of willingness from the community to participate and recruitment is slow. ✓ The participation rate of subjects in clinical trials of emerging diseases is not very high.
③ There is a lack of opportunities for human resources development for clinical trials on topics such as GCP training and protocol design.	✓ During the pandemic, it was difficult for hospitals to cope with new medication and treatment methods, and it was also difficult to continue conducting clinical research during the pandemic. The problem was that there was no protocol in the hospital for continuation of clinical and clinical research in such emergency. ✓ Indonesia cannot conduct clinical trials using domestic samples outside the country because it is prohibited to take domestically collected biological samples outside the country. Therefore, training of researchers such as basic GCP training is required. ✓ The number of clinical trials conducted at our university is not very large. The problem with conducting clinical trials is that there are not many people at Udayana University with experience in clinical trial protocol design, as many clinical trials already have protocols designed at CROs and other universities. ✓ At present, the Udayana University only conducts the requested clinical rrial and does not design the clinical trial itself, so basic clinical research skills are required.
④ The basic ability of each institution to carry out more research and development is insufficient, and equipment and financial capacity need to be strengthened.	✓ It is necessary to strengthen the capacity of clinical trial facilities and government and regulatory bodies (For example, the government's ability to allocate funds). ✓ We feel that technology transfer and capacity building are necessary to develop new vaccines. The capacity of drug discovery and vaccine research and development is still limited, and capacity building is necessary to raise the level. ✓ The lack of a formal clinical research center makes it difficult to participate in clinical research offered by other universities, in terms of the system, and in terms of the capacity and human resources skills of medical schools. ✓ There is a strong need to strengthen the capacity of the Academic Hospital to conduct more clinical research and trials as a clinical research center in the future. In the future, a CRSU function similar to that of the University of Indonesia will be established at UUH.

Figure 2-60 Interview results of medical research institutions and hospitals (Indonesia)

There are four main requests for pilot activities. (1) Lateral support such as procedural and investigative support for clinical trials is desirable. Specifically, support is required for administrative assistance and research. (2) Knowledge sharing and training in various fields including protocol design, statistical analysis and vaccinology are required. (3) Equipment and financial support are required to strengthen the capacity of each institution. (4) There is a need for training on building the infrastructure for conducting clinical trials, including data management and how to establish a clinical research support unit (CRSU).

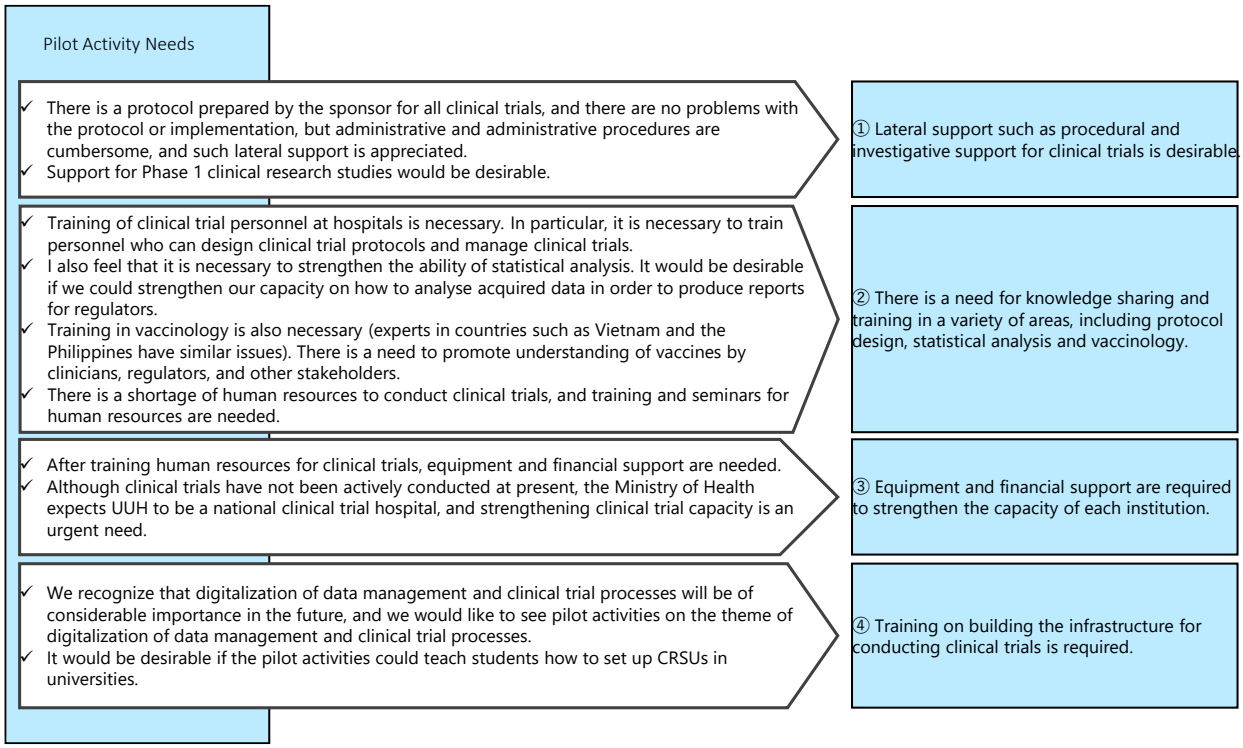


Figure 2-61 Pilot activity needs of medical research institutions and hospitals (Indonesia)

(3) CROs

Interviews with CROs revealed that (1) insufficient funds are available for research and development, and sufficient clinical trials cannot be conducted. (2) There is currently a lack of understanding of clinical trials in Indonesia. (3) The ethics review process takes time and needs improvement. (4) The capacity of clinical trial institutions is insufficient.

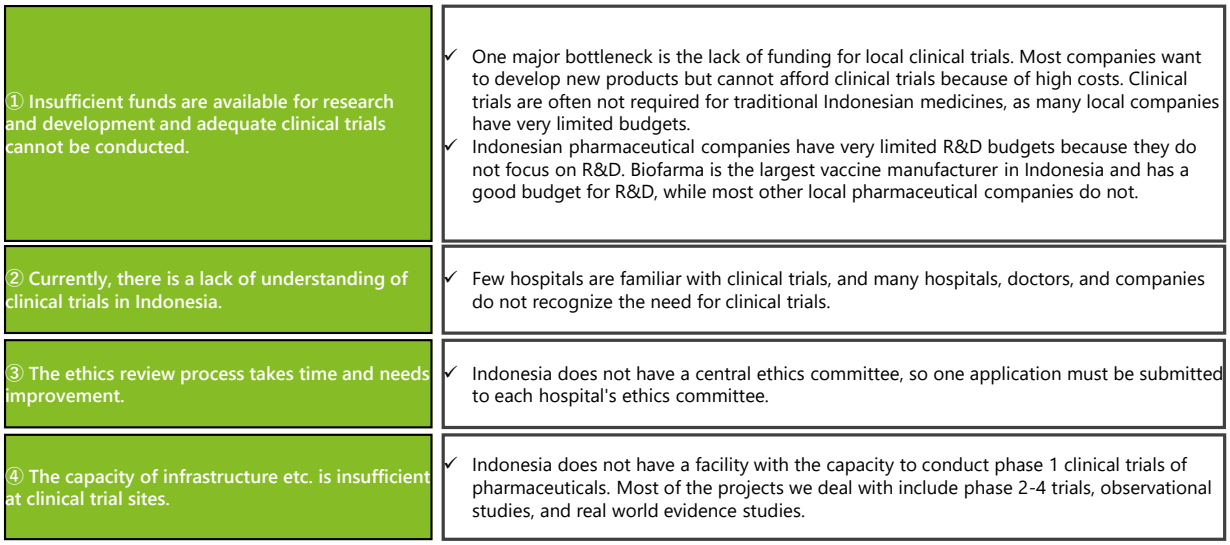


Figure 2-62 Interview results of CROs (Indonesia)

There are three main requests for pilot activities. (1) There should be opportunities to learn about how to conduct clinical trials. (2) Support for capacity building of clinical trial institutions, such as technology transfer, is required. (3) In order to conduct clinical trials smoothly, there is a need for an opportunity that can lead to network building.

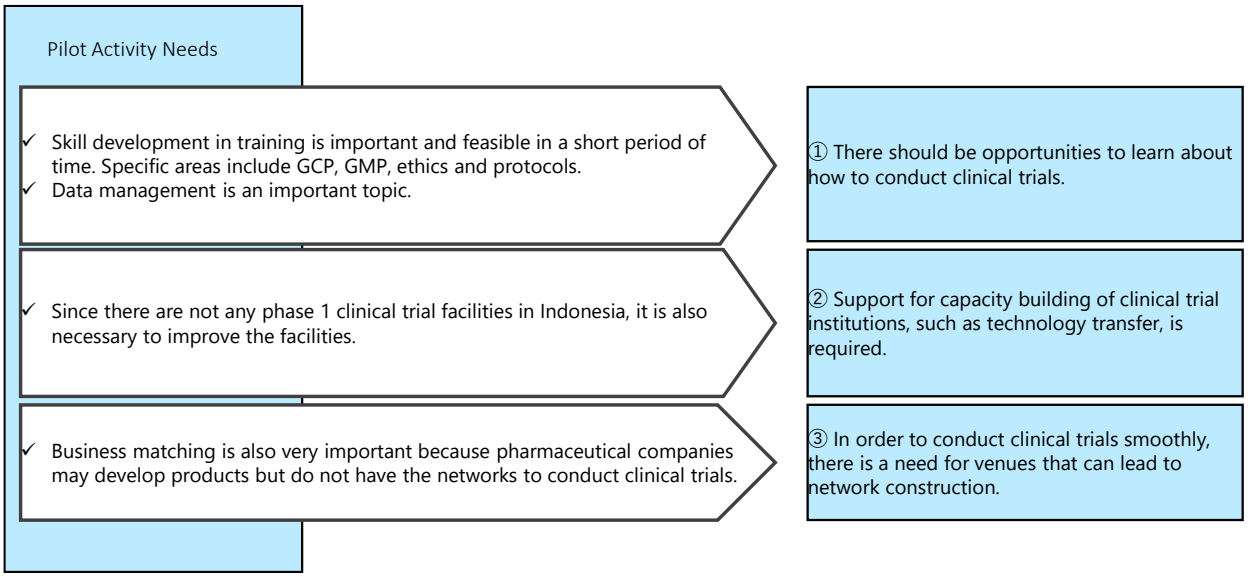


Figure 2-63 Pilot activity needs of CROs (Indonesia)

(4) Industry associations and private companies

Interviews with industry groups and private companies revealed four main issues. (1) There is a lack of emergency preparedness and a need for a manufacturer's center to recruit and procure talented resources. (2) Due to COVID-19, supply chain management must be reviewed. (3) Stringent pharmaceutical regulations in the country are affecting clinical trial timelines. (4) There is a lack of clinical trial infrastructure and a need for increased capacity.

① The government does not have a system in place to respond to emergency situations, and it is necessary to establish a center for manufacturers to hire and procure talented human resources.	✓ Because of the impact of COVID-19 and the situation in Ukraine on travel, exports and imports, it is necessary to select a manufacturer in consideration of the availability of talented personnel in Japan who can handle issues and the local availability of necessary parts.
② COVID-19 needs to review its supply chain management.	✓ The impact of COVID-19 has made it very difficult to manage the entire supply chain, including the procurement of raw materials, due to production adjustments.
③ Drug-related restrictions in Indonesia have affected the timeline for clinical trials.	✓ BPOM has strict regulations. It is difficult to compare the situation with other countries, but I feel that it will take a long time for approval. ✓ Another challenge is that it is difficult to obtain samples for clinical trials from overseas through customs clearance.
④ There is a lack of infrastructure to conduct clinical trials and a need to strengthen capacity.	✓ There are few laboratories in Indonesia that can evaluate samples.

Figure 2-64 Interview results of industry associations and private companies (Indonesia)

The requests for pilot activities include (1) training for clinical trialists and provision of content aimed at improving their performance. In addition, (2) the pricing of drugs that manufacturers want to sell in Indonesia is strict, and negotiations for measures such as preferential treatment for manufacturers are required.

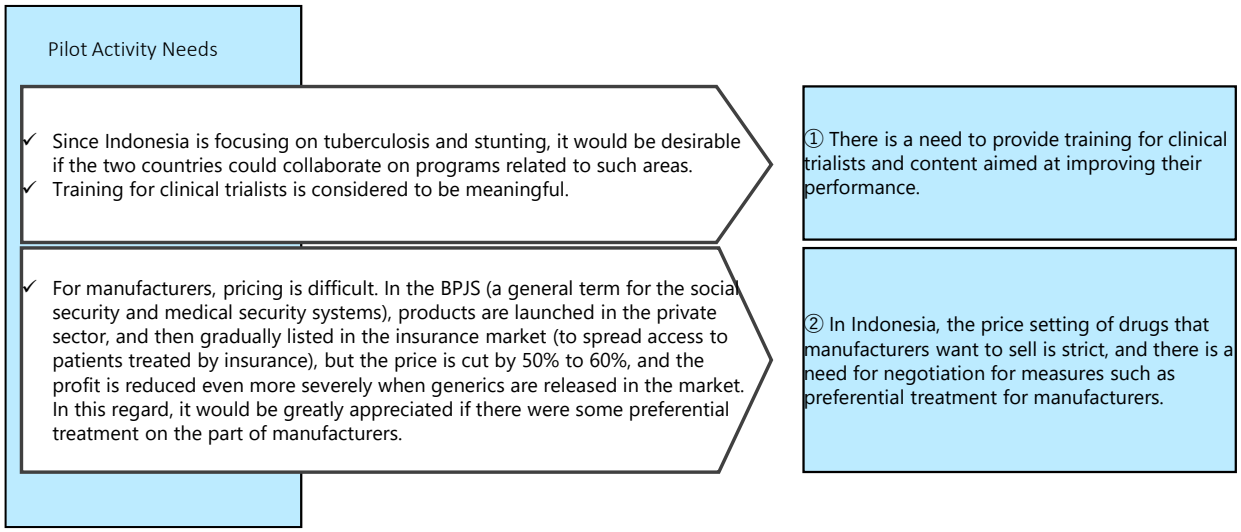


Figure 2-65 Pilot activity needs of industry associations and private companies (Indonesia)

2.7.6 Kenya

A total of 22 interviews were conducted with relevant institutions in Kenya, 3 interviews with international organizatons and non-profit organizations, 5 interveiews with government agencies and regulatory authorities, 5 medical research institutions, 1 interview with CRO, and 8 interviews with industry organizations and private companies.

(1) International organizations and non-profit organizations

Interviews with international organizations and non-profit organizations revealed that there are two chakkenges: (1) inadequate efforts to improve efficiency of and streamline screeining process, and (2) a lack of human resources and infrastructure and funds for clinical trials.

① Efforts to improve the efficiency and facilitation of the review process are insufficient.	✓ The problem is that the examination takes too long. Regulatory authorities and institutional ethics committees need training to conduct assessments and monitoring.
② There is a lack of human resources to conduct clinical trials and the infrastructure, resources and funding required to conduct clinical trials.	✓ There are not many experienced in quality control. ✓ Few hospitals have the resources to devote to clinical trials. ✓ Lack of skilled personnel to conduct clinical trials (At various levels, including PI, coordinator, and lab analysis) is cited. Also, lack of infrastructure and funding are also challenges. ✓ In addition to clinical trials, necessary information and data, such as patient information during the pandemic, are not properly organized at the hospital level.

Figure 2-66 Interview results of international organization and non-profit organizations (Kenya)

There are three major requests for pilot activities: (1) support activities to build the capacity of regulatory authorities and ethics committees of relevant institutions, (2) information mapping on the capacity of clinical trial sites, and (3) building equal partnership.

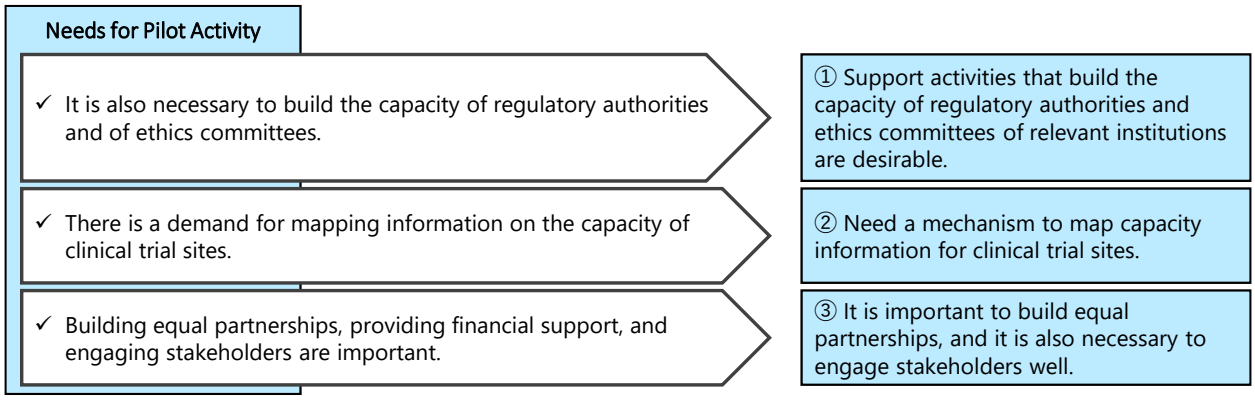


Figure 2-67 Pilot activity needs of international organization and non-profit organizations (Kenya)

(2) Government agencies and regulatory authorities

Interviews with government agencies and regulatory authorities revealed that there are two challenges in clinical trials and vaccine and drug manufacturing system. Specifically, two main challenges are (1) a lack of human resources for regulatory review and local manufacturing and (2) improving data collection, management, and analysis capabilities to promote digitization of the application and aprroval process.

① There is a lack of human resources for regulatory review and for local production, and insufficient training to enhance capacity and capacity.	✓ It feels understaffed and difficult to complete reviews on a defined timeline. ✓ As we are still building capacity for GCP screening, we need to strengthen our capacity to conduct GCP screening, which requires comprehensive and ongoing training and training. ✓ Training in quality assurance, quality control and production management is required for local production personnel.
② It is necessary to promote digitization of the application and approval process and to improve data collection, management and analysis capabilities.	✓ Digitization, such as online application and approval, must be performed. ✓ Although there is a large amount of data, it is not yet possible to analyze the data as "information" and use the large amount of data to determine various directions as a regulatory body. ✓ The Department of Health is currently working to establish a data management system that will archive all health care data, but the challenge is that health data is part of national security, making it difficult to obtain and provide data and limiting access.
③ Efforts to support local production from a policy perspective are still insufficient, and it is necessary to create an environment and system that facilitates local production.	✓ Only a few percent of the products on the Essential Medicines List can be produced in Kenya, and the product category is limited. ✓ It is important not only to promote local production but also to promote government procurement of locally produced products based on an accurate analysis of the market structure of the country. ✓ The problem is that raw materials for pharmaceuticals are extremely dependent on imports. ✓ In order to promote local production of pharmaceuticals, it is important to integrate multiple initiatives related to financial resources and human resources. ✓ There is a GMP roadmap, but it is important to raise the bar for companies with poor performance and low levels of compliance.

Figure 2-68 Interview results of government agencies and regulatory authorities (Kenya)

There are four major requests for pilot activities: (1) human resource development in clinical trials, training to strengthen the capacity of regulatory authorities and to promote local manufacturing, (2) support to reform, streamline, and establish interoperability of IT systems related to clinical trials, and support to strengthen data management capabilities, (3) technology transfer from Japanese companies to promote local manufacturing, and (4) establishment of partnership and networking between regulatory bodies and experts in Japan and Kenya.

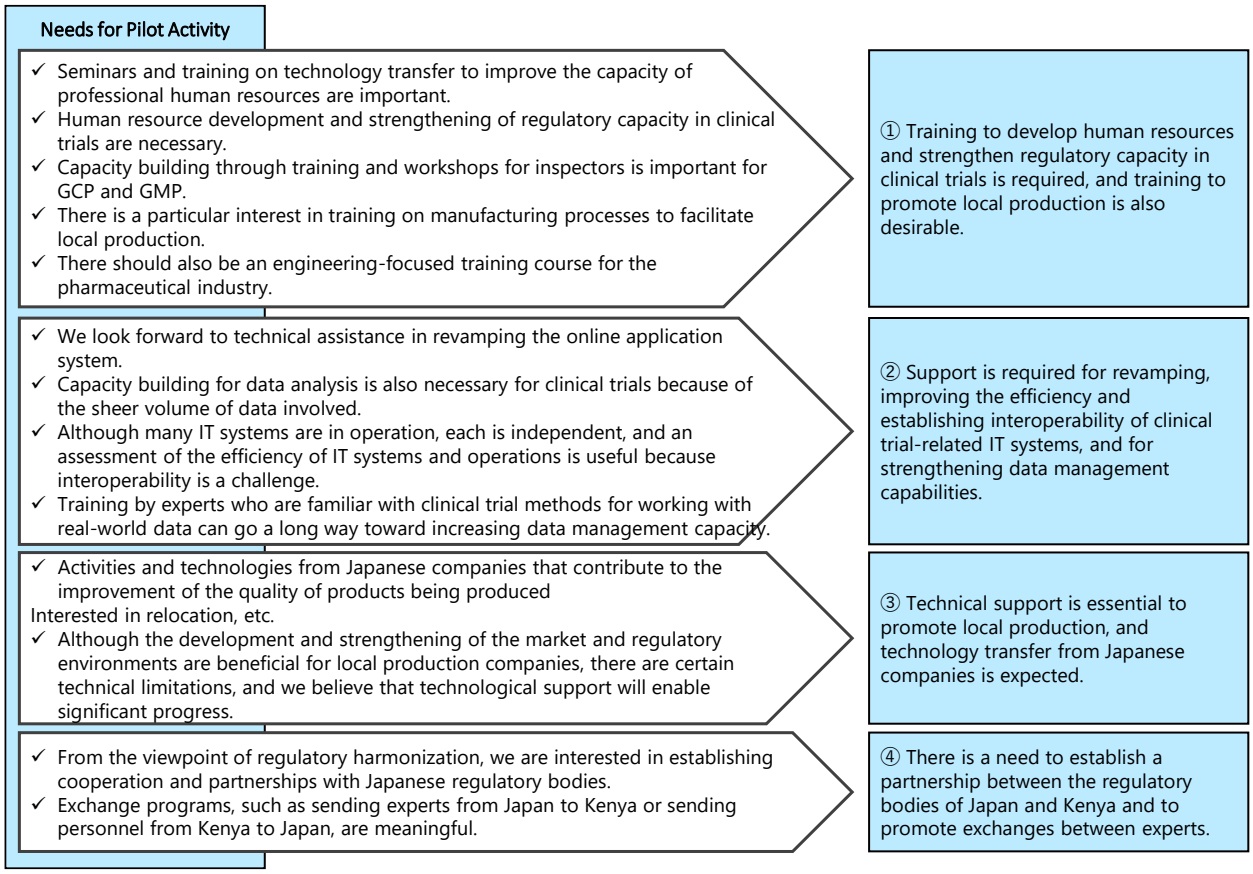


Figure 2-69 Pilot activity needs of government agencies and regulatory authorities (Kenya)

(3) Medical research institutions

Interviews with medical research institutions revealed that there are four challenges in clinical trials and vaccine and drug manufacturing system which are funding, human resources, equipment and infrastructure, and regulations. Specifically, (1) insufficient budget and funding for clinical research and clinical trials implementation and financial support for R&D, (2) a lack of human resources with technical expertise in clinical trials, clinical research, and vaccine R&D and quality control, and needs to secure the trained personnel and establish them in field, (3) insufficient equipment, laboratories, and upgrade of functions for clinical research and trial, and maintenance of equipment is expensive, and (4) establishment of mechanisms to facilitate clinical trials and improve and streamline the regulatory review and approval process are raised as major challenges.

① Budgets and funding for clinical research and the conduct of clinical trials and financial support for R & D are inadequate.	✓ One of the challenges with R & D is funding, and sometimes the financing capacity is not enough to commercialize a product. ✓ Securing government funding for clinical research is important and funding for clinical trials is also needed. ✓ Policies to create an environment should be developed so that the cost of running a company in Kenya is high and corporate activities are easy to carry out.
② There is a shortage of human resources with technical expertise in clinical trials and clinical research, vaccine research and development, and quality control.	✓ In Kenya, there is not much training in clinical research. ✓ There is a shortage of people with technical expertise, including staff who can conduct vaccine research, and a shortage of people who are knowledgeable about quality control. ✓ How to reduce the outflow of human resources from clinical trials and establish human resources in clinical trials is an issue. ✓ Trained personnel are available, but there is a lack of sustainable planning.
③ Equipment and laboratories for clinical trials and research are lacking, and upgrading of the functions of related facilities is insufficient, raising the cost of equipment maintenance.	✓ There are facilities that conduct phase 1 clinical trials, but the functionality is not up-to-date. ✓ Outdated equipment is also a challenge, as many of the equipment is imported from overseas and hiring overseas engineers is expensive, making maintenance in Kenya difficult. ✓ Although there is financial support, it is allocated to each field, resulting in a lack of equipment and labs for large-scale research.
④ It is necessary to establish a mechanism to facilitate the implementation of clinical trials and to improve and improve the efficiency of the regulatory review and approval process.	✓ The fact that the approval process takes a lot of time (one of the reasons for the delay is that there are multiple approval processes) is a challenge, and the capacity of the PPB needs to be strengthened. ✓ The problem is that the structure of clinical trials is dispersed among institutions and is not organized into a unified institution or process.

Figure 2-70 Interview results of medical research institutions (Kenya)

With regards to requests for pilot activities, there was a high level of interest in training for human resources development, networking activities to promote communication and collaboration with relevant stakeholders and visiting Japan. Specifically, opinions were raised about the following needs: (1) training on clinical trial frameworks and processes, training to increase contact with new technologies and personnel development in the areas of quality management and biomedical engineering; (2) establishment of a forum for opinion sharing and discussion that enables two-way communication among stakeholders, including networking activities, interactions among regulatory authorities, and conversations among stakeholders involved in drug manufacturing; (3) human resource development in clinical trials and pharmaceutical manufacturing, visiting Japan and other developed countries that lead to sharing of technologies and knowledge, and establishment of equal partnerships.

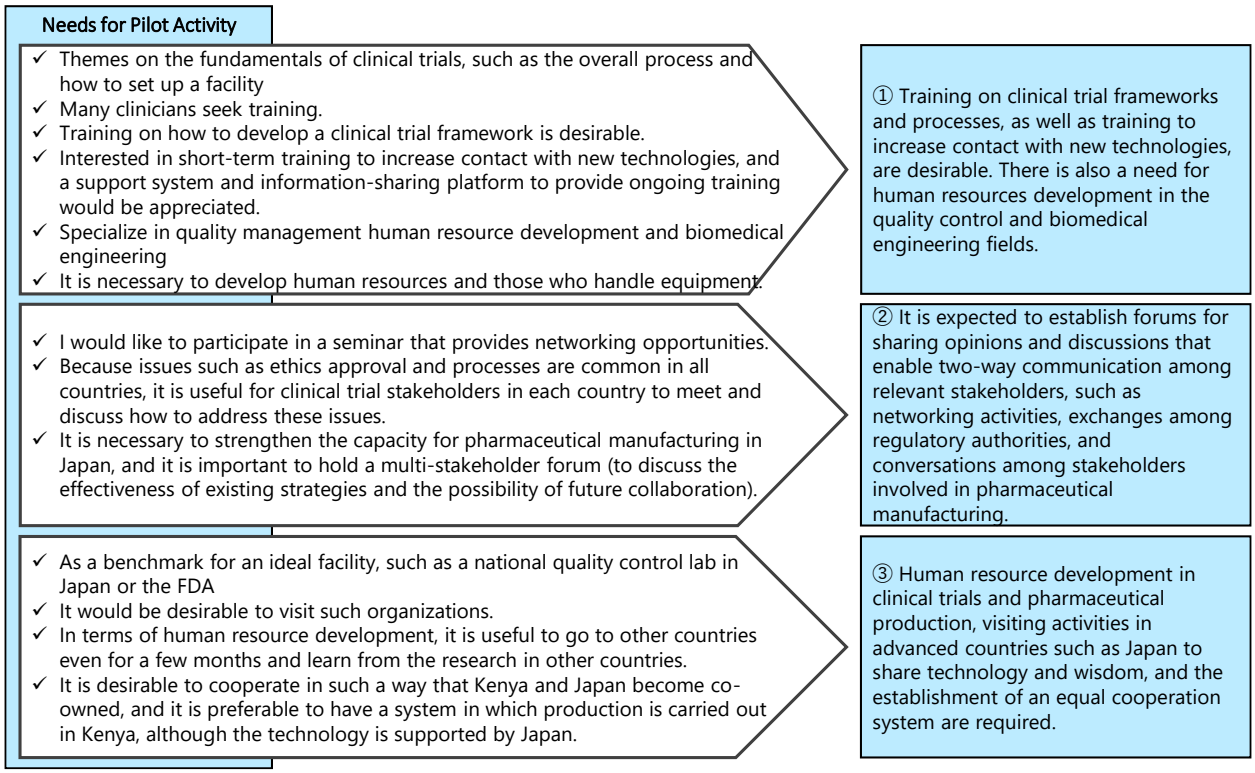


Figure 2-71 Pilot activity needs of medical research institutions (Kenya)

(4) CROs

From the interview with CRO, three challenges in clinical trials and vaccine and drug manufacturing were mainly mentioned. These included (1) the complecity and delay of the clinical trial review and approval process, (2) the enhancement of local manufacturing efficiency in line with the GMP, and (3) capacity building for the data collection and analysis of clinical trials.

① The complexity and delay of the review and approval process of clinical trials is a challenge.	✓ The complexity and delay of the regulatory process for clinical trials is a problem, and delays are caused by the need to go through various approval processes.
② More efficient local production in line with GMP has not yet been achieved.	✓ In local production, it is necessary to strengthen technical aspects that enable efficient production in line with GMP.
③ Capacity building for collection and analysis of clinical trial-related data is not yet sufficient.	✓ Technical enhancements such as data collection and data analysis are needed to enable more efficient clinical trials, and it is desirable to have technologies that enable remote data collection. ✓ It is important to strengthen the data management ability of clinical trial human resources and to create opportunities for medical students to know clinical research. ✓ More investigators are needed for clinical trial personnel.

Figure 2-72 Interview results of CROs (Kenya)

There were four major requests with regards to pilot activities, and they include (1) equipment support (data analysis and management software), (2) technical support for local manufacturing (transfer of technology and knowledge), (3) support for strengthening the capacity of human resources involved in clinical trials, and (4) funding support.

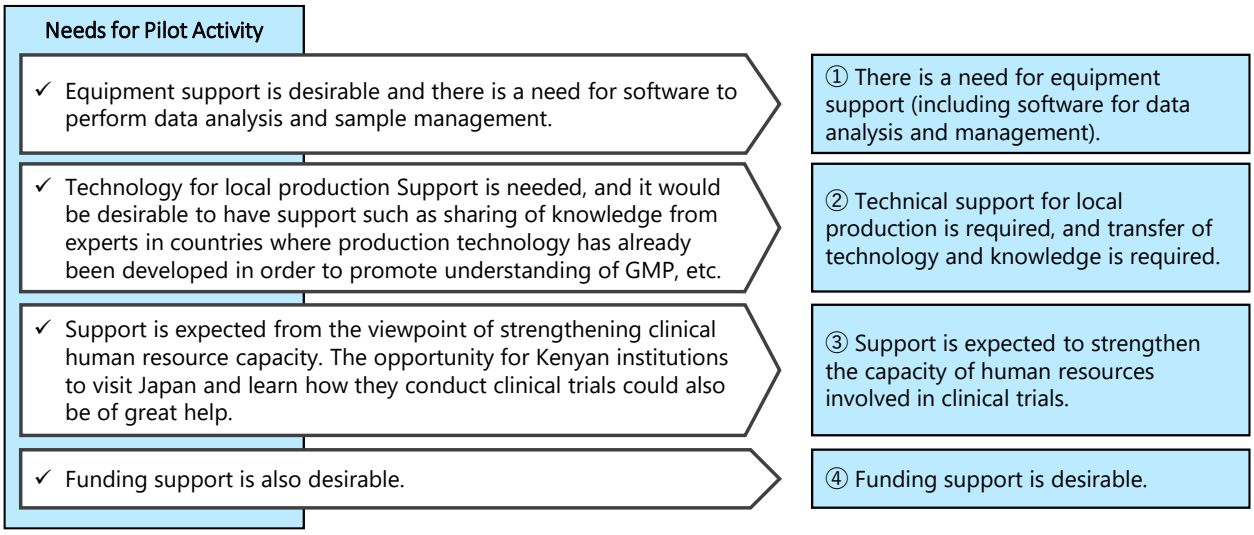


Figure 2-73 Pilot activity needs of CROs (Kenya)

(5) Industry organizations and private companies

Interview with industry organizations and private company revealed three major challenges in clinical trials and vaccine and drug manufacturing systems. Specifically, the following challenges were raised: (1) a lack of policies and tax measures to promote the establishment of a system for local manufacturing and sustainable drug supply, and insufficient support to improve the efficiency of facilities and equipment for local manufacturing, (2) lack of guidelines to support drug discovery and policy and regulatory frameworks to promote clinical trials, and (3) a lack of capacity (human resources, funds, and etc.) to conduct clinical trials.

① There is a lack of policies and tax measures to promote the establishment of a local production and sustainable pharmaceutical supply system, and insufficient support for efforts to improve facilities and equipment for local production and improve efficiency.	✓ Cost-effective local production of raw materials such as APIs has not yet been achieved, and a system is needed to enable sustainable supply of pharmaceuticals without recourse to overseas imports. ✓ Although there are policies to encourage local production, the actions and activities associated with it have not been implemented. ✓ To promote local production and manufacturing, policy changes are needed to limit the amount of imports to some extent and to establish a system to meet domestic needs through local production. Policies to promote production should be considered so that tax measures are also favorable to local companies. ✓ With regard to local manufacturing, support is required for the maintenance of facilities and equipment and efforts to improve efficiency. ✓ There is not much capacity to develop new products such as new drugs.
② There is a lack of policies to promote clinical trials, appropriate regulatory frameworks and efficient institutional design and operation, and guidelines to support drug discovery.	✓ Appropriate regulatory frameworks are needed to facilitate smoother drug/vaccine clinical trials, and training of regulatory personnel is also important. ✓ Approval of clinical trials needs to be easier and faster, not only from a regulatory perspective but also from operations such as customs and import licensing. ✓ Overall, there is a lack of national policies to promote clinical trials. ✓ Delays in the application and approval processes for clinical trials are a major challenge and require more efficient institutional design and operation. ✓ Clinical trial guidelines have yet to be developed to support the movement of innovator companies conducting global clinical trials on drugs in development.
③ The capacity to conduct clinical trials is insufficient, there is a lack of relevant human resources and funding, and the results and knowledge of clinical research and clinical trials are not being returned to the field.	✓ There is insufficient capacity to conduct clinical trials and the clinical trial process is not well understood. In addition, clinical trials are expensive and present considerable hurdles for local manufacturers. ✓ Lack of human resources for clinical trials and clinical research (few people have specialized training), lack of funds, lack of capacity of non-medical institutions such as clearance of samples, and delay in response are cited. ✓ As for cooperation with foreign institutions, data are always owned by foreign institutions, and data are not accumulated on the ground in Kenya, so the establishment of knowledge in Kenya has not been realized (research results have not been returned to Kenya).

Figure 2-74 Interview results of industry organizations and private companies (Kenya)

There were four major requests with regards to pilot activities, and they include (1) participation in events and networking activities involving a wide range of stakeholders, and visiting activities to learn about Japanese technologies and knowledge, (2) participation in training on topics such as clinical research,

clinical site management, GMP, and vaccine quality control, (3) support for the development of regulatory frameworks and implementation of policies to strengthen regulatory capacity and harmonize regulations, and (4) provision of equipment and facilities for clinical trials and local manufacturing and technology transfer (including knowledge on data collection, management, analysis, and operation).

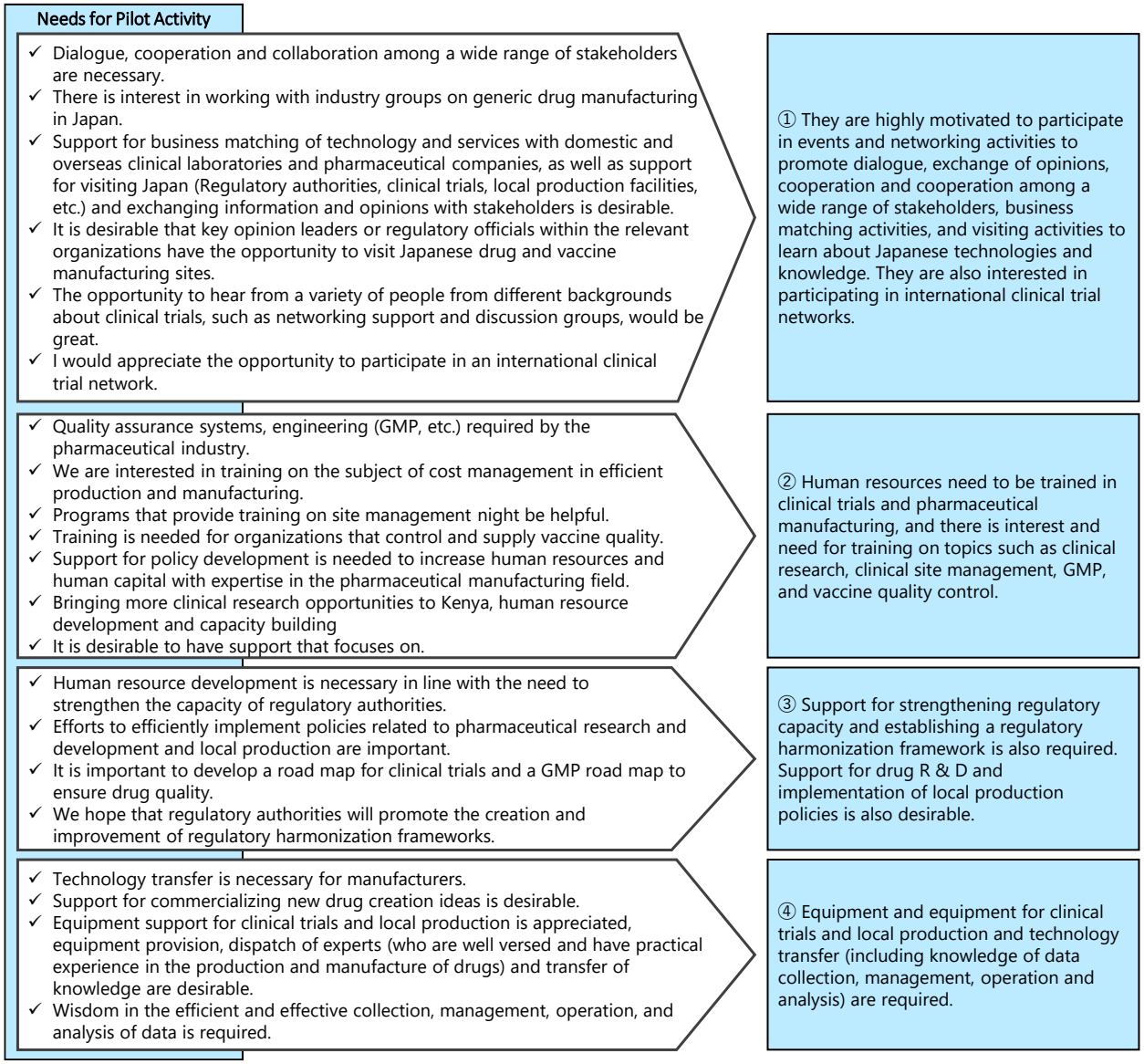


Figure 2-75 Pilot activity needs of industry organizations and private company (Kenya)

2.8 Interview results with relevant organizations in Japan

2.8.1 Results of discussions with relevant organizations in Japan

Interviews were conducted with relevant organizations involved in the implementation of clinical trials in Japan. In addition to the outlines and initiatives of each organization, interviews were conducted mainly on issues and countermeasures in the implementation of smooth clinical trials overseas and the realization and expansion of the international collaborative trial platform. The agencies are divided into five categories (Regulatory agencies, clinical trial sites, clinical trial implementation promotion organizations and networks, private companies and industry associations) and their comments are summarized below.

(1) Regulatory agencies

Interviews were held with one regulatory organization. For the realization of the international joint clinical trial platform, there was mention of presenting benefits to partner countries with a view to building long-term relationships and providing incentives to private companies to promote international cooperation. In addition, there was mention of Thailand, Indonesia, and Malaysia, because JICA and other experts were dispatched to target countries that Japan should cooperate with as a priority. In addition, since Thailand has shown advanced development in the field of clinical trials in ASEAN, there was an opinion that it should cooperate with ASEAN as a lead country in order to spread its effects to ASEAN. In addition, it was pointed out that shortening the review period may increase the speed of vaccine development and reduce confidence in the quality of drugs.

Table 2-1 Comments from regulatory agencies

No.	Discussion Points	Comments
1.	Japan's contribution to the realization of a global clinical trial platform	• In order to build a long-term relationship, it is necessary to consider how to create a win-win relationship that benefits the other country. • It is important to create a system that can respond promptly by involving multiple stakeholders from a broad perspective. • It is important to provide incentives for private companies to participate in international cooperation in a context where there are few advantages to enter a new market.
2.	Countries that Japan should cooperate with as a priority	• JICA experts are dispatched to Thailand, and has a good relationship with Japan. Thailand is one of the leading countries in ASEAN, and if Japan can influence Thailand, it may become easier to impact other ASEAN countries. • JICA experts are also dispatched to Indonesia and Malaysia and have long-standing connections and networks.
3.	Issues in the pharmaceutical approval process in Japan	• The shortening of the screening period has raised public distrust. It is difficult to strike a balance because shortening the examination period is not always necessary, and it is also important to prove that the examination is reliable.

(2) Clinical trial sites

Interviews were conducted with 3 clinical trial sites. Regarding the promotion of clinical trials in Asia, it was mentioned that the environment and support for clinical research are hindrances. It was also pointed out that in countries such as India, the environment for registration systems and data collection is insufficient, and IT-related development is a problem in order to smoothly exchange information between countries. In addition, opinions were gathered on the development of human resources using Japanese know-how and resources as an area where Japan can contribute to the implementation of the international joint examination. Regarding the cooperation between Japanese clinical trial institutions and overseas, it was also mentioned that the Academic Research Organization (ARO) from overseas has never been accepted from the institutions that play a central role in clinical trial implementation in Japan.

Table 2-2 Comments from clinical trial sites

No.	Discussion Points	Comments
1.	Establishment of a support system for conducting clinical trials in Asia	• When ASEAN, Japan and the whole are combined, the number of cancer patients is comparable to that in the United States, but global companies overseas are not as enthusiastic to expand their business compared to Western countries. This is because Asian markets are smaller than those in Western countries. • Asia has enough capacity, however the environment and support for clinical research is a bottleneck.
2.	IT-related challenges	• When talking to doctors at high-volume hospitals in India, IT challenges such as registration systems and data collection are common. • In India, IT challenges are often mentioned. Once the issues regarding IT are settled, more specific support will be possible.
3.	Japan's contribution to the realization of a global clinical trial platform	• By participating in international clinical trials, countries can acquire knowledge on clinical research and develop human resources. • The aim is to utilize Japan's knowledge, resources and platforms to conduct international clinical trials in the future. • Financial support is important, it is important to build trust with other countries face-to-face. • Rather than thinking about starting a new network, considering a partner to work with is also important. • In addition to establishing international clinical trials and manufacturing bases, Japan will be able to contribute to human resource development in these areas. It will also increase the possibility of promoting regulatory science in Asia. • It would be a good idea to establish a cooperative relationship if there are better seeds overseas, rather than just focusing on Japanese pharmaceutical companies and ventures.
4.	Collaboration system between Japanese clinical trial institutions and overseas	• Although our organization has been appointed as an advisor by various universities and provides clinical research support, we have never accepted the Academic Research Organization (ARO) for clinical research from overseas.
5.	Regulatory development of international clinical trial platforms	• Regarding regulatory science, it is necessary to improve regulations for building a platform for new drug discovery. Creating a platform that involves developing countries will enable drug discovery with high efficacy and safety. • If we can build capacity to improve the quality of new drug discovery in developing countries, we can contribute to the international community while supporting developing countries.

(3) Clinical trial implementation promotion organizations and networks

Interviews were conducted with 3 organizations. The main areas in which Japan could contribute to the realization of a global clinical trial platform were human resource development, technology transfer, and financial assistance. In particular, regarding technology transfer, it was mentioned that support needs for equipment capable of conducting Phase 1 studies and equipment for storing specimens are high, and that local expectations are high for the development of systems for integrating medical data, etc. In addition, there was a reference to a support system for private companies to conduct clinical trials overseas, and there was a comment that it was necessary to share information on the pharmaceutical approval system, etc. of the partner country, and to follow up on ongoing implementation of local business.

Table 2-3 Comments from clinical trial implementation promotion organizations and networks

No.	Discussion Points	Comments

1.	Japan's contribution to the realization of a global clinical trial platform	• Human resources development
		  • Training of human resources is undoubtedly necessary for smooth clinical trials abroad and for the realization and expansion of global clinical trial platforms.
		  • Human resource development requires commitment over the medium to long term and preparation and commitment from peacetime.
		• Technology transfer
		  • When visiting the target country institutions, we often hear about the need to have facilities capable of conducting Phase 1 studies.
		  • There is also a high need for medical data integration systems and biobanks to facilitate clinical trials.
		  • It is difficult to collect samples in developing countries. There is also a problem of not being able to procure dry ice and equipment to freeze and store specimens. Any support for this equipment would be appreciated.
		• Financial aid
		  • Southeast Asian countries also have sufficient systems and know-how for conducting clinical trials, but lack of budget is a problem, and there is a great need to acquire funds to conduct small clinical trials independently.
		  • The organization provides a fund and does not have a budget structure that needs to be digested every fiscal year, so it can support the development of researchers and the development of research in the long run.

2.	Support system for private companies to conduct clinical trials overseas	• In order to conduct clinical trials in developing countries, it is paramount that the motivation of companies and national policies are aligned. It is also important for companies to motivate themselves to develop clinical trials in Southeast Asia. • Barriers to motivating companies include (1) a lack of knowledge and experience in foreign country pharmaceutical approval systems and procedures, (2) a lack of firm confidence that there is a market to sell, and (3) a lack of understanding of distribution mechanisms. • If the public interest is high, the business advantage is generally small, and it is desirable to consider the burden of industry, government, and academia, and the indirect benefit, and to set milestones and go/no go criteria in advance. • In order to take root in local clinical practice, it is necessary to conduct preliminary research, develop strategies, build consensus, and then follow up on the business continuity of the company in charge of product management. • It is also useful to have national information on compensation for trial subjects, regulatory information on the importation of drugs for use in clinical trials, and regulatory information on sending test data, samples, and specimens obtained in trials overseas.
3.	Transparency in governance of clinical implementation agencies	• What Japan can learn from this organization is that it is an academia network and that the governance of the platform is transparent and lean. • This has resulted in a platform with high patient enrollment and rapid evidence base relative to the budget.
4.	Utilization of the "Japan" brand	• What Japan can contribute to the global clinical trial platform depends on whether it is made in Japan, or whether Japan should be involved even if ownership is not 100%.
5.	Importance of Japan's cooperation with overseas countries	• After successful trials, vaccines and drugs need to be supplied, and they need to be ready. It would be good to be able to match not only domestic CMOs and CMOs but also overseas CMOs and CMOs as needed. • With Japan lagging behind in the development and production of vaccines, cooperation with Southeast Asia is essential given the number of trial patients and the fact that it is not profitable to distribute vaccines after development or to sell them in Japan alone.

(4) Private companies

Interviews were conducted with five private companies. Since some companies do not have the means to find local partners to support them, they have been asked to help build a network with overseas clinical trial-related organizations, and they expressed their desire to utilize the connections of domestic organizations such as JICA. In addition, as an approach to encourage private companies to participate in the international joint clinical trial platform, it is expected that there will be accompanying support to support the process of obtaining local certification for each company's products.

Table 2-4 Comments from private companies

No.	Discussion Points	Comments
1.	Support for networking between private companies and overseas institutions	• Collaboration with institutions that actually use the kits is essential, and the first point of contact is often the local university or government health institute. • We are interested in the countries covered in this survey, but it is difficult to take the first step without ties with overseas countries. First of all, we would like to expand our network overseas, and would appreciate if you could help support us (including PoC). • We would like to utilize JICA's network with Southeast Asian countries, and first let the organizations in the other countries use our products to understand its excellence, and then we consider business development (consider working with private partners). • In Indonesia, Vietnam, and India, we would like to consider starting a new clinical trial, but we have not found a sponsor, so we would like to ask for your cooperation in starting a new trial.
2.	How to approach the private sector to encourage participation in the global clinical trial platform	• To involve the private sector, it is necessary to coordinate with the agenda of clinical trial-related facilities in Japan in a framework in which JICA provides funds. • In some cases, MOCs will be established between the two countries, but we hope that the MOC will go beyond the framework to certify products. Instead of stopping at MOC, we need to reduce it to practical work. • Thailand and the Philippines are already working on their own projects, so we would like to ask for support in expanding the business to other countries.
3.	Status of overseas business development	• We want to explore the possibility of manufacturing vaccines in Southeast Asia. We hope to get our company's vaccine on the emergency use list (EUL) first, and then supply more countries with the vaccine bilaterally or through COVAX. • In Indonesia, Vietnam, and India, we would like to consider the development of a test kit for dengue fever as a new launch. • The test kit has been developed and CE marking has already been obtained.

(5) Industry associations

Interviews were held with two industry associations. During the interview, there was information sharing on the efforts of Japanese organizations regarding training in Asia, etc., and there was mention that strengthening the capacity of clinical trial laboratories in Asia could serve as an outsource for clinical trials conducted by Japanese pharmaceutical companies. In addition, it was mentioned that it is important to increase the opportunities to input the content of the guidelines on drug regulation prepared by the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) in order to improve the implementation level of clinical trials in Asia as a whole, and that it is important to consider training tailored to the level of each country. Other issues related to TRIPS Waiver were also mentioned[141].

[141] The TRIPS Waiver temporarily exempts medical supplies from the obligation to protect their intellectual property and encourages increased vaccine production

Table 2-5 Comments from industry associations

No.	Discussion Points	Comments
1.	Initiatives of domestic rrganizations	• Some institutions have established a training center for pharmaceuticals and medical devices and provide training. • The Headquarters for Healthcare Policy from the Cabinet Office is engaged in activities related to the Strategy for Strengthening the Vaccine Development and Production System, and participates in meetings, etc. to select priority infectious diseases for the Asian region.
2.	Japan's contribution to the realization of a global clinical trial platform	• In the future, it will be possible to become an outsource of clinical trials for pharmaceutical companies by supporting clinical trial institutions in target countries to step up to their level, and Japanese companies will also benefit. • Japan will benefit from increased capacity in the Philippines and Indonesia, which are geographically close to each other.
3.	Inputs of drug regulatory guidelines	• Knowledge dissemination of ICH guidelines is essential in terms of increasing clinical trial partners globally. • In Vietnam, the level of the clinical trial system is increasing, and it is necessary to have training contents that are different from other Asian countries.
4.	Challenges related to vaccine development	• The TRIPS Waiver, which exempts countries from the obligation to protect COVID-19's intellectual property, was a challenge in developing the COVID-19 vaccine.

Chapter 3 Development and pilot implementation of support activities (pilot activities) results

3.1 Results of potential cooperation activities according to the identified issues

3.1.1 Method of developing potential cooperation activities

(1) Definition and purpose of pilot activities

In this study, priority issues and needs to be addressed will be identified through literature research, interviews, and field surveys, and based on these challenges and needs, a pilot activity plan will be considered and implemented in the study target countries or stakeholders concerned in Japan. Based on the verification of the effectiveness of the pilot activities, a long-term cooperation activity plan will be considered at the final stage of the study, with the aim of proposing concrete plans with details that will lead to the consideration of JICA's future program.

(2) Candidate pilot activities considered based on the challenges identified

First, information obtained from the literature research and interviews with local stakeholders, either online or during the field survey, was scrutinized and challenges related to each clinical trials and local manufacturing were comprehensively sorted out. The issues mentioned in the interview were extracted, especially those mentioned by multiple stakeholders.

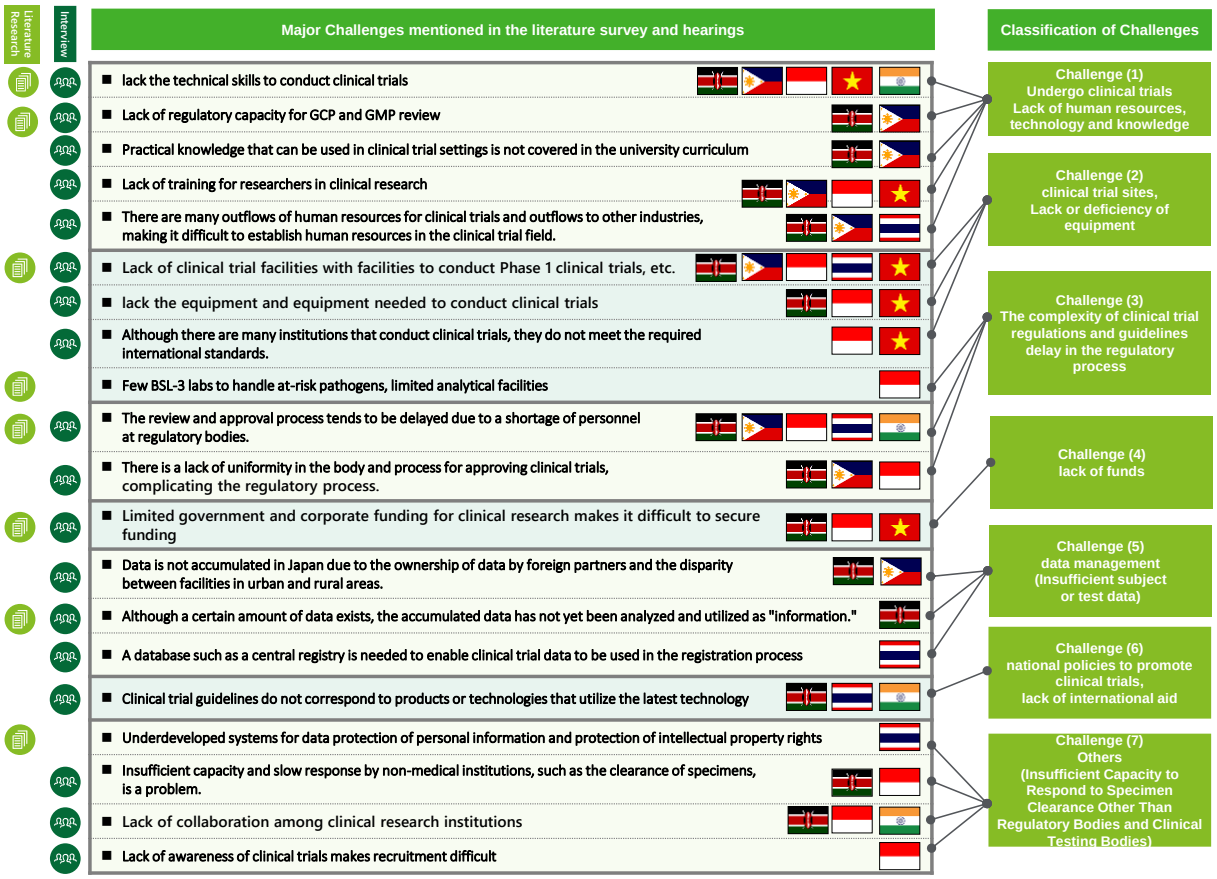


Figure 3-1 Callenges related to the clinical trials (6 target countries)

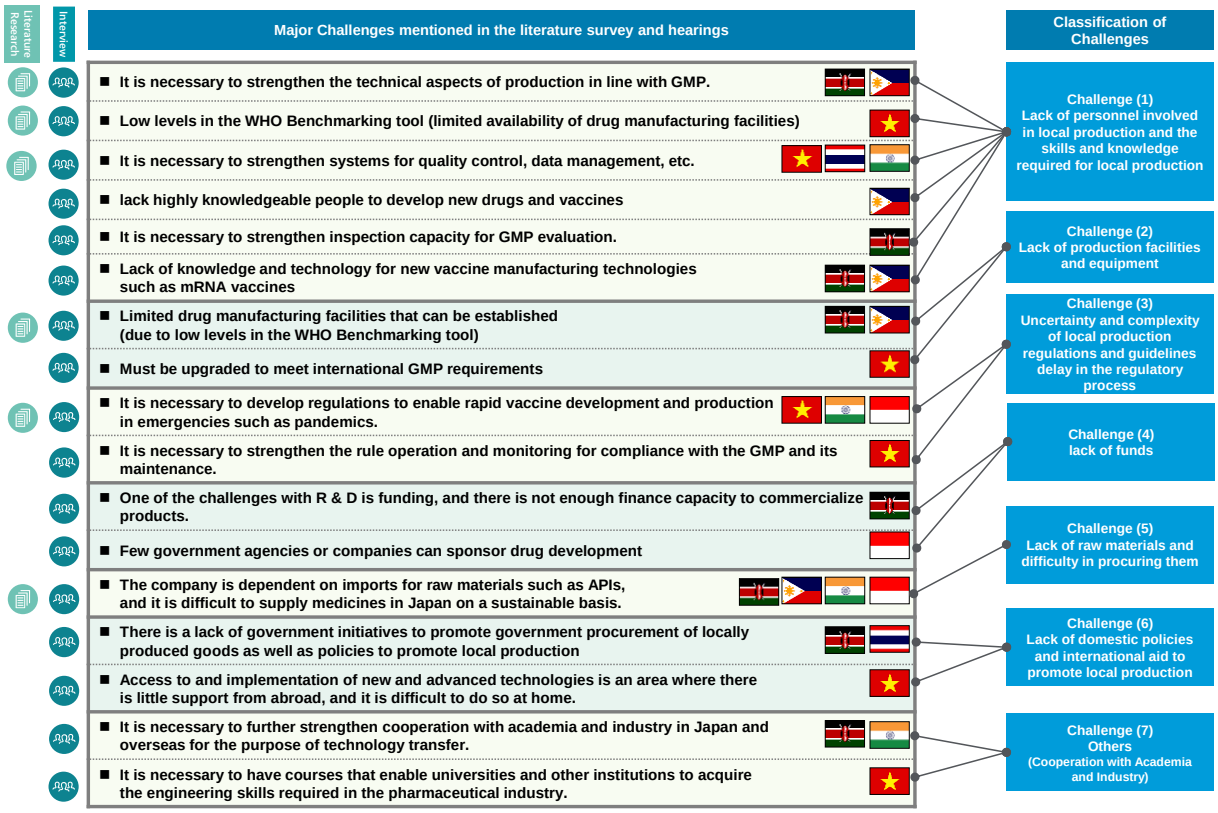


Figure 3-2 Challenges related to the local manufacturing (6 taget countries)

As a result of sorting out the challenges as described in above figure, the challenges related to clinical trials and local manufacturing have 7 groups of challenge based on each feature as shown in the table below.

Table 3-1 7 groups of challenges

Challenges of clinical trials	Challenges of local production
① Lack of human resources, skills, and knowledge for clinical trials	① Lack of personnel involved in local production and the skills and knowledge required for local production
② Insufficient or inadequate clinical testing facilities and equipment	② Lack of production facilities and equipment
③ Uncertainty and complexity of clinical trial regulations and guidelines, and delays in regulatory processes	③ Uncertainty and complexity of regulations and guidelines, and delays in the regulatory process of local production
④ lack of funds	④ lack of funds
⑤ Data management (lack of subject and test data)	⑤ Lack of raw materials and difficulty in procuring them
⑥ Lack of national policies and international aid to promote clinical trials	⑥ Lack of domestic policies and international aid to promote local production
⑦ Others (Insufficient Capacity to Respond to Specimen Clearance Other Than Regulatory Bodies and Clinical Testing Bodies)	⑦ Others (Cooperation with academia and industry, etc.)

In developing the pilot activity plan, the "challenges" extracted from the literature research and interviews (online and on-site interviews with stakeholders in the target countries), discussions with Japanese stakeholders, and "activity forms" for implementing the pilot activities were set as two keys, and then the activity plan was formulated.

Based on the needs and requests for pilot activities obtained from the relevant institutions in the target countries, the following seven types of pilot activities were drafted.

① Networking Support

② Matching Support

③ Seminar/ Workshop

④ Indivitual Training

⑤ Utilization of International Clinical Trial Platform

⑥ Equipment Support

⑦ Local PoC utilizing Japanese Technology

On the basis of the above, pilot activities that contribute to each group of challenge were examined for each activity forms, and consolidated into five activity proposals in consideration of feasibility factors such as budget, implementation period, and human resources: (1) matching, (2) networking, (3) equipment support/ training, (4) local PoC utilizing Japanese technokogy, and (5) training (seminar/ workshops/ individual training).

Theme

1. **Matching Needs and Solutions for Promoting Clinical Trials of Vaccines and Other Medicines**
   - Matching the needs and Challenges of the target country with the solutions and products that can be provided by Japan, and matching of related companies and institutions
2. **Construction of a raw material demand forecasting system to support local production of vaccines and other pharmaceuticals**
   - Development of demand prediction algorithms for raw materials, establishment of a mechanism to link supply and demand, and consideration of utilization methods

Purpose

1. **Addressing deficiencies in clinical trial facilities and equipment in target countries**
   - Identifying and identifying the needs and Challenges of target countries, Showing solutions and products that can be provided by Japanese companies, and creating opportunities for dialogue to achieve win-win matching
2. **Support for procurement of raw materials for local production of vaccines and other pharmaceuticals in target countries**
   - As part of local production support measures, we launched a demand forecasting tool to provide necessary support such as procurement of raw materials and supply of goods when there are signs of tight production conditions.

Summary

Number of countries covered	About 2~3 countries (The Philippines, Thailand and India)
applicable implementing agency	▪ On the Japanese side: Japanese pharmaceutical companies and medical device manufacturers, Japan Pharmaceutical Manufacturers Association ▪ Target countries: Local pharmaceutical and medical device manufacturers, trade associations, CROs, regulatory authorities, medical institutions, etc.

Implementation method

- **needs hearing on the part of the target country**
  - ✓ Conduct questionnaires and interviews with relevant organizations in target countries while utilizing the networks of PMDA and NCGM to **identify needs for clinical trial facilities and raw material procurement**
- **Cataloging the needs of the target country and the solutions of Japan**
  - ✓ List local needs and solutions that Japan can provide, and create a catalog as a consideration for matching
- **Setting up opportunities for online and offline interaction between domestic and overseas related companies and institutions**
  - ✓ Online/offline, Communication toward cooperation will be conducted by establishing a forum for dialogue between related companies and institutions of the target country and Japan.
- **Promotion of matching and implementation of post-matching follow-up by our association**
  - ✓ After matching the needs and solutions of both target countries and Japan, our association will support and promote matching in a way that meets the needs of both countries, and will consider and propose requirements, processes, schemes, etc. for collaboration.

Activities

- **Matching activities with Japanese solutions and products to meet the needs of target countries for pharmaceuticals such as vaccines and inadequate clinical trial facilities**
  - ✓ Listening and listing the needs of local clinical trial facilities, looking for Japanese companies that can provide the necessary facilities based on the needs, and introducing them to relevant organizations in the target country to establish a place for communication
  - ✓ Check with relevant organizations such as the Ministry of Health of the target country for the top diseases and the necessary vaccine needs of that country, and create and match a catalog that can be shown to Japanese pharmaceutical companies and research institutions.
- **Activities to introduce Japanese technologies and products to target countries and collect information on local clinical trial-related laws and guidelines, application and approval processes, etc.**
  - ✓ Introduce technologies and products from Japanese companies to target countries and Communicate with relevant parties such as regulatory authorities in target countries and Communicate about requests and confirmations of regulations from Japanese companies.
- **Activities to promote cooperation between Japanese companies, local companies and CROs, and to develop demand forecasting tools useful for both parties**
  - ✓ Engage in tie-up and matching with technologies, products and clinical trial services provided by local companies and CROs with Japanese pharmaceutical companies
  - ✓ An algorithm for predicting the future production status of feedstock producing countries is developed from the information provided by the International Collaborative Clinical Trials Network and data on the medical needs of each country, and the algorithm is used to support local production.

Figure 3-3 Overview of pilot activity plan ((1) matching)

Theme

- **Proposal 1: Meeting of the ASEAN Regional Human Resources Network for Pharmaceutical Research and Development**
- **Proposal 2: Holding of network meetings between pharmaceutical companies and clinical research organizations in target countries and Japanese pharmaceutical companies that wish to conduct clinical trials overseas**

Purpose

1. **Energizing conversations among stakeholders in the target countries**
   - Pharmaceuticals, R&D, conduct of clinical trials, production and delivery, Discussions on bottlenecks, harmonization, and desirable linkages in a range of processes, and Holding.
2. **Build a talent database**
   - Based on the information of the participants, the Human Resources Database and Creation for conducting drug R & D and clinical trials in the fields of industry, academia and government

Summary

Number of countries covered	Proposition 1 Four countries (Indonesia, Thailand, Philippines, Vietnam)	Proposal 2 All eligible countries
applicable implementing agency	▪ Country side: Governments, regulators ▪ Japan side: PMDA, Pharmaceutical Co-op, etc.	▪ Target countries: universities, hospitals, clinical research organizations such as CROs, and pharmaceutical companies ▪ Japanese side: Pharmaceutical cooperatives, pharmaceutical companies, etc.

Implementation method

- **Conducting face-to-face and online hybrid conferences**
  - ✓ One in-person, while the others participate online.
  - ✓ For in-person attendees, there will be enough room for networking, and for online attendees, there will be Zoom meetings and a stable connection.
- **Create breakout rooms per topic to select participants**
  - ✓ Tohmatsu will prepare questions that will deepen the interaction of the participants in advance, and advance each room.
  - ✓ Participants are free to enter and exit each room

Activities

1. **Present status of drug R&D, clinical trials, production and delivery in each target country**
   - ✓ Recognize the uneven distribution of knowledge and discrepancies in information in each target country through information sharing
2. **Stakeholders Discuss the following topics with each other**
   Proposition 1: Network between government and regulatory authorities in the target country
   - ✓ Export and import regulations for samples and test data
   - ✓ Insurance and guarantee system for clinical trial subjects
   - ✓ Biobanks use common data
   - ✓ Pros and Cons of the Purchase Guarantee Program

   Proposition 2: Network between clinical research institutions in target countries and Japanese pharmaceutical companies wishing to conduct clinical trials overseas
   - ✓ Strengthen networks with local clinical research organizations (including CROs), pharmaceutical companies, and Japanese pharmaceutical companies to promote technology alliances, overseas clinical trials, and the use of local CROs
3. **Building a human resources database**

Figure 3-4 Overview of pilot activity plan ((2) networking)

Theme

1. **Equipment and equipment support**
   - ➢ Support for facilities and equipment based on expert facility assessment of clinical trial institutions
2. **Equipment training and technical training**
   - ➢ Combined training program with equipment and equipment support

Purpose

1. **Increase capacity of clinical laboratories**
   - ➢ Facilitate the conduct of clinical trials, starting with local hospitals and research laboratories where equipment is scarce or the environment is not prepared
2. **Dissemination of Japanese corporate products and establishment of local sales networks**
   - ➢ Promote overseas expansion of Japanese equipment manufacturers over the long term

Summary

Number of countries covered	About 2 countries (Candidate Countries: Philippines, India)
applicable implementing agency	Country: ▪ Clinical trial institutions (hospitals and laboratories) ▪ government agency ▪ Organization that provides training for clinical trials Japan: ▪ Japanese clinical trial experts (NCGM, university institutions, etc.) ▪ Japanese equipment manufacturers

Implementation method

- ➢ **Select local clinical laboratories to support**
  - ✓ With the cooperation and advice of local organizations, select local urban hospitals, research institutes, and other institutions that have needs for equipment expansion.
- ➢ **On-site facility assessment**
  - ✓ Invite Japanese clinical trial experts to conduct on-site facility assessment
- ➢ **List the equipment you need and find a Japanese company that can provide the equipment**
  - ✓ List selected equipment based on the equipment assessment and present it to Japanese manufacturers
- ➢ **Provide technical training as well as equipment and equipment support**
  - ✓ Conduct technical training in cooperation with experts and local organizations in Japan

Activities

Examples of activities in the Philippines:

- ➢ With the cooperation of the Philippine Department of Health (DOH) and others, Needs for equipment expansion, Local clinical trial organizations, and Selected.
- ➢ Provide equipment and equipment support based on equipment assessment by Japanese experts, and conduct technical training in cooperation with NCGM, etc. and RITM/NCTTC (organizations conducting on-site training)

Looking ahead to future initiatives:

- ➢ List and catalog all necessary equipment for future cooperation programs
- ➢ From now on, you can send the equipment you need from the list and do technical training via video or online.
- ➢ We can also consider equipment support combined with matching support and individual training, which we have proposed separately.

Figure 3-5 Overview of pilot activity plan ((3) Equipment support)

Theme

1. **To measure the effectiveness of solutions utilizing Japanese pharmaceutical (reagent) technology in solving health care problems (especially in infectious disease control) in target countries**
2. **Based on the above measurement results, we will measure the possibility of lateral deployment of solutions in target countries and form future support projects.**

Purpose

1. **Trial introduction of highly sensitive virus (enteric viruses and respiratory viruses such as COVID-19) detection technology by sewage monitoring**
2. **Trial introduction of infectious disease testing technology**
   - ➢ Building relationships with local implementing agencies
   - ➢ Measurement of the possibility of lateral business development
   - ➢ Business formation with a view to lateral development in target countries
3. **Performance evaluation of new products of other companies**

Summary

Number of countries covered	Countries included in this study (Candidate Countries: Indonesia, India, Philippines, Vietnam)
applicable implementing agency	▪ Ministry of Health ▪ Local Health Authority and Sewerage Authority ▪ Target countries Epidemiology and Health Research Institute, etc. (India ICMR-NIE, Vietnam NIHE, etc.) ▪ local hospital

Implementation method

- ➢ Select local organizations interested in local PoC for solutions provided by Japanese companies in the countries covered by this survey.
- ➢ Establish an implementation structure with local organizations and implement PoC at local sites

Activities

- ➢ **Sensitive virus detection technology by sewage monitoring**
  - ✓ Selection of target countries (target regions)
    - Multifaceted development in Indonesia, where demonstration testing is already underway
    - Implementation of third countries through networking with health authorities of other countries
  - ✓ Support for procurement of reagents and freezers for reagent storage
  - ✓ Implementation of local PoC
    - In addition to sewage monitoring, we will also consider monitoring wastewater from food processing plants and aquaculture farms.
- ➢ **infectious disease testing technique**
  - ✓ Selection of target countries (target regions)
    - Select implementing partners with close ties to JICA, such as the Philippine Institute of Tropical Medicine and the Vietnam NIHE, for which ethics approval is easily obtained.
  - ✓ Implementation of local PoC
    - Implementation of demonstration experiments
    - Consider providing training and equipment to partner countries

  [Proposed Implementation]
  The introduction of a package of NIPRO MDR TB genetic testing drugs by JICA's private technology promotion project in the Philippines may also be considered in other target countries.
- ➢ **Support for performance evaluation of new products from other companies**
  - ✓ Genetic test kits for tuberculosis, dengue fever, etc.

Figure 3-6 Overview of pilot activity plan ((4) local PoC utilizing Japanese technology)

Theme

1. **[For incumbent engineers] Enhancing technical skills and knowledge related to clinical trials**
   - Sharing technical (expert) knowledge from NCGM and PMDA
   - Promoting understanding of new clinical trial trends (e.g., adaptive design and RWD) or GCP and ICH
2. **[For organizations that nurture relevant human resources] Nurturing human resources for future clinical trials and clinical research**
   - Conduct workshops on the formulation of training plans and the development of teaching materials and teaching methods for institutions that produce many human resources for clinical trials and educational institutions that offer related programs

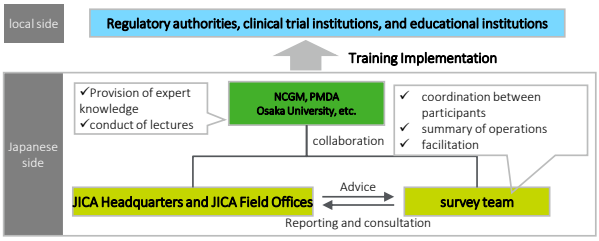
Purpose

1. In order to meet the increasing demand for clinical trials, the implementation system of clinical trial facilities and human resources will contribute to strengthening the capacity of existing implementation institutions.
2. Contribute to technical improvements in clinical trials for current engineers
3. Contribute to the development of human resources for clinical trials and research in the future

Summary

Number of countries covered	▪ Offline: 2 Assuming -3 countries ▪ Online: Joint implementation for all target countries
applicable implementing agency	▪ regulatory authority ▪ Clinical trials and research organizations (Universities, laboratories, hospitals) ▪ an educational institution that offers programs for clinical trials

Implementation method



*Assumed to be co-organized with the NCGM and PMDA in Japan

Activities

[Points of Attention]
- Themes and training participants should be considered together with local partner organizations, and then themes with local needs should be set and appropriate participants selected.
- When training is conducted, the needs and Challenges should be discussed in depth so that future cooperation programs can be considered.

[Proposed contents (one example)]
- seminar format
  - Conduct seminars in collaboration with NCGM, PMDA and local training organizations in Japan (for example, NCTTC and RITM in the Philippines)
  - Conduct panel discussions on the clinical trial-related policies and legal systems of the target countries and the Challenges facing each country in line with the movement for regulatory harmonization in the ASEAN region
- individual training
  - Provide training for the introduction of the clinical research supervisor system and the administrator system (* Mentioned in interviews with target countries)
  - (Increase clinical trial sites and look to future expansion of national capacity) Conduct training including needs assessment for multiple clinical trial sites such as local urban hospitals

Figure 3-7 Overview of pilot activity plan ((5) training)

(3) Evaluation axis in developing pilot activity proposal (affinity with the challenges, feasibility, involvement of relevant institutions, prospects)

From the five types of pilot activity proposal (matching, networking, equipment support, seminars/training, and local PoC of Japanese technologies), the activities were subdivided, and after evaluating the feasibility of each activity, the candidate activities were narrowed down to those to be implemented. In evaluating the feasibility, four evaluation keys were established as shown in the table below ((1) challenges and needs, (2) feasibility, (3) involvement of relevant institutions, and (4) prospects), and the feasibility of each activity component was evaluated according to the evaluation axis. As a result of the evaluation, six activity components were selected which are framed in red in the table below.

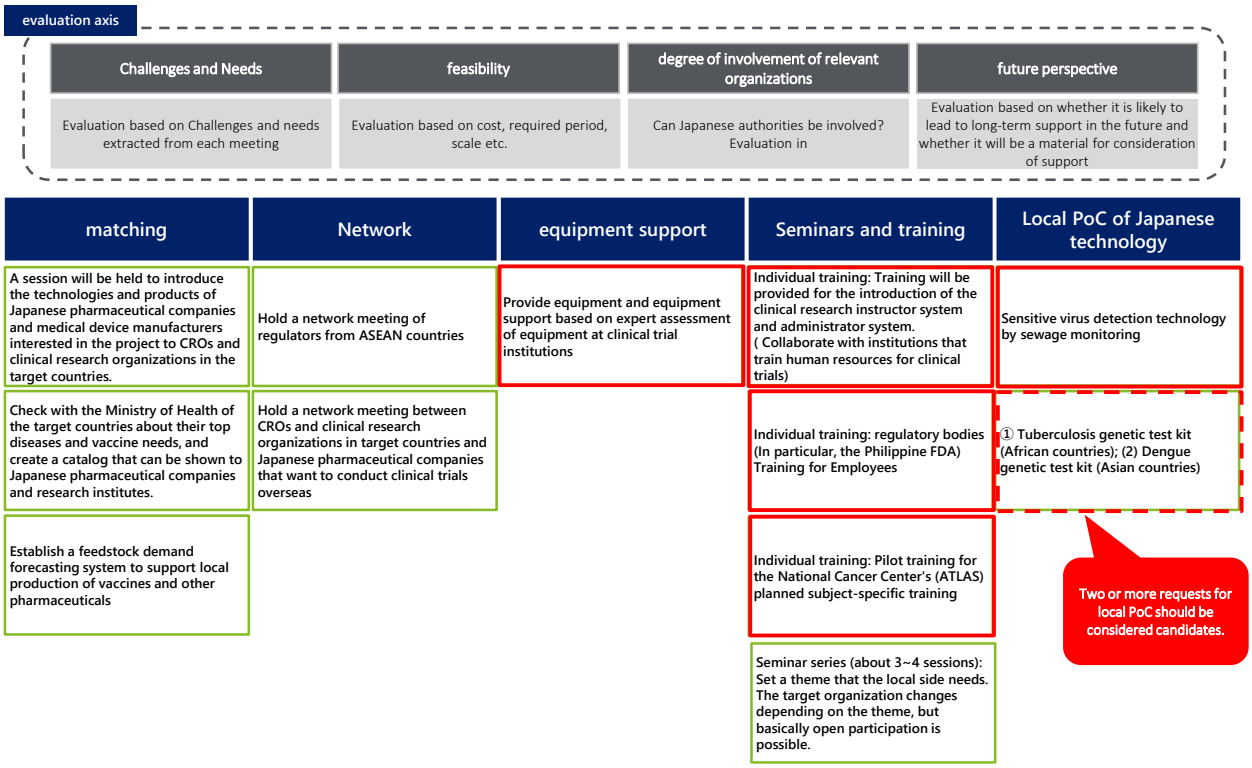


Figure 3-8 Narrowing down of the pilot activities

(4) Reason for selection

The table below shous the evaluation of the six pilot activities selected as candidates for implementation in the four-evaluation axis.

Activities		Challenges and Needs	feasibility	Degree of involvement of relevant organizations	future perspective
		Evaluation based on Challenges and needs extracted from each meeting	Evaluation based on cost, required period, scale etc.	Can Japanese authorities be involved? Evaluation in	Evaluation based on whether it is likely to lead to long-term support in the future and whether it will be a material for consideration of support
Equipment support	Provide equipment and equipment support based on expert assessment of equipment at clinical trial institutions	There are many needs for equipment support for local clinical institutions and phase I clinical trial facilities.	The budget has been secured. Support is fully possible by narrowing down the target of support.	It is necessary to confirm from which institution the clinical expert can be trained.	Is it not effective to provide equipment support to organizations that are candidates for long-term support?
Seminars and training	Individual training: Training will be provided for the introduction of the clinical research instructor system and administrator system. (Collaborate with institutions that train human resources for clinical trials)	There is a need to develop leaders for clinical research management from multiple sources, and to develop trial data and protocol managers.	Introductory training for existing instructors and managers in Japan, including system design and curriculum structure, is available.	It is necessary to confirm whether it is possible to cooperate with research managers and related organizations that provide training for instructors.	It may be developed into a technical cooperation project.
	Individual training: regulatory bodies (In particular, the Philippine FDA) Training for Employees	In particular, there is a strong request from the Philippine FDA.	It is feasible in terms of cost, duration, and scale.	It is necessary to confirm whether cooperation can be obtained from the Asian Training Center of PMDA.	It may be developed into a technical cooperation project.
	Individual training: Pilot training for the National Cancer Center's (ATLAS) planned subject-specific training	It is necessary to meet the common needs of infectious diseases and NCDs.	It is possible to build on the PoC already implemented in Indonesia and expand it laterally.	The National Cancer Center expressed its intention to organically connect and collaborate with JICA.	We are already in the stage of considering training for each subject for FY 24, and from there it is possible to develop it into a technical cooperation project.
Local PoC of Japanese technology	Sensitive virus detection technology by sewage monitoring	Interests expressed by the Philippines, India, etc.	It is possible to build on the PoC already implemented in Indonesia and expand it laterally.	Cooperation with Japanese pharmaceutical companies is quite possible.	An operational protocol for sewage epidemiological studies has been developed and could be deployed in future projects through proposals to Indonesian central and provincial officials.
	① Tuberculosis genetic test kit (African countries); (2) Dengue genetic test kit (Asian countries)	Only one organization in the Philippines expressed interest.	It has already been certified in Asian countries and can be promoted mainly by Japanese medical device manufacturers.	You need to see if you can get help from a company that provides testing kits.	There is a possibility that PoC can be used as a springboard for product dissemination, but it may be difficult to develop it as an ODA project because it targets products of one company.

Figure 3-9 Evaluation of the pilot activities

3.1.2 Results of developing potential cooperation activities

Based on the results of online interviews and field survey, the six pilot activities that were narrowed down as candidates for implementation were rearranged and consolidated into four pilot activities as shown in the figure below.

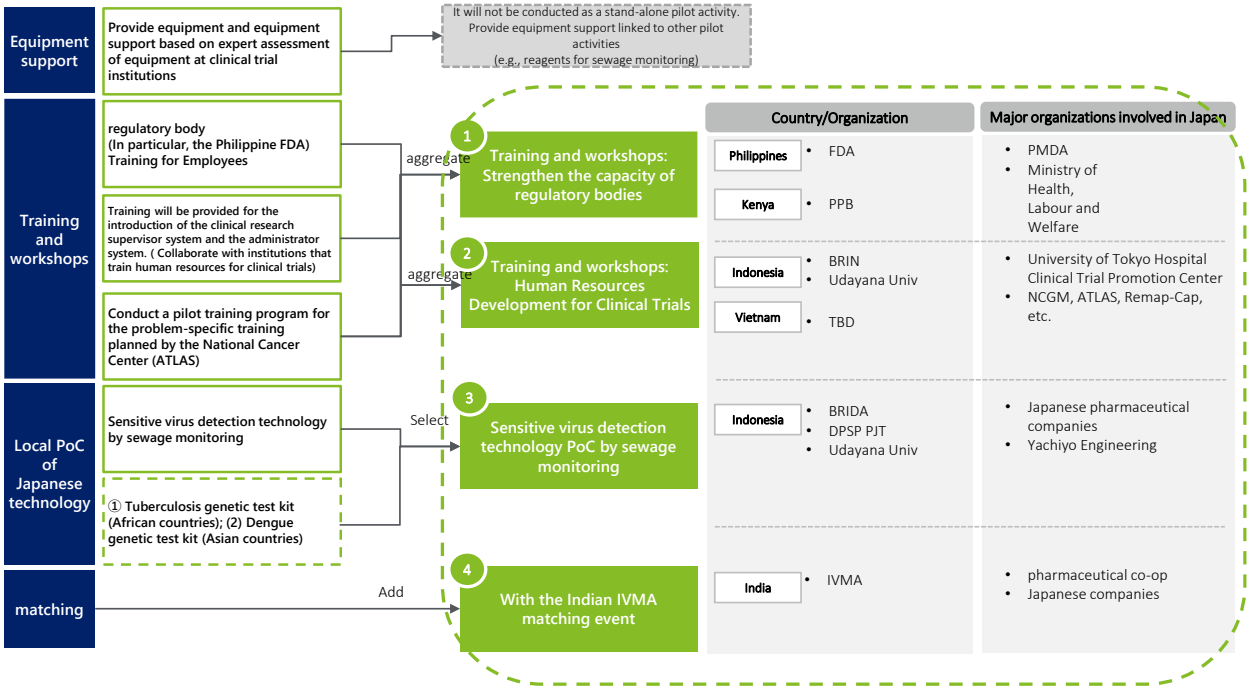


Figure 3-10 4 pilot activities

① Training and Workshop "Strengthening the Capacity of Regulatory Bodies"

The Philippines FDA and and Kenya PPB were selected as the target candidates since they showed strong interest in participating in the pilot activities during the interview and specifically mentioned what they would like to learn from Japan and to collaborate (or obtain cooperation) with Japan. Another reason for the selection was that they are still at WHO Maturity Level 1, and there is an urgent need to strengthen their capacity considering the experience of the delayed supply of vaccines and medicines due to COVID-19.

② Training and Workshop "Human Resources Development for Clinical Trials"

Udayana University Hospital in Indonesia and Ho Chi Minh Medical and Pharmaceutical Hospital in Vietnam, both have needs to strengthen their clinical trial implementation systems, were selected as candidates for the project because the same reasons with the one described in (1) above and specific proposals were shared. Furthermore, in Indonesia, there are national expectations to strengthen the clinical trial implementation system as an "Academic Hospital", and education and training to comply with international research standards, such as Good Clinical Practice (GCP) training for hospital personnel, are focused on.

The invitation to Japan for the "human resources development for clinical trials," the first pilot activity, collaborated with the symposium conducted by NCGM and PMDA.Therefore, stakeholders from University of the Philippines, the University of Indonesia, Bio Farma, and Sirirato Hospital who attend the symposium joined the pilot activity in addition to Udayana University Hospital in Indonesia and Ho Chi Minh Medical and Pharmaceutical Hospital in Vietnam.

③ Sensitive Detection Technology PoC by Wastewater Surveillance

In collaboration with a PoC by Yachiyo Engineering for sensitive detection technology by wastewater surveillance in Indonesia, it was decided to conduct the verification of the effectiveness

of a new technology to detect COVID-19 in wastewater with sensitive detection technology of pharmaceutical company A.

④ Matching Between Indian and Japanese Companies

Based on the expectations expressed by Indian private companies, public institutions, and industry associations for the creation of opportunities for matching Indian and Japanese companies, it was decided to conduct support for matching the needs and challenges of Indian companies with solutions and products that can be provided by Japanese companies, and for bringing together interested companies. Matching support with IVMA （Indian Vaccine Manufacturers Association） was not listed as a candidate for pilot activities at the time of narrowing down proposals, however, it was added since strong expectations for collaboration on an equal footing and in a mutually win-win manner was raised. In particular, a strong desire for matching with Jaoanese companies and research institutions from IVMA member companies was raised.

3.2 Pilot activity results 1

3.2.1 Japan visit

Based on the results of the developing potential cooperation activities, a total of 12 participants from five countries (Philippines, Thailand, Kenya, Indonesia, and Vietnam) were invited to Japan for three days from July 19 to 21, 2023, for the pilot activity. At the stage of developing the pilot acticities, it was considered to conduct the pilot activities separately for strengthning the capacity of regulatory bodides and human resource development for clinical trials. However, it was decided to jointly conduct the workshops in order to enhance the effectiveness of Japan visit since the institutions to visit and the content of workshops during the Japan visit were effective for both participants from regulatory bodeis and clinical trial institutions, and it would be a great opportunity to discuss challenges all together from both categories.

12 participants who joind Japan visit were shown in the table below, and a total of 3 were invited from Kenya and the Philippines to strengthen the capacity of regulatory bodies, and 9 were invited from the Philppines, Thailand, Indonesia, and Vietnam to develop human resources for clinical trials.

In order to have better understanding regarding the regulatory challenges faced by clinical research providers, good practices of clinical trials conducted in various countries, and possible solutions to the challenges, the pilot activity collabolated with the 2nd ARISE-PMDA Joint Symposium for Asia Clinical Trials (hereinafter referred to as "symposium")[142] and included the Follow up session for the symposium into the program. Participants 8 through 12 in the list below are member of ARISE or from clnical research institutions affiliated with ARISE and were invited to Japan visit with the aim of continuing collaboration with related institutions in Japan after their return to their countries.

[142] The symposium, hosted by NCGM and PMDA, provides an opportunity to understand regulatory issues in Asia and discuss potential collaboration between industry, government, and academia on First Patient In and accelerated approvals.

Table 3-2 Participants of Japan visit

#	Country	Organization	Department	Category
1	Indonesia	Udayana University Hospital	Microbiology, Faculty of Medicine	CT
2	Indonesia	Udayana University Hospital	Faculty of Medicine	CT
3	Vietnam	University of Pharmacy and Medicine, Ho Chi Minh City	Faculty of Public Health	CT
4	Vietnam	University of Pharmacy and Medicine, Ho Chi Minh City	Faculty of Public Health	CT
5	Kenya	Pharmacy and Poisons Board	Product Safety, Clinical Trials Division	RA
6	Philippines	Food and Drug Administration	Clinical Research Section, Product Research and Standards Development Division, Center for Drug Regulation and Research	RA
7	Philippines	Food and Drug Administration	Regional Field Office	RA
8	Philippines	University of the Philippines, Manilla	Institute of Molecular Biology and Biotechnology, National Institutes of Health	CT
9	Philippines	University of the Philippines, Manilla	Institute of Clinical Epidemiology, National Institutes of Health	CT
10	Indonesia	BioPharma	Surveillance and Clinical Research	CT
11	Indonesia	University of Indonesia	Department of Pharmacology, Faculty of Medicine	CT
12	Thailand	Siriraj Institute of Clinical Research	-	CT

The themes for each program during the Japan visit were as shown in the figure below with the aim of exploring project measures to address challenges that each participants' institutions have in the areas of human resource development and capacity building for regulatory agencies in clinical trials. The three-day program was designed to introduce examples of Japanese initiatives in line with the major needs of the participants' institutions, organize and narrow down challenges and needs, discuss specific future action plans that each institution should address, and identify future support by Japan.

	① Human Resources Development for Clinical Trials	② Strengthen the capacity of regulatory bodies
Theme	Explore solutions to help the challenge of shortage of clinical trial workers and lack of training opportunities in hospitals and research institutions	Exploring changes in regulations in preparation for the pandemic, future directions, and business strategies that contribute to strengthening the capacity of regulatory staff with a view to clinical trial quality control and acceleration
Target	Udayana University Hospital (Indonesia)/ Ho Chi Minh University of Medicine and Pharmacy (Vietnam)/ University of the Philippines (Philippines)/ BioPharma (Indonesia)/ University of Indonesia (Indonesia)/ SiCRES (Thailand)	PFDA (Philippines)/ PPB (Kenya)

Date	Program	Target	Summary	Purpose
Day1 7/19	training briefing	①＋②	Explanation of the contents and purpose of this training, and greetings from relevant stakeholders	Understand the overall schedule and purpose of this training
	Clinical Research Promotion Center at University of Tokyo Hospital	①＋②	Explanation of the role, management system, and human resource development of the Clinical Research Center	Learn about the management structure and human resource development of clinical research centers in Japan, leading to the enhancement of individual capabilities
	REMAP-CAP (Nerima Hikarigaoka Hospital)	①＋②	Introduction of new clinical trial methods and initiatives, flow of trial implementation, and stakeholders	After learning the methods and approaches of clinical trials, we will review our own efforts and seek solutions to problems.
	National Cancer Center	①＋②	Expectations for each partner country and explanation of ATLAS	After learning about ATLAS, they will become aware of how their country can participate and deepen their understanding of future cooperation with Japan.
Day2 7/20	Workshop 1	①＋②	Based on the interviews we have conducted so far, we have organized the issues and needs of each country and narrowed down the priority items.	Narrowing down issues and needs in preparation for the second pilot, while also learning about how to respond to challenges that arise during the pandemic
	NCGM/PMDA Symposium	①＋②	Discuss ways to collaborate to create a conducive environment for medical research and development through regulatory harmonization, acceleration of first patient in, and the use of new tools in the conduct of clinical research	Understand the regulatory issues faced by researchers, good practice examples of clinical trials conducted in different countries, and possible solutions to problems
Day3 7/21	PMDA	②	PMDA ' s Existing Efforts to Strengthen Regulatory Capacity (International Activities and Human Resource Development) and Introduction to the Japanese Clinical Trial Regulatory Framework and Recent Regulatory Changes	Concretely consider the second pilot activity for regulatory authorities and the long-term support measures provided by JICA
	Follow up session	①	Discuss future cooperation with Japanese organizations and project proposals	Provide prior input in considering specific future projects and collaboration plans at the country-specific WS
	Workshop 2	①＋②	Identify possible future collaborations with JICA, NCGM, PMDA, and other organizations, as well as future project and collaboration plans	Deepen awareness of feasible projects and collaboration plans that will lead to future collaboration and business formation
	Wrap-up	①＋②	Summary and review of the content discussed in the WS	Lead to future business formation and second and subsequent pilot activities

Figure 3-11 Details of Japan visit

Participants' interests, objectives, and intentions of collaboration was collected in advance of the Japan visit and the responses are as shown in the following table. Many of the institutions mentioned the need to strengthen their capacity in terms of human resources and clinical trial implementation, and participants visited Japan with the aim of reflecting the Japanese model in their own institutions and improving on the challenges they face.

Table 3-3 Interests and objectives of participants (1/2)

	Country	Organization	Interests or Objectives	Purpose of participation and intention to cooperate
clinical research institute	Indonesia	Udayana University Hospital	• Good Clinical Practice (GCP) Training • Building networks with government agencies, medical facilities, industry associations, pharmaceutical companies and medical device manufacturers • Experimental Medicine • Strengthening clinical trial capacity	Research has not yet become a top priority for doctors at Udayana University Hospital, and there is a shortage of personnel to operate the international standard, The Clinical Research Unit and Biostatistic (CRUB), which can provide high-quality, integrated research services. Therefore, through this training, we aim to raise awareness of research, acquire knowledge and know-how, and improve the quality of clinical trial research services.
	Vietnam	University of Pharmacy and Medicine, Ho Chi Minh City	• How to structure and create clinical trial research protocols • Japanese government and corporate priorities in clinical research • Views on cooperation with Vietnam in clinical trials • Building a unit capable of conducting Phase 1 clinical trial research • Japanese medical school or hospital operating model	The majority of clinical trial sites in Vietnam lack specialized clinical trial institutions and centers, and there are no clinical research centers equipped with site management functions or centers capable of conducting phase 1 trials. Therefore, we aim to develop centers of excellence for clinical research by learning the operational policies and models of Japanese universities and hospitals.
regulatory body	Philippines	Food and Drug Administration	• Evaluation of clinical protocol • Review of submissions for clinical trial approval • Review of newly designed clinical trial protocols • biosimilar review • on-site monitoring • Review of Submissions for Marketing Authorization	Enhancing the capacity of the FDA and training evaluators and examiners in clinical trials has been identified as an issue, and the goal is to achieve Maturity Level 3. Therefore, in this training, we will learn from Japanese regulatory authorities such as PMDA about the framework of clinical trial regulation and marketing regulation in Japan and the efforts to strengthen the capacity of FDA.
	Kenya	Pharmacy and Poisons Board	• Acceptance of clinical trial applications and review of applications • Timeline for review and approval of clinical trials • Implementation of GCP inspection • Regulation of Ethics Committees in Japan • Pharmaceutical costs paid for clinical trial review and monitoring • Expiration extensions and labeling of products under investigation	PPB has limited personnel and needs to increase capacity for protocol review and GCP review. Therefore, through workshops and individual visits, we will learn about Japan's existing efforts to strengthen capacity from the regulatory authorities, lead to cooperation and partnership with Japanese regulatory bodies in the future from the viewpoint of regulatory harmonization, and aim to achieve

Table 3-4 Interests and objectives of participants (2/2)

	Country	Organization	Interests and Objectives	Purpose of participation and intention to cooperate
clinical research institute	Philippines	University of the Philippines, Manilla	■ How to establish a rigorous clinical trial facility operated by an academic research institution ■ Standards required by regulatory authorities to operate regulated MRCTs (Minimum equipment and facilities, personnel requirements, quality control and assurance, SOPs) ■ Operating model and design of clinical trial centers capable of conducting preclinical studies, phase 1 to phase 4 clinical trials ■ New clinical trial design ■ Priority of clinical trials and medical devices ■ Strategies and steps to speed up initial patient enrollment	We look forward to learning about Japan's best practices, requirements, and strategies for establishing rigorous clinical trial sites that meet stringent regulatory requirements and conduct MRCT, strengthening our existing collaboration with NCGM Japan, and further expanding our network of academic and regulatory partners in Japan and Southeast Asia. We hope to strengthen the network of the Philippine National Clinical Trials Honyaku Center by using the knowledge learned in this JICA project to create a template on how to establish a clinical trial facility and to reproduce it as a model in multiple facilities throughout the Philippines.
	Indonesia	University of Indonesia	■ Capacity Building for Multiregional Clinical Trials ■ Potential for further collaboration in clinical research ■ Exchange of perspectives and ideas on the conduct and opportunities for post-pandemic clinical research	The University of Indonesia is actively engaged in a number of clinical studies, both at home and abroad. There are several barriers to conducting multilateral research, including legal and ethical disparities between countries, differences in health systems, and differences in policies. It therefore hopes that, as a representative of its institutions, it will be able to enhance its clinical research networking with other participants from industry, academia and regulatory agencies. It would like to explore opportunities for sharing knowledge and resources in the conduct of clinical research, strengthening human resource capacity and further collaboration in clinical research.
	Indonesia	BioFarma	■ Cooperation and friendship among countries, hospitals, government agencies, the medical industry and support agencies ■ Strengthening clinical trial capacity ■ Sharing clinical trial experience	Understand the harmonization of clinical trial guidelines in Asian countries to see if the same consensus has been reached, and reduce the time to conduct clinical trials and to market products. We would like to learn the operational procedures of clinical research in Japan and aim to develop a center of excellence for clinical research.
	Thailand	Mahidol University	■ FIH trial ■ Startup Timeline ■ Product Development (Pharmaceuticals, Chinese medicines, and medical devices)	It hopes to strengthen clinical research in Sirilat through network partners and to share experiences in the development of clinical research services and the potential of human resources in order to make clinical trial facilities multicenter.

The program included individual visits to various Japaense institutions related to clinical trials such as The University of Tokyo Hospital Clinical Research Promotion Center, REMAP-CAP (Nerima Hikarigaoka Hospital, a member of REMAP-CAP), NCC, and PMDA. The program also included attending

symposium and workshops to prioritize challenges and generate ideas for action plans that will contribute to resolving challenges in each country. The ojectives, contents, and results of each program are summarized below.

(1) The University of Tokyo Hospital Clinical Research Promotion Center

Visiting the University of Tokyo Hospital Clinical Research Promotion Center, which is a core hospital for clinical resaech and has its own clinical research supervisor system, was included in the program based on the result of interview. Stakeholders in each country mentioned the need to strengthen human resource for clincal trials and clinical trial capacity to resolve the shortage of human resources and supervisors/managers to ensure high quality clinical trials.

The lecture was given on the initiatives at the University of Tokyo Hospital Clinical Research Promotion Center (hereafter referred to as "center"), with the aim of learning about the role of the clinical research promotion center, their management system, human resource development system, and capacity building. After the lecture, the participants toured the center's clinical trial facilities and had explanation of the clinical trial equipment (e.g., Phase 1 unit) and test management.

Many participants commented that the lecture and facility tour were very beneficial. In particular, participants from Indonesia, which is on the process of establishing a Clinical Research Unit in their country, commented tha t the lecture provided them with ideas to promote the establishment of such a unit while oher participants commented that this visit was helpful to understand the overall picture of the clinical trial implementation system in Japan and the efforts to improve the quality of clinical trials.

Many people commented that the visit to the University of Tokyo was very useful. Specifically, the following
[Example comments]
- inspired the idea of establishing a clinical research center in Indonesia
- It also helped me with the research I'm trying to do in my own organization.
- A comprehensive overview of the operation of academic research and clinical core hospitals is useful and an impressive model to benchmark
- The overall image of the clinical trial support system was grasped.
- We were able to obtain information on initiating clinical trial development.

Lessons Learned from visiting the University of Tokyo

They learned about the mechanism of the entire clinical training center of the University of Tokyo (Human resources, hospitals, organizations, functions, etc.).

The details of the answers given are as follows
- business scale
- human resources
- Helping independent investigators improve the quality of clinical trials
- Training system for researchers and clinical trial investigators by taking necessary credits before engaging in clinical trials
- Functions of the clinical research center departments
- Methods for monitoring and evaluating clinical studies
- Increase in hospital trials
- Method for setting up clinical trial ward
- Organization and functions of the Clinical Research Promotion Center

Figure 3-12 Questionnaire result of the University of Tokyo visit

(2) REMAP-CAP (Nerima Hikarigaoka Hospital, a member of REMAP-CAP)

The lecture on initiatives at REMAP-CAP (A Randomized, Embedded, Multifactorial, Adoptive Platform trial for Community-Acquired Pneumonia)[143] and facility tour were given by the Nerima Hikarigaoka Hospital which is one of the members of REMAP-CAP.

REMAP-CAP is a large-scale international platform that collaborates with medical professionals around the world to find the best treatment for severe community-acquired pneumonia as early as possible. REMAP-CAP promotes Randomized Controlled Trial (RCT) which is a method of conducting trials in which modifications are made as needed based on data collected after the start of the trial, in order to take patient safety into consideration, to obtain results quickly, and to reflect the results back to the field.

[143] It is operated by a diverse group of experts, including medical professionals involved in the world's major emergency medical services, as well as medical professionals capable of responding to pandemic and infectious disease outbreaks, viral and immunology researchers, and statisticians. It is a large international platform with more than 1,100 registered participants at 218 sites in North America, Europe, Oceania, and other regions, and is designed to operate global surveillance in normal times to detect and respond to abnormalities in normal times at an early stage.

The overview and role of REMAP-CAP, new clinical trial methods and approaches, and the flow of conducting trials under REMAP-CAP were explained in the lecture.

Many participants found their approach innovative and mentioned the advantages of the multinational and multicenter international collaboration, such as the ability to obtain prompt and comprehensive research data and to conduct effective clinical trials even under special circumstances, such as pandemics.

Many participants have the impression that the initiative itself is new and innovative, and there are positive opinions that it will be an opportunity for international joint research.

Lessons Learned from REMAP-CAP Visits

There were positive comments about the platform and features, as well as the recognition of issues in collaboration and communication.

Other specific comments are as follows:

- Multinational, multicenter collaborations provide rapid, comprehensive research data and are cost-effective
- Effective clinical trials can be conducted even in limited facilities or special settings such as pandemics

Figure 3-13 Questionnaire result of REMAP-CAP visit

(3) National Cancer Center Research Institute (NCC)

The participants visited NCC, which manages the ATLAS Project (Asian Trial Network for Adverse Aspects of Cancer Surgery)[144], which provides support for education and training, develops infrastructure for conducting clinical trials, and conducts international joint research in Asia.

The lecture provided was on overview of the ATLAS project, the partnerships and initiatives of the project, and other important elements for multi-country collaboration, to deepen understanding of how their institutions can collaborate internationally in the future, using the ATLAS project's networking initiatives with other Asian countries as a model. The importance of participation in their own country's network and participation in the ATLAS project was also explained. In addition, in order to consider the possibility of participation in the network in his country and future collaboration with Japan, the initiatives in Thailand and the construction of a network of clinical trial sites overseas was explained by the Director of ATLAS Thailand.

After the explanation of the NCC's efforts in the ATLAS project, comments were made indicating an interest in participating in the ATLAS network, as it would enable enhanced cooperation with the clinical network in Asia.

[144] The official name of ATRAS is the "Asia Clinical Trials Network for Cnacers Project." The mission of ATRAS is to support education and research on the soft side, develop the infrastructure for conducting clinical trials on the hard side, and conduct multiple international collaborative studies in parallel, with the aim of building a system to conduct at least five international collaborative studies at any given time in the Asian region using the framework of the Asia Clinical Trials Network and they are calling for further stakeholder participation.

While some respondents commented they learned from cancer research, others said some aspects of ATLAS activities were difficult to understand.

- I learned from NCC's research in cancer treatment.
- I learned how to conduct international joint research.
- I understood some of the activities of ATLAS, but some of them were difficult.
- Clinical trials in oncology are complex but necessary

Lessons Learned from National Cancer Center Visits

There have been a number of comments about the ATLAS network and a number of comments about the possibility of joining ATLAS.

- UMC Hospital has the potential and confidence to join the network
- interested in strengthening cooperation with the Asian Clinical Network

Other

- International collaboration can improve data collection on disease incidence and increase patient participation
- NCCH is the best hospital for cancer patients
- It was good that they talked about MASTER KEY ASIA and how to participate in clinical trials.

Figure 3-14 Questionnaire result of NCC visit

(4) PMDA

Among the lectures given by PMDA as part of the JICA training and dialogue program "Pharmaceutical Administration for Appropriate Supply, Quality Control and Use of Medicines," the participants participated in a lecture on "Practice of Drug Review in Japan" to deepen their understanding of the mechanism of drug approval review and actual examples of pharmaceutical administration in Japan. During the Q&A session, participants asked questions about the necessity of PMDA approval, the difference in timing of inspections between PMDA and the participants' countries, and the possibility of expediting the review process by having overseas data. Three participants from the Regulatory authorities participated in this program.

Participants commented that they gained insight into the regulatory system and the implementation of guidance to other regulatory authorities, new drug approval methods and timelines, comparisons with their own countries, the importance of expedited approval, and the importance of collaboration with clinical research.

Comments on Lessons Learned about the clinical trial approval process were received, with many commenting that it was beneficial overall.

- I learned that PMDA's regulatory system complies with international standards and provides guidance to other regulatory bodies.
- I was able to learn about the new drug approval methods and timelines of PMDA.

Others commented that it was good that the staff of the PMDA were well prepared for their job descriptions and for explaining the performance of the organization.

Lessons Learned from PMDA Visits

Many people commented that they learned about the specific process of the PMDA clinical trial.
[Excerpt from comments]

- We were able to learn about the clinical trial process at PMDA and the differences in the process from our own country.
- We learned that patient safety is a principle of regulatory oversight.
- learned the importance of rapid approval for clinical trials and other regulatory matters
- We learned the importance of collaboration in clinical research including regulatory agencies.

Figure 3-15 Questionnaire result of PMDA visit

(5) Symposium

Participants attended in "The 2nd ARISE-PMDA Joint symposium for Asian Clinical Trials" jointly organized by NCGM and PMDA to have a better understanding of the regulatory challenges faced by researchers, good practices and possible solutions for clinical trials conducted in various countries. The symposium featured keynote speeches from various organizations and institutions, presentations on challenges and experiences by speakers from each country, and panel discussions to learn about regulatory issues and examples of Good Clinical Practice (GCP) in clinical trial implementation in each country and possible solutions to these issues.

Overview

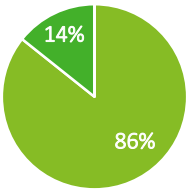
Date and Time	July 20th, 2023 (Thu) 13:00-18:00
Background	■ The international community has focused on the continuing threat of the spread of infectious diseases as a result of globalization, and the COVID-19 pandemic has made it clear that achieving a robust system of medical product R&D and health security is imperative, in which international cooperation has a major role to play. ■ Asian countries will discuss the cooperation needed to harmonize regulations, accelerate First Patient In (FPI), and create a favorable environment for medical research and development through the use of new tools in the conduct of clinical research.
Objectives	■ Update information on the latest regulatory strategies in medical research and developmentUnderstand the regulatory issues facing researchers, good practices of clinical trials conducted in different countries, and possible solutions to problems ■ Present the latest tools/approaches to accelerate clinical trials and regulatory approvals ■ Discuss addressing barriers, accelerating FPI and approvals in Asia, and industry-academia-government (regulatory) collaboration

Program

KEYNOTES: Latest regulatory strategy in medical research and development
1. Developing the Asian clinical research collaboration through the ARISE network activities
2. Cooperation for patients in Asia
3. Regulatory strategies to achieve the 100 days mission
Session 1: Regulatory issues surrounding clinical trial in Asia
1. Navigating Clinical Trials in Asia: A New Landscape and Horizon
2. Experiences of WHO Solidarity Trial in the Philippines
3. Clinical Trial for COVID-19 vaccine development
Session 2: First patient in Asian clinical trials
1. Barriers/challenges to FPI in Southeast Asian countries
2. Efficient process for IND review in Japan
3. Experiences of SICRES to accelerate FPI in Thailand
4. Accelerating Clinical Trial: Bio Farma Experience in COVID-19 Vaccine Development
Session 3: Utilization of new tools & approaches in clinical trials
1. Guidance on Decentralized Clinical Trials (DCT)
2. Experience of REMAP-CAP Platform Trial
3. Current status and expectation of DCT in Japan ~ from the industry stand point~
Panel Discussion: How academia, regulators and industry can work together to address barriers to accelerate FPI and approval in Asia

Figure 3-16 Overview and programs of symposium

The symposium was well-received by many stakeholders and they commented that the symposium provided them with knowledge and clinical trials that can be used in their own countries.



Discussions with participants in each country allowed for more specific brainstorming sessions, which led to deeper understanding.
- It was fascinating to think about the next action for the participants
- productive exchange of ideas on priorities and issues
- I was able to learn about the action plan for what clinical trials to do in my country.

Lessons Learned from Symposium

Many commenters commented that they were able to learn about the common/specific problems faced by Asian countries and consider the challenges of joint research in Asia.
[Excerpt from comments]
- Participants from each country were able to learn about their challenges and barriers (Epidemiological and religious reasons, links between academics, industry and regulatory authorities)
- We were able to think about the challenges of clinical trials, what we need to do about the challenges, and what action plans we need to make towards that.
- We learned that we need to have a deeper understanding of clinical trials and collaboration between Japan and Asian countries.
- There is a need for greater understanding of JICA's activities
- Some commenters said they learned of available Japanese funding agencies.

Figure 3-17 Questionnaire result of symposium

(6) Follow up session

A follow-up session to the symposium was conducted with nine participants from the "human resource development for clinical trials" side (other three participants from the "strengthning the capacity of regulatory bodides" joined PMDA which is the program conducted at the same time). Following the lectures and panel discussions at the symposium on the previous day, findings and ideas were shared among the participants, and future collaboration and business proposals with Japan were discussed based on the two themes of "Regulatory Challenges in Clinical Trials from the Researchers' Perspective" and "First Patient In." Participants were divided into group of three include participants from multiple countries and discussed current issues and their solutions.

In the first theme, "Regulatory Challenges in Clinical Trials from the Researcher's Perspective," the participants discussed regulatory challenges in clinical trials in general from the researcher's perspective. The main challenges raised were the length of timelines for review, differences in systems and responses in each country, and lack of cooperation with related organizations.

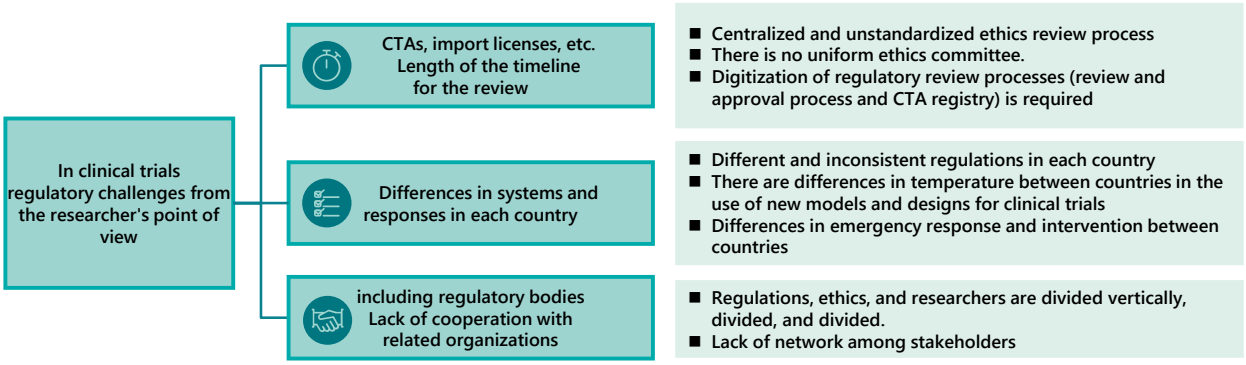


Figure 3-18 Discussion result of Theme 1

In the second theme, "First Patient In," the same kind of challenges as in clinical trials in general were raised, and establishing organizations from collaboration, and providing training for clinical trial conductors to have in-depth discussions from the initial stage and strengthening the capacity of regualtory agencies were mentioned as the solution.

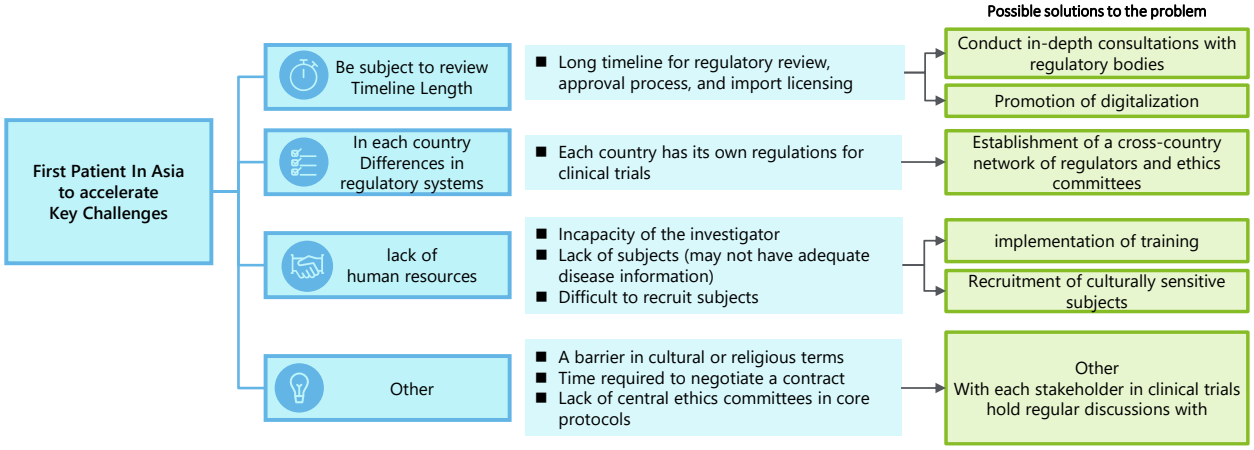


Figure 3-19 Discussion result of Theme 2 (1/2)

In the discussion on how academia, capacity building of regulatory authorities, private companies, and industry associations can work together to promote First Patient In, many comments were made about the importance of having a forum like program during the Japan visit which stakeholders from different institutions can come together to discuss the challenges across boundaries.

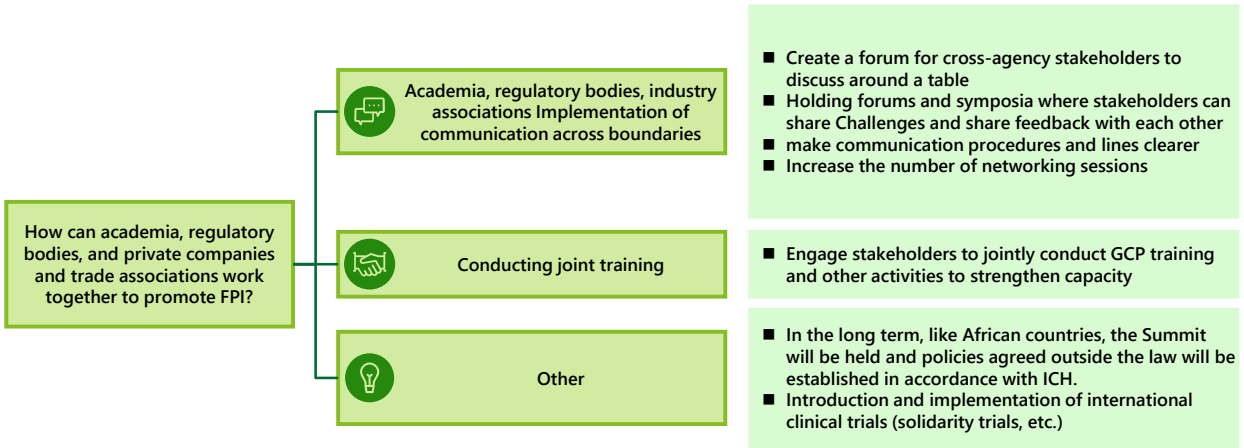


Figure 3-20 Discussion result of Theme 2 (2/2)

Some participants commented that the follow-up was a good brainstorming opportunity to consider next actions, since it was conducted based on the actual symposium panel discussions and lectures. Some participants also felt that the fact that the follow-up was conducted with multiple countries, rather than on a country-by-country basis, made it possible to exchange information on ideas and actual initiatives in neighboring countries, which led to more effective discussions.

Discussions with participants in each country allowed for more specific brainstorming sessions, which led to deeper understanding.
- It was fascinating to think about the next action for the participants
- productive exchange of ideas on priorities and Challenges
- I was able to learn about the action plan for what clinical trials to do in my country.

Lessons Learned from Symposium

Many commenters commented that they were able to learn about the common/specific problems faced by Asian countries and consider the challenges of joint research in Asia.
[Excerpt from comments]
- Participants from each country were able to learn about their challenges and barriers (Epidemiological and religious reasons, links between academics, industry and regulatory authorities)
- We were able to think about the challenges of clinical trials, what we need to do about the challenges, and what action plans we need to make towards that.
- We learned that we need to have a deeper understanding of clinical trials and collaboration between Japan and Asian countries.
- There is a need for greater understanding of JICA's activities
- Some commenters said they learned of available Japanese funding agencies.

Figure 3-21 Questionnaire result of Symposium

(7) Workshop and wrap-up session

In order to narrow down the challenges and needs identified in the literature research and interview survey to those of high priority, and to generate ideas for feasible project and collaboration proposals that will lead to future cooperation and project formation with relevant Japanese institutions that address those challenges and needs, Workshops 1 and 2 were conducted during the two days of training in the following figure (Day 2 and Day 3). The participants were divided into groups by country and held Workshops 1 and 2 as shown in the figure below. Afterwards, in a wrap-up session, each country gave presentations on the action plans developed during the workshops, received feedback on their action plans from the Japanese stakeholders, and exchanged opinions among the participants.

Workshop 1

Review the listed challenges in each country and Prioritize the challenges

- You will refer to the handout, consisting of Challenges that were brought up in previous interviews with each target country and perform the work below.
  - ✓ Review the Challenges and mutually agree on each of them（modify the list based on the group discussion)
  - ✓ Prioritize the Challenges

— Handout of the List of Challenges —

Workshop 2

Brainstorm Ideas for future collaborations based on the challenges

- Among the Challenges prioritized in Workshop 1, you will select the Challenges categorized as “Top Priority” and “High Priority," and come up with ideas for potential future collaborations.
- Each group will utilize the same worksheet to brainstorm ideas.

Presentations・Wrap-Up

Group Presentations
Feedback Session, Wrap-Up

- You will present the ideas you came up with in Workshop 2. (using the action planning worksheet)
- Presentation Feedback（JICA, PMDA, The University of Tokyo Hospital）

Figure 3-22 Overview of Workshops

i. Workshop 1

Workshop 1 fostered a common understanding by reviewing the challenges and needs that their countries have, referring to the challenges and needs that had been interviewed, and discussed which challenges were particularly important and whether there were any challenges that should be added. Based on the discussions, each issue was prioritized based on "importance" and "feasibility of improvement".

Regarding the results of the discussions, each country presented its priorities and the reasons for those rankings. The most cited priority challenges were strengthening of human resource capability, followed by the need for capacity in terms of equipment, and facilities, and securing the personnel, and the need to improve the review and approval process.

Table 3-5 Summary of challenges in the five target countries (high priority challenges)

	Indonesia	Kenya	Philippines	Thailand	Vietnam
① equipment and facilities, human resource capacity Need to strengthen	The capacity of clinical trial facilities and government and regulatory bodies must be strengthened. MTA required.	It is necessary to strengthen the capacity of facilities and facilities in PPB labs.	Low levels of the FDA's WHO Benchmarking tool. Private institutions lack the capacity to develop vaccines.	N/A	The clinical trial site does not meet international standards. It is necessary to establish a new clinical trial promotion center. Increased capacity for pragmatic clinical trials is needed.
② Need to improve review and approval process	The application process takes time because there is no central ethics committee. There is no uniform review or evaluation process.	N/A	N/A	It takes more than three months to obtain an FDA license. Experts at the Thai FDA did nothing to improve the approval process. Regulatory processes for Phase 1 clinical trials have not been established.	N/A
③ Inadequate government efforts	N/A	Policies and initiatives to promote local production have not been implemented well. Research requires government funding.	Legal protection is lacking. There is a lack of funding for researchers.	N/A	New regulations are needed in the systems of major hospitals conducting clinical trials.
④ Lack of human resources	N/A	There is a shortage of human resources for GMP screening. There is a shortage of investigators.	It is difficult to retain human resources who are familiar with drug development research and vaccine manufacturing, and many of them move to overseas or other professional positions.	N/A	N/A

Table 3-6 Summary of challenges in the five target countries (top priority challenges)

	Indonesia	Kenya	Philippines	Thailand	Vietnam
① human resource capacity strengthening	Lack of training opportunities for clinical trial personnel.	Lack of technology and expertise in vaccine research.	a shortage of specialists and research-oriented physicians.	N/A	Human resource capacity for GMP, GCP and GLP inspections needs to be strengthened.
		Capacity to conduct GCP and GMP inspections needs to be strengthened.	lack of overall knowledge.		Lack of human resources to handle and conduct clinical trials.
		Lack of human resources in regulatory bodies.	There are few skilled people in rural areas.		Lack of technology, including protocol design, data management, and statistical analysis.
			Training of evaluators and inspectors in clinical trials is necessary.		
② Support and support for physicians in the conduct of clinical trials	N/A	N/A	It is necessary to establish a scientific advisory committee.	The implementation and introduction of investigator-initiated clinical trials are necessary to solve serious health problems such as tuberculosis and dengue fever.	Requires access to new and advanced technologies through overseas networks.
			Database construction required.		
			A one-stop shop for investigator-initiated clinical trials is needed.		
③ Review of regulatory and review processes and organizational structures	It is difficult to go through customs clearance.	N/A	Policy revision of product registration certificate is required.	N/A	N/A
	The politics inside the university hospital are complicated.		Harmonization of regulatory and ethical processes is necessary to avoid increasing political complexity within the organization.		
④ Raising awareness and communication with stakeholders	Communication between stakeholders is necessary.	It is necessary to raise awareness among stakeholders.	N/A	N/A	N/A
⑤ Collaboration and Collaboration	N/A	N/A	A joint ASEAN review is required.	N/A	N/A
			Cooperation with the Ministry of Science and Technology is required.		

Comments such as Workshop 1 was a good opportunity to reorganize and prioritize challenges in their own countries, which led to a common awareness of challenges in each country, and a good preparatory work to formulate action plans for high-priority issues in Workshop 2 were raised.

The results of the questionnaire showed that many participants were able to recognize and clarify the Challenges at their institutions, which led to their awareness of the Challenges, and led to the workshop being able to lead to the next steps.

- The current Challenges and the Challenges to be prioritized in terms of feasibility were clarified.
- prioritized the Challenges to be solved
- Very useful in bridging the gap between regulators and clinical trialists on the problems faced in conducting clinical trials not only in their own countries but also in other Asian countries
- The idea of future joint research came up
- what was needed to improve clinical research and what was prioritized

Lessons Learned from Workshop1

In the workshop, as shown on the left, it was mentioned that they were able to recognize the Challenges and the recognition that leads to the next step.
[Excerpt from comments]

- We've identified what needs to be done to improve clinical trials in Thailand.
- Assessed Challenges and led to solutions
- Awareness of local Challenges related to clinical trials and clinical trials and recognition of priority Challenges to be addressed
- The importance of regulation for the development of clinical research was recognized.
- Awareness of problem resolution and potential for improvement

Figure 3-23 Questionnaire result of workshop1

ii. Workshop 2

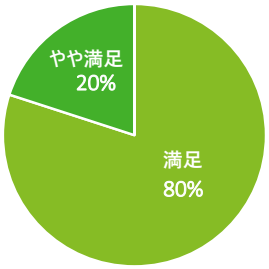
In Workshop 2, the country groups selected two or more challenges of high priority from the prioritization in Workshop 1 and developed action plans that included future project and collaboration proposals to address each challenge. The table below summarizes the results of the Action Plan formulation for each country.

Table 3-7 Overview of action plan for each country

clinical trial site
regulatory body

	Theme	Action Item	covered institution	Timeline (Start)	Partnership	
Thailand (SiCRES)	Development of new tools to accurately and cost-effectively identify people at high risk for tuberculosis	• Development of Thailand's Operation Plan to End Tuberculosis • Plan cohort settings to identify acute Serial Interferon-Gamma Release Array (IGRA) seroconversion.	Siriraj Hospital	Short-term (1 year)	GHIT (financing), private sector (FF), JICA/NCGM experts	priority area for infectious diseases Strengthening research and development
	Enhanced vaccine production capacity for neoplasms	• Technology transfer (production capacity) • human resources development • Infrastructure Development (Equipment)	government pharmaceutical agency (GPO)	Short-term (1 year)	SCARDA (Fundraising), JICA Experts	
Kenya (PPB)	Comprehensive training of CT staff on protocol review and evaluation/GCP inspection	• PMDA Training Review (3 months) • Development of a training programme/package on the study protocol Review Assessment/GCP Inspection in collaboration with PMDA (6 months) • Practical training sessions for CT staff (minimum 1 week)	PPB/CT Department	Short-term (1 year)	PMDA, WHO	PPB Human Resource Development Awareness of clinical trial stakeholders
	stakeholder sensitization	• List of stakeholders around clinical trials • Planning and implementation of sensitization workshops for stakeholders		Short-term (1 year)	JICA, KEMRI, MSH (NGO)	
Vietnam Ho Chi Minh University of Medicine and Pharmacy	Establishment of a clinical trial promotion center including a P1 Unit	• General Principles for Planning and Drafting International Clinical Trials Training • Training on conducting clinical trials (CRC development, data management, safety management, etc.) • site visit to the university hospital	Ho Chi Minh University of Medicine and Pharmacy	Mid-term (3 years)	Clinical Research Promotion Center, Tokyo University Hospital	Establishment of a clinical trial promotion center based at Ho Chi Minh University of Medicine and Pharmacy and transformation into a clinical trial core hospital
	Building a network of clinical trial core hospitals	• Establishment and selection of criteria for clinical trial core hospitals (for tertiary hospitals) • Receive technical assistance from ARISE	Vietnam Ministry of Health/Ministry of Science, Vietnam National Tertiary Hospital	Mid-term (3 years)	JICA, ARISE	
Philippines (FDA, University of the Philippines)	Development of human resources development and regulatory support tools for regulatory agencies	• Competency Development Program for Examiners and Evaluators (Clinical trial application review, GCP, new drug approval) • Development of manuals for regulatory examiners and assessors • Development of an information technology platform to support regulatory activities in clinical trials	FDA/ Center for Drug Regulation (CDRR)	Mid-term (3 years)	PMDA-ATC	FDA Human Resource Development Improve operational efficiency
	Capacity building for clinical trials	• Specialized training for CRC and NTTC core staff • Technical assistance in the development of SOPs and quality assurance mechanisms • Technical support for performance monitoring capabilities and indicators • Scoping support for research capacity and needs assessment at various research institutes/testing sites in the Philippines	University of the Philippines NIH/NCTTC	short-term (1) -1.5	NCGM/ARISE, PMDA, NCC/ATLAS, Tokyo University Hospital, JICA	ARO based on University of the Philippines NIH/NCTTC yesterday strengthening and facility renovation
	Support for renovation of new UP NIH building space allocated by UP-NCTTC	• Financial Assistance in the Design and Renovation of NCTTC Space in the New UP NIH Building • Development and purchase of software for electronic data capture systems for clinical trial data management • Establishment of data archiving and biobanking facilities		mid-term (2-5 years)	JICA, NCGM	
Indonesia (Udayana University Hospital, University of Indonesia, BioFarma)	Establishment of the National Clinical Research Support Center	• Benchmarking of the University of Tokyo Hospital/Invitation of experts • infrastructure development • Organizational structure and program development • stuffing	Udayana University Hospital	mid-term (2-5 years)	JICA, AMED, BPOM, Indonesian Association of Teaching Hospitals	Udayana University Hospital based on clinical research support With the establishment of the center Enhancement of clinical trial capacity
	Human Resources Development for International Clinical Trials	• CT Competency Training Needs Analysis • Training programs (CT design, GCP, GLP, GMP, ethics, site management,		short-term (1 year)		

Comments such as the discussion of actions in Workshop 2, based on the results of organizing the issues and necessary responses in Workshop 1, provided a good opportunity to think about more concrete solutions and their feasibility were made.



There are many positive opinions that we learned a lot by formulating a concrete action plan for the problem.

[Excerpt from comments]
- Prioritization and feasibility of clinical trials in Thailand were confirmed.
- It was an opportunity to think about solutions to Challenges and concerns.
- Satisfied as a forum to present national needs to improve the quality and procellability of clinical trials
- We were able to formulate and discuss specific action plans to address key Challenges

Lessons Learned from Workshop2

There were a number of comments indicating that participants understood the priorities of what should be done in response to their country's challenges, and several participants cited human resources Challenges (e.g., human resource development) as challenges.

[Excerpt from comments]
- Excellent action plan, the need to maintain regional health security, and coordination with Japanese institutions
- Action plan for regulation, action plan for clinical trial implementation, support from JICA
- Prioritize Challenges to facilitate the regulation of clinical trials and new drug applications, communicate with stakeholders on areas of focus, and identify high-risk areas of focus
- How to rank to meet challenges, determine timelines, and address challenges through collaboration
- The top two countries that want to improve and support are manpower and facilities. Regulators and clinical trialists should work together to improve the quality of clinical trials in their countries, WS allowed network expansion
- Most developing countries struggle with human resources in clinical trial regulation. Making clinical trials a global standard requires a large financial investment, and the interaction between researchers and regulators is fundamental to the success of clinical research

Figure 3-24 Questionnaire result of workshop 2

iii. Wrap-up Session

Each Group presented the action plans developed in Workshop 2, and Japanese stakeholders (Mr. Daisuke Tanaka, Director, Asia First Division, International Department, PMDA; Ms. Eiko Ogata, Director, Scientific Committee and Advanced Science Division, RS Management Department; Mr. Tatsuya Maruyama, Deputy Director, University of Tokyo Hospital Clinical Research Promotion Center, Ikuo Takizawa, former Director, Office for the Promotion of Cooperation to Combat New Coronavirus Infections, Human Development Department, JICA), made questions and gave feedback on the action plans of each country, and opinions were exchanged among the participants. The table below shows the main feedback and opinions.

Table 3-8 Key opinions for presentation from each country

Thailand	Strengthening research and development in key areas of infectious diseases	• It is easier for private companies to cooperate because they are more flexible, he said, citing the partnership with Fujifilm. Technical and equipment support could be provided to allow companies to negotiate low-cost access to new vaccines once they have been developed and manufactured. • If we want to provide technical and equipment support for future vaccine production, we will need to find a private company partner.
Kenya	PPB human resource development Awareness of clinical trial stakeholders	• The PPB does not provide training for regulators and needs to find partners and other regulators who can provide the training. • Collaboration and collaboration between regulators, clinical trial researchers, and drug manufacturers is critical. • There is a forum called the African Vaccine Regulatory Forum where regulators are coming together in an effort to establish a common template in evaluation procedures.
Vietnam	promotion of clinical trials Establishment of the Center clinical trial core hospitalisation	• We believe that it is necessary to establish a clinical trial promotion center. We would like to make the center capable of designing and introducing clinical trials and conducting phase I clinical trials. • It is necessary to establish a network of major hospitals to conduct clinical trials.
Philippines	Improve efficiency of FDA human resource development operations	• At the FDA, many of its staff members are contract employees sent through the government. The team that regulates clinical trials and approves new drugs for safety and efficacy review consists of only 12 employees, most of whom have been with the company since 2021. • The FDA does not have the capacity to provide specialized training on its own.
	Enhancing ARO functions and renovating facilities based on the University of the Philippines NIH/NCTTC	• In the Philippines, where clinical trials are sponsored and CRO-led, ARO enhancements are needed to increase the number of academia-led clinical trials. • Since there are gaps in capacity and capacity among clinical trial sites, we want to create a template that can be standardized and used and implemented at any clinical trial site, starting from the University of the Philippines.
Indonesia	Establishment of Clinical Research Support Center based at Udayana University Hospital and strengthening of clinical trial capacity	• We want to establish a national clinical trial support center and unify the standards and capacity of all clinical trial centers. • With 157 hectares of land, Udayana University has the capacity to establish a clinical trial support centre. It is also located in Bali, making it ideal for being a core hospital based in Bali.

The wrap-up was highly satisfactory, as the participants received feedback from the Japanese stakeholders, which provided them with items for consideration and advice or suggestions that they had not been fully aware of. There was also a comment that ask for continued support from Japan in the future.

The participants are more satisfied with the good advice given to the comments of the reviewers.

[Review]
- It was an opportunity to receive great advice, useful encouragement and feedback from the PMDA staff.
- Thanks to the representatives of JICA, the University of Tokyo and PMDA for their comments and suggestions on the input of the participants.

[Overall]
- Very good communication and facilitation
- Information sharing and action plans were established in each country.
- Satisfied with the opportunity to present national needs to improve the quality and process of conducting clinical trials in each country

Lessons Learned from Wrap Up Sessions

It can be understood that by clarifying the recognition of the Challenges in the country, it was possible to clarify the matters that will be necessary in the future.
In addition, several people expressed a desire for JICA's continued support in this field.

[Excerpt from comments]
- For JICA's support
  - We want JICA to guide clinical researchers and regulators to achieve their goals.
  - in regulation
  - I learned the procedure for applying for funding through JICA.
  - need to contact JICA's field office for assistance
- About the whole thing
  - We understand that clinical research requires a team effort between regulators and researchers.
  - What the participating countries want to improve and support is manpower and facilities
  - I was able to expand my network through the workshop.
  - Support from JICA, action plans in regulations, and action plans in conducting clinical trials
  - Dr. Takizawa of JICA gave us useful advice on tuberculosis research, vaccine production and technology transfer in Thailand.
  - Information was obtained on future research trends, especially DCT.

Figure 3-25 Questionnaire result of wrap up

3.2.2 Follow up initiatives as a result of the Japan visit

Based on the action plans of each country developed in the workshop, follow up initiatives for each country to be implemented in this study were drafted. For each country's action plan, we drafted the initiatives of on-site dispatch and seminars, and identified and organized the prerequisites, such as cooperation from Japanese institutions, that would be required for each initiative. Based on the discussions, five plans were proposed as follow up pilot activities, as shown in the table below.

Table 3-9 Pilot activity plans for each countries

regulatory body
clinical research institute

	Action planning (draft)		Types of action	Theme	Activities (example)	collaborating institution	Prerequisites
Indonesia (Udayana University Hospital, University of Indonesia, BioFarma)	national clinical research Establishment of Support Center conduct of international clinical trials human resource development for	Based on Udayana University Hospital Establishment of clinical research support centers and strengthening of clinical trial capacity	1 field dispatch	Introduction of the Clinical Research Support Center	• Resource (Facilities, equipment, and human resources) assessment for the establishment of the center • Training to introduce organizational theory for building centers • Training needs analysis of clinical trial competencies	[Domestic] • University of Tokyo Hospital Clinical Research Promotion Center [Country] • Udayana University Hospital • Ho Chi Minh University of Medicine and Pharmacy	• To conform to Dr. Maruyama's schedule at the University of Tokyo Hospital.
Vietnam Ho Chi Minh University of Medicine and Pharmacy	P1 Building a Clinical Trial Promotion Center Including a Unit	based at Ho Chi Minh University of Medicine and Pharmacy Establishment of the Clinical Trial Promotion Center					
Philippines (FDA)	Human resource development of regulatory agencies Development of regulatory task support tools	FDA Human Resource Development Improve operational efficiency	2 field dispatch or seminars, etc. (face-to-face or online)	Building and strengthening human resource development systems at regulatory bodies	• Assessment of training needs by regulatory bodies • Formulation of training program proposals • Development of an implementation plan for the proposed program	[Domestic] • PMDA [Country] • PPB • PFDA	• Getting cooperation from PMDA • Scope 1 country depending on cooperation of PMDA
Kenya (PPB)	Comprehensive training of CT staff for protocol review and evaluation/GCP inspection	PPB human resource development					
	stakeholder sensitization	clinical trial Stakeholders enlightenment	3 Seminars, etc. (face-to-face or online)	stakeholder sensitization	• Network Seminars with Hospitals, Research Institutes, Pharmaceutical Companies, and Industry Organizations Based on Regulatory Organizations	[Domestic] • PMDA [Country] • PPB • African Vaccine Regulatory Forum	• Getting cooperation from PMDA
Philippines (University of the Philippines)	Capacity building for clinical trials UP-NCTTC's assistance in renovating new UP NIH building space	ARO enhancements based on the University of the Philippines NIH/NCTTC facility renovation	4 field dispatch	Strengthen ARO functions in the Philippines	• Specialized training for CRC and NCTTC core staff • Technical support for the development of SOPs and quality assurance mechanisms • Technical support for performance monitoring capabilities and indicators • Facility assessment of the new UP-NIH building	[Domestic] • National Cancer Center (ATLAS) Or • NCGM(ARISE) [Country] • University of the Philippines/NIH/NCTTC	• Cooperation from ATLAS or ARISE • Aligning with ATLAS or ARISE's base development activities
Vietnam Ho Chi Minh University of Medicine and Pharmacy	Building a network of clinical trial core hospitals	clinical trial With the establishment of core hospitals Network	5 Seminars, etc. (face-to-face or online)	Strengthening international network with clinical trial core institutions	• Holding of network seminars with clinical trial core institutions based on ATLAS • Support for ATLAS's activities to promote cooperation in Asia	[Domestic] • National Cancer Center (ATLAS) • REMAP-CAP [Country] • Clinical trial centers in major cities in Asia • Clinical trial network groups in Asian countries • Ministry of Health	• Cooperation from ATLAS and REMAP-CAP.

As a result of the discussion with JICA regarding the above five proposed follow-up pilot activity plan taking into consideration such factors as "ease of linking with future projects," "implementation schedule," and "cooperation with relevant Japanese institutions," the following table shows the establishment of the follow up pilot activities (follow up in each country after the Japan visit). The newly added additional pilot activities are (1) follow up activities after the Japan visit and (2) dispatch of experts to the countries.

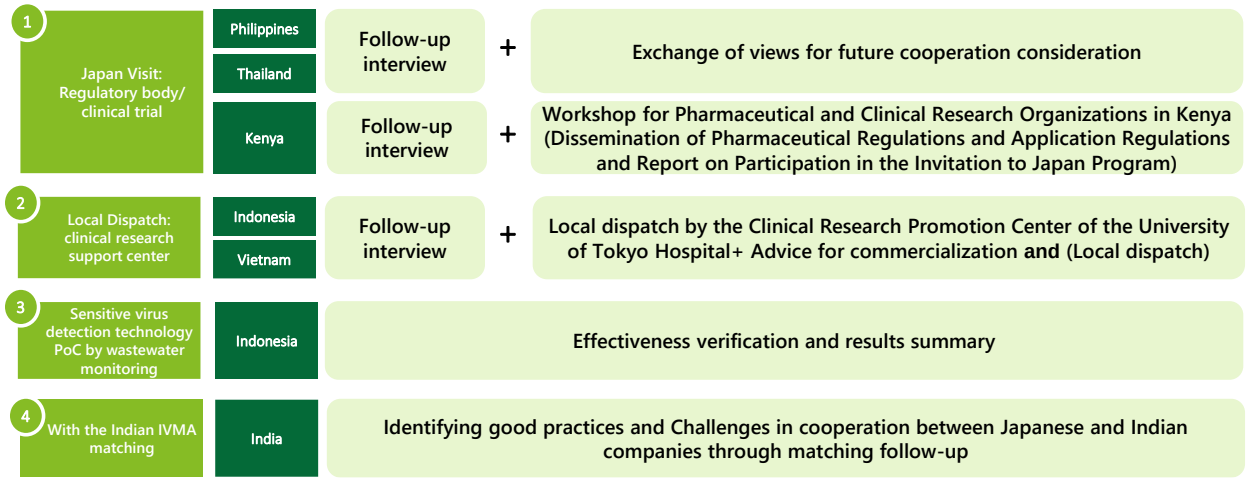


Figure 3-26 Project planning

(1) Post pilot activity plan (Follow-up after Japan visit) (Target countries: Thailand, Philippines)

For Thailand and the Philippines, based on the results of the Japan visit in July, dialogue for the future commercialization of the project was hold including JICA's local offica.

The support project plan was blasshed up by organizing the results of the Japan bisit and discussions with counterparts in Thailand and the Philippines and discussing with counterparts in Thailand and the Philippines. With the consideration of utilizing JICA's technical experts such as dispatching experts and providing equipment, matching, and collaborating with Japanese companies, discussion with counterparts in Thailand and the Philippines was held to develop the support project plan into as much concrete proposal as possible aiming to make this plan into actual project. After consideration with counterparts, discussion including JICA's local offices was held to discuss feasibility and utilization of support project plan, and to confirm the steps necessary for realization.

The implementation of actions and activities after the proposal is made shall be outside the scope of this project.

(2) Post pilot activity plan (Follow-up afer Japan visit) (Target country: Kenya)

For Kenya, it was decided to have sensitization seminar which will be joined by various actors who involve in clinical trials such as universities, research in stitutions, ethics committees, industry associations, and private companies with the PPB’s organizing to promote a common understanding and collaboration on challenges and measures of clinical trial regulations. It was also decided to discuss about the details of content and design with PPB after summarizing the objectives and details of the seminar and discuession with JICA to be on the same page.

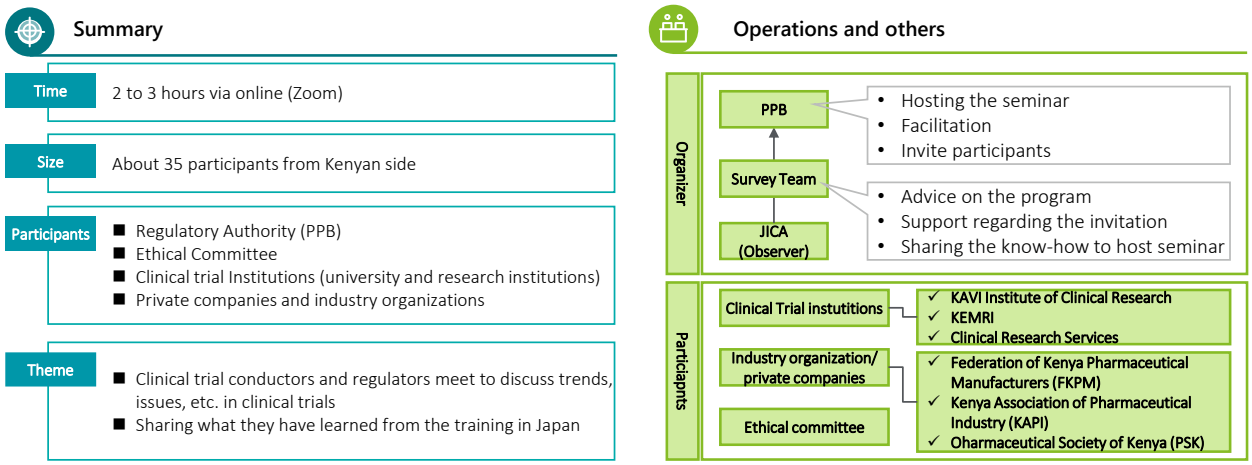


Figure 3-27 Image of the sensitization meetingr

(3) Post pilot activity plan (Follow-up after Japan visit) (Target countries: Indonesia, Vietnam)

Since "introduction of a clinical research support center (or clinical research unit) function" was cited as an action plan by Udayana University Hospital (UUH) in Indonesia and the University of Medicine and Pharmacy at Ho Chi Minh City (UMP) in Vietnam, it was decided to conduct more detailed needs assessment locally for the introduction of a clinical research support center (or clinical research unit) function at both UUH and UMP. The University of Tokyo Hospital Center for Clinical Research Promotion Dr. Tatsuya Maruyama, Deputy Director, was dispatched as a technical advisor to conduct the needs assessment and to provide technical advice and exchange opinions with the local institution.

As a result of follow-up interviews with both UMP and UUH in late September 2023, both reported the action plan to their superiors and confirmed that there is no conflict in their policy to introduce and strengthen the clinical research promotion center function (or clinical research unit) as institutions. As for Indonesia, a Health Ministerial Decree was issued by the Indonesian Ministry of Health in July 2023, notifying a policy to promote the establishment of the Indonesian Clinical Research Center (INA-CRC) and Clinical Research Units (CRU) in hospitals as a whole country, and it was cleared that the introduction of CRU functions in hospitals was in line with the national healthcare policy.

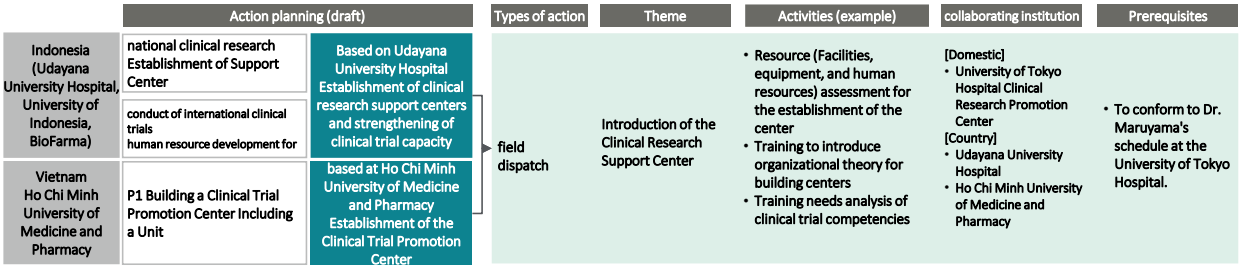


Figure 3-28 Pilot activity plan for Indonesia and Vietnam

3.2.3 Follow-up initiative for Thailand/Philippines

For Thailand and Philippines, duscussions were held with each of the institutions of stakeholders who joined Japan visit to determine their detailed needs and to develop a concrete plan for future support projects based on the results of the workshop as a follow up to the Japan visit.

(1) Follow-up with Thai SiCRES

With the aim of considering future JICA projects, an interview with SiCRES in Thailand was conducted

as a follow up to Japan visit in order to understand more detailed needs for the preparation of a support project proposal.

Based on the results of the workshop, two support projects was proposed: (1) collaboration with Japanese private companies in TB-LAM, and (2) dispatching experts to strengthen the capacity for conducting investigator initiated clinical trials.

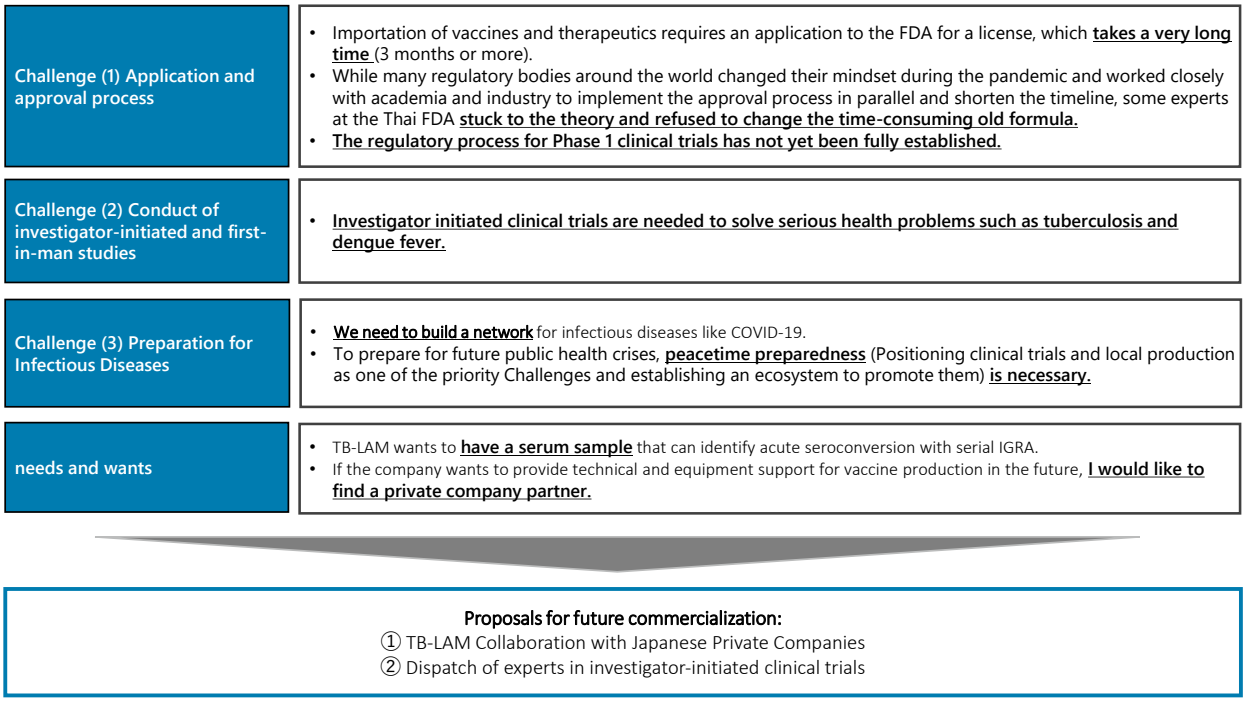


Figure 3-29 Challenges and needs of SiCRES which is indicated in Workshop

As a result of the interviews conducted, it was confirmed that there is a high need for assistance in the implementation of the Action Plan related to TB. Specifically, they need assistance to conduct a cohort study to detect seroconversion in newly infected TB patients, including financial support for the use of storage facilities and technical assistance in detecting new biomarkers.

Through these interviews, it was learned that interest in latent TB is growing in many countries and that there is a high need for support for validation of the IGRA test to detect patients with seroconversion. The "Project for Validation of IGRA Tests for Detection of Seroconversion" was considered as a project proposal to support SiCRES in Thailand.

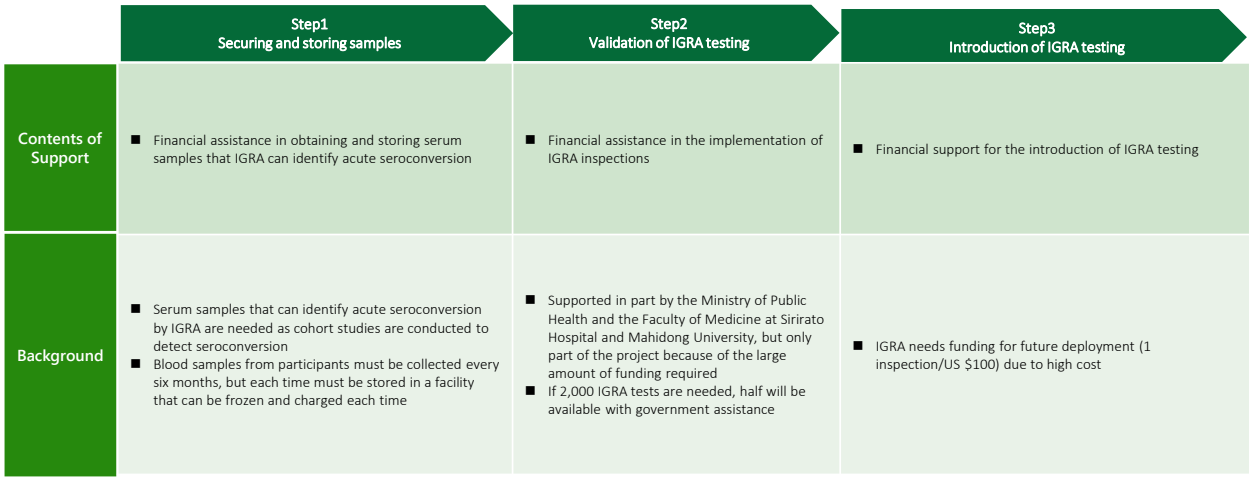


Figure 3-30 Support project plan for SiCRES

On the other hand, as a result of the discussions with JICA, further consideration was suspended, as the IGRA's efficacy cohort study for identifying latent TB is not a joint research project with a Japanese research institution and it is difficult to provide financial support for the project. Therefore, we informed SiCRES that this proposal would be difficult to support under the JICA scheme, and the follow up was completed with this study.

In addition, although it could not be discussed at this time, preparedness for infectious diseases was raised as a challenge, and needs were expressed for the establishment of a network for infectious diseases such as COVID-19 and for preparedness from normal times (positioning clinical trials and local manufacturing as one of the priority challenges and establishing an ecosystem to promote them). The need to prepare for pandemics was also expressed. Capacity of Vaccine manufacturing was also a major theme as part of the response to a pandemic, and strengthening manufacturing capacity, human resource development, and infrastructure development were also mentioned as needs.

(2) Follow-up with University of the Philippines

In order to understand the needs in detail for the preparation of the support project proposal, interview with the University of the Philippines was held as a follow up to the Japan visit, for the purpose of considering future JICA projects.

Based on the results of the Japan visit, the challenges and needs of the University of the Philippines were organized as follows, and two projects were proposed: (1) Curriculum development related to research, and (2) Technical cooperation for the establishment of the NCTTC (National Clinical Trial and Translation Center). The two project proposals were as follows.

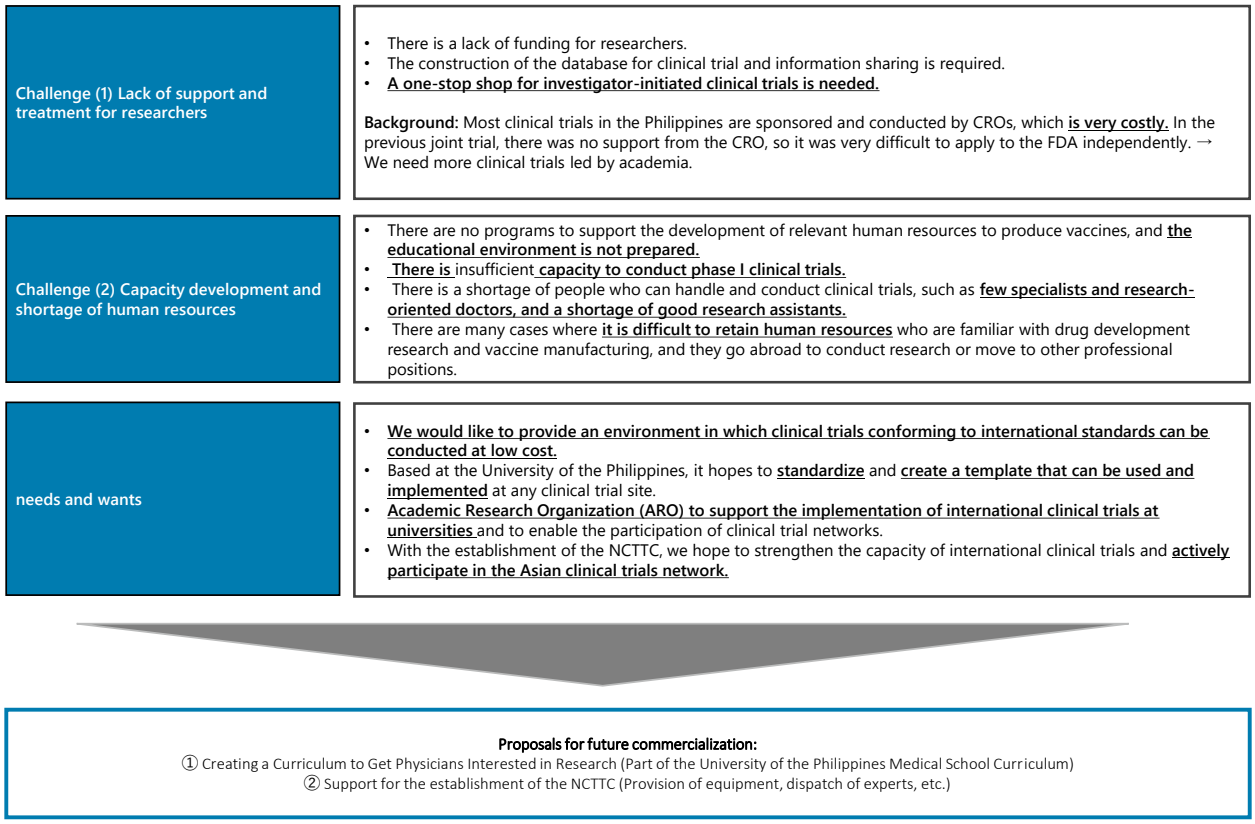


Figure 3-31 Challenges and needs of University of the Philippines which is indicated in Workshop

Based on the above figure, interview was conducted with the University of the Philippines, and the following comments were made, confirming that there is a high need for support for the newly established NCTTC.

Philippines (University of the Philippines)

Discussion

Action Plan (1) Introduction of a new curriculum dedicated to clinical trials and research

- It is difficult to establish a new curriculum because only a limited number of departments can introduce it when targeting clinical trials, etc., but we hope that existing curriculum programs and others will be strengthened.
- Since we are also actively introducing double-degree programs, we would like to ask you to support exchange programs (cooperation and networking) with Japan.
- In addition, we would like to provide opportunities for Masters and PhD students who are writing theses to collaborate with Japanese institutions and academia, so we would like you to create a foothold in networking. They also want to actively participate in ATLAS and other networks.
- For researchers, capacity needs to be strengthened in areas such as adaptive design and hybrid design.

Action Plan (2) Support for the establishment of the NCTTC (Technical assistance, financial assistance, equipment provision, etc.)

① Technical assistance (high priority)

✓ For technical assistance from experts, we would like advice on how to function as knowledge and ARO in Design and Design of NCTTC Space in New UP NIH Building.

✓ Assessment of clinical trial sites in the Philippines is already underway, and proposals for efforts to assess the needs, skills, and expertise of local researchers have been submitted.

② Financial assistance (high priority)

✓ The University of the Philippines is also providing funding, but further funding is required in the renovation of the NCTTC space in the new UP NIH building.

③ Provision of equipment (low priority)

✓ The NCGM has already cooperated in the provision of equipment, and the necessary equipment has been secured in the initial stage of the establishment of the NCTTC, but the necessary equipment is expected to increase in the future as the NCTTC expands. (NCGM has a presence at the University of the Philippines and is working with)

Figure 3-32 Discussion detail of follow up meeting with University of the Philippines

Regarding support for the newly established NCTTC requested by the University of the Philippines, interviews with NCGM were held in order to understand the specific support provided by NCGM and the possibility of collaboration since NCGM has already provided support for equipment and human resource development, etc.

The current status of the NCGM is that support for the NCTTC, which was provided for the AMED grant

project, was completed in FY2022, but since the new NIH building has not yet been completed, the NCGM is expected to continue to follow up until its completion in FY2023 and beyond. The direction of NCGM appears is to be to generate new clinical trials and clinical study projects as a result of its support for NCTTC. As for JICA's future collaboration, funding for the development of infrastructure for international clinical trials and training for starting clinical trials were mentioned. In addition, a project to develop a new technology to diagnose hepatitis patients at the University of the Philippines is scheduled to begin in January 2024 and run for two years, and we have received comments that supplemental funding is needed. The possibility of collaboration between JICA and NCGM in this type of support is also considered.

(3) Follow-up with Philippines FDA

As a follow-up to the invitation to Japan, interviews were held with the PFDA in order to understand their needs in detail for the development of a support project proposal, with the aim of considering future projects by JICA.

Based on the results of the workshop, we summarized the challenges and needs of PFDA as follows and proposed a support project for the development of a manual for GCP inspectors.

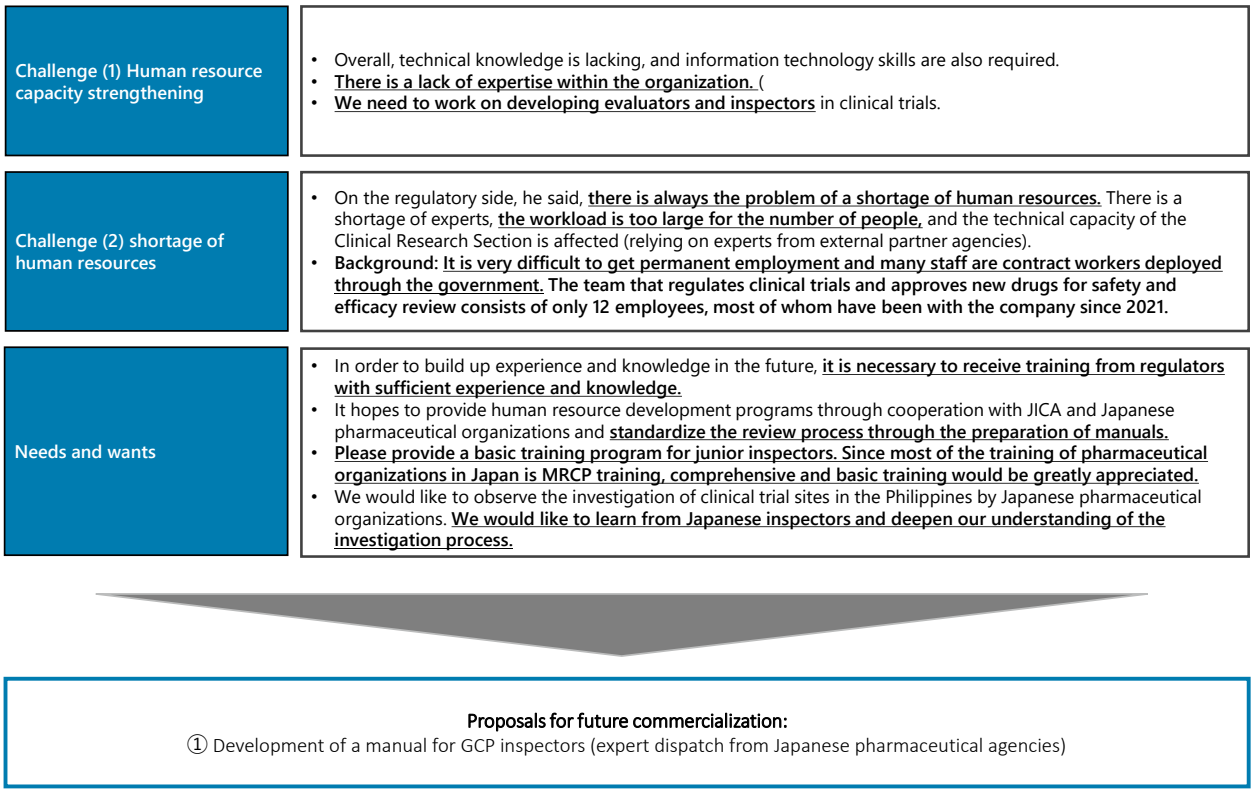


Figure 3-33 Challenges and needs of PFDA which is indicated in Workshop

Interview with PFDA was held based on the above figure, and specific support details for the action plan is described as following figure.

Philippines (Philippine FDA)

Discussion

Action Plan: Development of manuals and capacity building for FDA personnel

Support: Dispatch of experts
① GCP inspectors preparing manuals
② Manuals for the review of clinical trials of medicinal products
③ Manuals on Review of clinical trials of medical devices

Supposed experts: experts of Japanese pharmaceutical organizations
✓ Experienced in reviewing clinical trials in Japan
✓ Those who can respond in English

Duration: Approximately five years for Phase1 and Phase2
✓ Phase1: Draft the manual (assuming expert deployment of 3 months or so), review the draft within the FDA, and complete the manual (assuming expert follow-up online or on short trips)
✓ Phase2: Support for implementation in accordance with the manual, revision of the manual based on implementation results (Expect experts to provide short-term travel support, with experts providing lectures to staff as needed and support until the second or third manual revision)

Figure 3-34 Discussion detail of the follow up meeting with PFDA

Based on the results of the interview, a second interview was conducted to discuss specific capacity building needs in order to brush upu on a project proposal that can be considered in the future.

Challenges	• There is a shortage of skilled personnel, and new hires are being made, but training has not caught up. • The shortage of human resources is a challenge and the workload is too high for the number of people, affecting the technical capacity of the Clinical Research Section • Only 12 teams and 5 GCP inspectors implement new drug approvals for clinical trial regulation and safety and efficacy review • Standardization of the review process through the development of evaluators and inspectors in clinical trials and the development of guidelines is necessary.
Current status	• No manual for review of drug-related clinical trials (review of documents submitted at the application stage before clinical trials are conducted) • There is a manual for GCP surveillance, but improvements are needed, and a manual for clinical trials on medical devices is currently being developed
Needs	• In order to bring more knowledge and experience to the Philippines, it would be good if Japanese educators could travel to the Philippines and train more experts directly. This will also allow Japanese experts to see the situation on the ground. • It is also necessary to send experts who have actual experience in the Philippines to Japan and make them powerful trainers based on their efforts in Japan.

Figure 3-35 Challenges and needs of PFDA

As a result of the discussion about the needs of the capacity building, it was found that they are audited about WHO global benchmark in October 2023 and required to reach Maturity Level 3 in 2 years. This proposal project can be part of the support for the initiative to reach the required level as well; therefore, PFDA is very positive about the support in capacity building.

With challenges such as a lack of skilled human resources and manuals on clinical trial review, the main needs identified included support for guideline formulation, training by experts and observation of inspections by Japanese regulatory authorities with the aim of learning from Japanese knowledge and experience.

Based on the needs identified in the previous interviews, discussion was held with the PFDA and JICA to explore the feasibility of proposal project. In the discussion, JICA side mentioned that the proposed projects need to be determined based on the availability of Japanese resources, feasibility as well as the priority and the criteria of the country. If the PFDA has specific requests for assistance, it is expected that the PFDA will consult with JICA after coordination within the Philippine government.

3.2.4 Kenya PPB sensitization seminar

For Kenya, based on the action plan, it was decided to have sensitization seminar (hereinafter referred to as "seminars") hosted by the PPB, as the regulatory authority, for various stakeholders involved in clinical trials, including universities, research institutions, ethics committees, industry associations, and private companies.

As for the purpose of holding the seminar, given that the PPB, as a regulatory body, promotes collaboration among those involved in clinical trials, the main objective was to create a opportunity where regulatory bodies and institutions conducting clinical trials could meet and share their know-how and knowledge with each other.

To ensure effective implementation of the seminars in this study, regular meetings with PPB were held to provide lateral assistance in program content and outreach to participants. During the discussions, it was decided that the themes would focus on emerging trends in clinical trials and the challenges and opportunities for collaboration faced by both regulatory agencies and clinical trial sites.

The seminar was held on January 22, 2024, and was opened with a presentation by Dr. Benson Kanji on the differences between the clinical trial environment in Japan and Kenya, based on the insights gained from his visits to Japanese institutions at the Japan visit. This was followed by six presentations including one about new clinical trial applications and about reviews by the Expert Committee on Clinical Trials (ECCT). After the presentations, a panel discussion was held to discuss the efforts to conduct efficient clinical trials, collaboration among institutions, and securing researchers. The discussion was very active, with many questions from the participants. The details of the program are shown in the table below.

Table 3-10 Program

Time	Program	Facilitator/ Speaker
8:00-9:00	Arrival and Registration of Participants	Dr. Rosemary Njogu (PPB)
9:00-9:30	Opening Prayers Introduction of Participants	Dr. Samuel Kerama (PPB)
9:30-9:45	Opening Remarks	PPB CEO
9:45-10:15	Regulation and Clinical Trials: Kenya and Japan Perspective	Dr. Benson Kanji (PPB)
10:15-10:35	Overview of New CT Applications	Dr. Rosemary Njogu (PPB)
10:35-10:55	Study Protocol and Assessment	Prof. James Kimotho
10:55-11:20	Tea Break	
11:20-11:45	Post Approval Considerations; Progress Reports, Amendments, Shelf-life Extension	Dr. Kevin Wangokho (PPB)
11:45-12:15	Study Monitoring; Good Clinical Practice Inspections, Deviations, Safety Reporting and Monitoring in Clinical Trials	Dr. Samuel Kanji (PPB)
12:15-12:35	Handling of Investigational Medicinal Products; A Clinical Site Perspective	Dr. Faith Riziki (KEMRI Walter Reed)
12:35-1:00	Q&A	Dr. Benson Kanji (PPB)
1:00-2:00	Lunch Break	
2:00-2:45	Panel Dscussion Opportunities and Challenges in Clinical Trials	Modelator: Dr. Mikal Ayiro (PPB) • Dr. Samuel Kerama (PPB) • Dr. Daisy Cheruiyot (SERU) • Dr. Kalerwa (NACOSTI) • Dr. Lucas Otineo (PI)
2:45-3:00	Q&A	
3:00-3:10	Closing Remarks	
3:10-4:00	Tea and Departure	

A total of 36 participants attended the seminar from various institutions involved in clinical trials, including clinical trial sites, medical institutions, and industry associations.

Table 3-11 Institutions of the participants

Category	participating institution
research institute	KEMRI (Kenya Medical Research Institute) • RCTP • KILFI • KISUMU • CRDR (SIAYA and KISUMU) • USAMRU-K Kericho • CGHR • SERU
	KAVI Institute of Clinical Research
	VIBRI (Victoria Biomedical Research Institute & KEMRI WRP)
	Clinical Research Society of Kenya
	STRATHMORE-CREATES
medical institution	Kenyatta National Hospital
	Moi Teaching and Referral Hospital
	Aga Khan Hospital
	ICI (International Cancer Institute)
public institution	NACOSTI (The National Commission for Science and Technology and Innovation)
	ECCT (Expert Committee on Clinical Trials)
regulatory authority	PPB (Pharmacy and Poisons Board)
trade association	KNH UoN Ethics and Research Committee
	MTaPS (The Medicines, Technologies, and Pharmaceutical Services Program)
Other	AMREF Health Africa
	KAPI (Kenya Association of Pharmaceutical Industry

As noted above, the seminar featured six presentations and panel discussion on clincal trials. A summary of each presentation and discussions in each session is as follows.

① Regulation of Clinical Trials: Kenya and Japan Perspective

The first presentation was given by Dr. Benson Kanji, a participant of Japan trip. Information on the clinical trial environment and situation in Japan was shared, as well as a comparison of the situation in Japan and Kenya based on information obtained during his visit to Japanese. He shared his view that Japan has a favorable environment for clinical trials in terms of a strong regulatory framework for clinical trials, population size of each age group, highly skilled clinical trial personnel, easy access to advanced technology, and government funding. He noted that the timeline needs to be improved in Kenya, where it takes 60 days for approval, compared to about 30 days in Japan.

② Overview of New Clinical Trial Application

This presentation was presented by Dr. Rosemary Njogy, a member of PPB, who shared the requirements for submitting a new application, the information needed, the applicant, and the mistakes that can occur, in order to improve basic understanding of the application. She also mentioned that it takes 5 days to verify the accuracy and completeness of the application and the post-submission process.

③ Study Protocol and Assessment

Prof. James Kimotho, a member of the Expert Committee on Clinical Trials (ECCT), presented the guidelines available on PPB portal. He shared the role of the ECCT and its review perspective and timeline based on actual cases. The ECCT's review focuses on trial safety, subject health, and integrity of trial data, and it was noted that some of the trials reviewed lacked or were unclear about necessary information and data.

He also mentioned that the timeline needs to be improved and that a parallel review mechanism is currently being considered to shorten the time to approval.

④ Post Approval Considerations

Dr. Kevin Wangokho, a member of the PPB, gave a presentation on progress reports, corrections, and shelf-life extensions that need to be addressed after approval.

Specifically, Dr. Wangokho provided information on the data and timing required to apply for modifications and extensions, as well as the content and reporting timeline of important progress reports.

⑤ Study Monitoring

Dr. Samuel Kerama, a member of the PPB, gave a presentation on monitoring clinical trials and explained the importance of adverse event and drug reaction reporting and GCP inspections, emphasizing that such reporting is an important process for the safety of not only researchers but also subjects.

Regarding GCP inspections, he also mentioned the specific process up to the inspection, the types of inspections, and the responsibilities of the sponsor.

⑥ Handling of Investigational Medicinal Products

Dr. Faith Riziki of KEMRI Walter Reed gave a presentation on the handling of investigational drugs from the perspective of a clinical trial site. He discussed how investigational drugs are procured, stored, and distributed in each clinical trial, the challenges faced at each step, and the critical importance of trial management and data reliability to improve subject and patient safety and maintain efficacy.

He also mentioned that handling investigational drugs requires a certain amount of capital investment, and that on-the-job training, capacity building, and technology transfer are also necessary in terms of human resources to keep up with technological changes.

⑦ Panel Discussion

The panel discussion was conducted lively with panelists Dr. Benson Kanji (PPB), Dr. Samuel Kerama (PPB), Dr. Daisy Cheruiyot (SERU-KEMRI), Dr. Godfrey Kalerwa (NACOSTI), and Dr. Lucas Tina (Victoria Biomedical Research Institute (VIBRI)) as panelists. The themes and the opinions and topics raised by the speakers on each topic are shown in the table below.

Table 3-12 Themes and discussion details

Themes	Details and Topics
1) Strengths and challenges in clinical trials in Kenya	■ Strengths 1. Law that empowers and a strong regulatory framework 2. Robust guidelines for clinical trials 3. Adoption of an online platform for clinical trials in Kenya 4. Skilled staff and expert committee on clinical trials at PPB 5. Improved turn around time at SERU 6. 2-tier review system at SERU 7. 3 divisions activated to support clinical trials 8. SERU has built a rapport with PPB and NACOSTI 9. Such stakeholder consultations/meetings are helpful 10. Prioritization of health research at NACOSTI 11. Quick responses at NACOSTI ■ Challenges 1. Funding inadequate to monitor clinical trials 2. Lack of regular capacity building opportunities 3. Process of informed consent can be complex 4. There is a gap in NCDs

	5. Timelines are long 6. Poor infrastructure for clinical trials 7. Incomplete applications submitted to NACOSTI 8. Lack of responses from applicants 9. Multisite applications submitted to NACOSTI 10. Individual applications as opposed to applications made by institutions 11. Lack of compliance – e.g., report submission 12. Expired documents submitted 13. Mismatch in documentation 14. Increased workload
2) How do you address efficiency in clinical trials among the regulator?	■ NACOSTI 1. Automation 2. Having a common platform where regulators and researchers interact 3. Increased awareness among stakeholders on clinical trials processes and procedures ■ PPB a) Internally (processes and procedures) 1. Optimizing timelines 2. Improving human resource within the clinical trials division 3. Capacity building models for new entrants 4. Parallel review of application submissions b) Externally 1. Ensuring that stakeholders are conversant with processes and procedures 2. Regular stakeholder engagement
3) What is your perspective on ERC, PPB, NACOSTI working together? Do we have trust issues amongst ourselves?	■ There have been unethical issues that have come up in the past that may have affected the working relationship ■ Research integrity could also be an issue ■ Lack of full disclosure among researchers ■ Silo mentality among stakeholders ■ Historical influences/experiences could be a factor ■ Confidence and beliefs as to whether roles should be complementary ■ Mistrust in timelines
4) Do you thing we can have enough researchers to conduct clinical trials?	■ Biggest challenge is that good researchers eventually end up doing administrative duties/roles ■ Capacity building and transition plans must be put in place
5) How do you want to foster confidence in clinical trials?	■ Collaborate and make a clear pathway for clinical trials ■ Regular stakeholder engagement is important ■ Training of individuals to understand the submission portal is important ■ Parallel and joint reviews may also help with the timelines ■ Knowledge sharing among stakeholders ■ Publication of success stories ■ Intentionally leveraging on technology/online system of application submission ■ Optimize on timelines ■ Involving external individual experts ■ Capacity building on existing staff working in clinical trials ■ Intentionally pushing a positive narrative

	■ Maintaining an open door policy at PPB

⑧ Q&A

During the Q&A session, many questions were asked about measures to deal with the lack of resources at the PPB, the online system for applications, and possible causes of delays and possible countermeasures during the review process, each of which was answered by the organization related to the question. The details of the questions and answers are listed below.

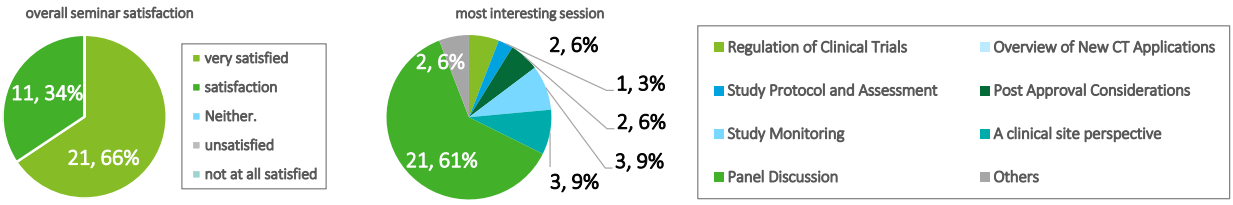
Table 3-13 Q&A

Questioner	Question	Respondent	Answer
KEMRI-KERICHO	What is the timeline for allocating a protocol to a reviewer? Can we bring down the 30days/15days?	PPB	It takes 30 days for the protocol to be reviewed and evaluated and 15 days to ensure that the queries raised by the reviewer have been addressed. It is possible to shorten the number of days and that is why we are here. Parallel submissions can help reduce timelines and we are open to proposals that will not compromise time and quality.
Aga Khan University Hospital	Are we learning from other countries? Do we have any data from them?	PPB	✓ We have visited Ghana and found that they have 15 staff handling clinical trials ✓ Concerning timelines, we are more or less at the same level with Ghana ✓ We have more applications submitted for clinical trials than Ghana ✓ As for Nigeria, we are doing better than them ✓ In Uganda, most trials are phase 3 or 2 ✓ South Africa and Egypt are performing much better than we are ✓ We don't have data from Tanzania
MTaPS	What do you see as the options for resources given the current low resources at PPB?	PPB	✓ Collaboration with other frameworks ✓ Provision of reliance mechanisms ✓ Strategic development partners ✓ Fees for service to facilitate efficiency/work
KEMRI-KERICHO	Is there a technological problem with the online system?	PPB	We are currently working on Version 3 of the system.
AMREF	At which step is there much delay in getting feedback from the ERC?	PPB	We are increasing sensitization to streamline our processes.

KEMRI-KILIFI	Do you have a subdivision for Clinical Trials in NACOSTI?	NACOSTI	We have dedicated science schedules.
STRATHMORE-CREATES	How do you carry out monitoring of clinical trials? How do you manage IMPs given that storage and compliance is a big problem?	VIBRI	Being vigilant to make sure that generators are running. We also usually have someone to monitor the storage conditions remotely and physically. We have installed solar panels for back up.
ECCT-PPB	Coordination between stakeholders, CROs and PPB?	PPB	GCP inspection is a regulatory requirement by law, hence that function cannot be transferred. CROs are not bound by law. We are willing to work with available staff.
KAPI	Is there a proposed feedback framework to improve timelines for clinical trials? Safety reporting, what is the way forward?	PPB	We already have parallel review committees in clinical trials. We have a plan. On safety reporting, we can take this discussion offline.
CRSK	Is PPB considering GCP alternative procedures in Kenya?	PPB	Kenya is reviewing and further updates will be provided. Go ahead and submit applications plus letters for GCP and PPB will verify.
KAVI-ICR	What is your position on researchers having to also pay county fees?	NACOSTI	Payment of county fees may not only be for researchers and a plan of action may be required for continuous improvement.
CRSK	Can PPB consider working with centers and implement best practices, e.g., from SAHPRA? Can we have a dedicated portal for clinical trials for applying for import permits? Domestication of AVAREF procedures locally?	PPB	PPB takes the final position of AVAREF and only does administration duties. Import and export procedures involve many agencies. We may have to consult further to see how some of these processes can be streamlined.
Moi Teaching and Referral University	Where is the boundary between IRB and PPB?	PPB	PPB's major focus is quality, safety, and efficacy of IMPs. Our major concern is clinical development. IRB's focus more on ethical procedures. We have a team of reviewers which is advertised every three years through a tendering process.
Aga Khan University Hospital	Would PPB be open to having trainees/fellows do a 1-month rotation and learn from adjunct reviewers? As you train PPB reviewers, can you also train institutional	PPB	Yes, this is something PPB can consider once the frameworks are in place.

	IRB reviewers as well who may need refresher courses?		

A questionnaire was collected after the seminar, and responses were received from 32 out of the 36 participants (a response rate of approximately 88%). Regarding overall satisfaction with the seminar, about 66% answered "very satisfied" and about 34% answered "satisfied," indicating that the seminar was extremely satisfying for the participants. About 63% answered that the most interesting session was the panel discussion, mainly because of the openness of the discussion and the fact that many challenges in Kenya were covered in the discussion.



[Reasons for the most interesting session]
Regulation of Clinical Trials
- Development has been seen in cooperation and support
- Improve the function and operation of the Kenya PPB

Study Monitoring/ A Clinical Site Perspective
- had something to do with one's own business

Panel Discussion
- Open and transparent discussion was. It was very exciting because all stakeholders were working positively towards making Kenya an important country in clinical trials, we were able to take FB from participants openly and hear about the process for improvement, so it was very exciting. We look forward to continuing discussions.
- It was very meaningful because it was a place to share Challenges and discuss possible responses to those Challenges for each stakeholder. In addition, each stakeholder was able to directly share with each other where improvements were needed.
- In Kenya, much of what was now a challenge was covered in the discussion.

[Other comments on the seminar as a whole]
- As this was a good opportunity for networking and learning knowledge and know-how, I hope that similar efforts will be made in the future.
- Trust and confidence in regulatory authorities have increased.
- A very fruitful meeting It was a positive step and I would like you to follow up based on the comments and advice of stakeholders.

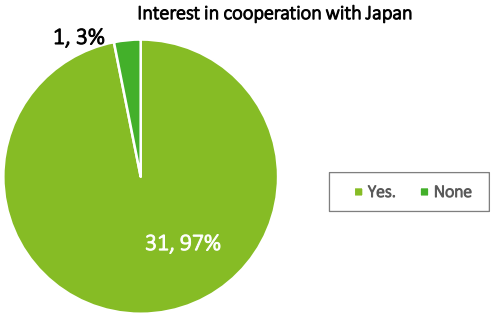
Figure 3-36 Answers of overall satisfaction

Regarding the level of understanding of each session (on a of 1 to 5), the average for all sessions was generally 4.5 or higher, indicating that the sessions were not one-way sessions from the presenter's side, but that a high level of understanding of the content was obtained from the participants as well. Detailed comments on the level of understanding and learning from each session are provided below.

Table 3-14 level of understanding lessons learned

Program	Average	Comments on Learning
Regulation of Clinical Trials: Kenya and Japan Perspectove	4.66	■ Collaboration initiatives and future possibilities. ■ After comparing Kenya with the Japanese regulatory body, we found that Kenya needs to improve its timeline. ■ I realized the importance of meetings that bring stakeholders together. ■ Improving the regulatory framework requires collaboration among stakeholders. ■ To avoid delays, it is important to fill out and submit the form appropriately.
Overview of New CT Applications	4.63	■ Provisional application schedules and the importance of ensuring that appropriate submissions and requirements are met to shorten the schedule. ■ I understood the process of submitting a new application. ■ A deeper understanding of the checklist and process done.
Study Protocol and Assessment	4.66	■ I understood how to manage the protocol at the evaluation stage. ■ I was able to understand the time and timeline for the review in Kenya and the time required for each person involved. ■ The main reason why the delay actually occurred until now was the study. Appropriate protocols must be submitted to expedite the review process.
Post Approval Considerations; Progress reports, amendments, Shelf-life Extension	4.56	■ You now have a deeper understanding of the conditions, procedures, and reports required for approval. ■ Responsibilities and points to be noted by the institution conducting the clinical trial after approval. ■ Type of amendment and importance of submission of amendment. ■ The progress report and its schedule. ■ about deficiencies.
Study Monitoring; Good Clinical Practice inspections, Deviations, Safety reporting and, Monitoring in Clinical Trials	4.84	■ Rather than being punitive, GCP inspections are an important and necessary means of enhancing compliance and ensuring quality at clinical trial sites. ■ The importance of research monitoring was understood. ■ The guideline was reconfirmed. ■ I was able to understand the PPB requirements in depth. ■ Clear division of RA responsibilities and gaps in effective financing methods in this aspect
Handling of Investigational Medicinal Products; A clinical site perspective	4.84	[Investigational product (IMP)] ■ Critical steps in management and storage, Maintenance of high efficiency and quality, importance of correct treatment for safety of trial participants, challenges that may arise during importation, Expediting the import process, Need for, compliance with protocols and guidelines, etc. [Intellectual Property Management] ■ Basic knowledge Challenges, processes, handling, best practices, etc. [Others] ■ Challenges at trial sites
Panel Discussion (Opportunities and Challenges in Clinical Trials) & Q&A	4.75	■ There were open questions and answers about various Challenges in clinical trials. ■ Need for multi-agency cooperation and have and are willing to cooperate. It also became a good opportunity to have cross-institutional discussions. ■ Experienced panelists were able to get experience, opinions and FB from. ■ It was meaningful to hear opinions from the viewpoints of various institutions and researchers. ■ I felt it was important to share success stories. ■ The discussion clarified areas that need improvement and cooperation among stakeholders. [Points that need to be improved in clinical trials and regulations in Kenya] ■ Building trust among regulators is necessary to improve efficiency. ■ Shorter time to approval required. ■ As a response to the lack of funds, we need to think about a fund-raising strategy. ■ There are many unexplored areas in clinical trials.

In particular, the presentation by Dr. Benson Kanij provided an opportunity to increase interest in collaboration with Japan. In the questionnaire, question to ask whether or not they would like to collaborate with Japan and, if so, in what areas and with which Japanese institutions were included. Some of the comments clearly mentioned specific institutions and companies that they want to collaborate, and several commented on the interest in strengthening their capacity to conduct clinical trials in general as an area of collaboration. Other comments included the possibility of utilizing Japan as a benchmark to improve the clinical trial environment in Kenya to achieve a higher standard, and the need for more detailed information on the potential for collaboration.



[Comments of interest]
- Some comments indicated the names of specific institutions and companies.
- There were also many comments indicating the nature of the assistance, such as capacity building, infrastructure development and program expansion.
- I hope we can discuss collaboration online.
- I would like to know the details in order to obtain approval from the organization for cooperation.

Support request with the name of the institution clearly indicated

agency	support area sought
JICA	training and training opportunities
	capacity strengthening
	Strengthening and growing the Kenya Clinical Research Society
	unspecified (3)
Regulatory Agencies & JICA	Capacity Building in PPB
National University Hospital	Clinical trial training and laboratory capacity building
Japanese companies	clinical trial
Japan Research Agency	Study on cervical cancer
Research institution (no specific institution name)	_

The most common areas of hope for capacity strengthening were:

Capacity building
- Regulation (both regulatory and ethics committees)
- GCP inspection
- Development of systems for clinical trial supervision and supervision
- Conduct of clinical trials
- Improved application and approval timelines
- Setting Benchmarks for Ethical Review

Expansion of initiatives
- Collaboration to expand pilot clinical research skills and capacity development projects

opportunity development
- Developing opportunities as an institution for conducting clinical trials, basic science research, and immunological and observational research

Other
- cancer research

Figure 3-37 Comments on collaboration with Japan

Since this seminar attracted a certain number of various clinical trial-related organizations in Kenya, we also included questions regarding challenges related to pharmaceutical regulations and the clinical trial field in Kenya, as well as solutions for challenges requiring support.

In addition to (1) timelines and review schedules, which were the most frequently commented challenges, the following five issues were frequently mentioned: (2) lack of facilities and equipment, (3) opportunities for discussion and collaboration, (4) lack of funds, and (5) lack of human resources, technology, and knowledge. Some commented that they have lost sponsors due to delays in approvals, resulting in insufficient funds, etc., and that tells that each of these five issues is correlated with the others.

Regarding the solutions that should be taken to address the above challenges, there were multiple references to "developing human resources involved in clinical trials" and "promoting collaboration among stakeholders," mainly based on the PPB.

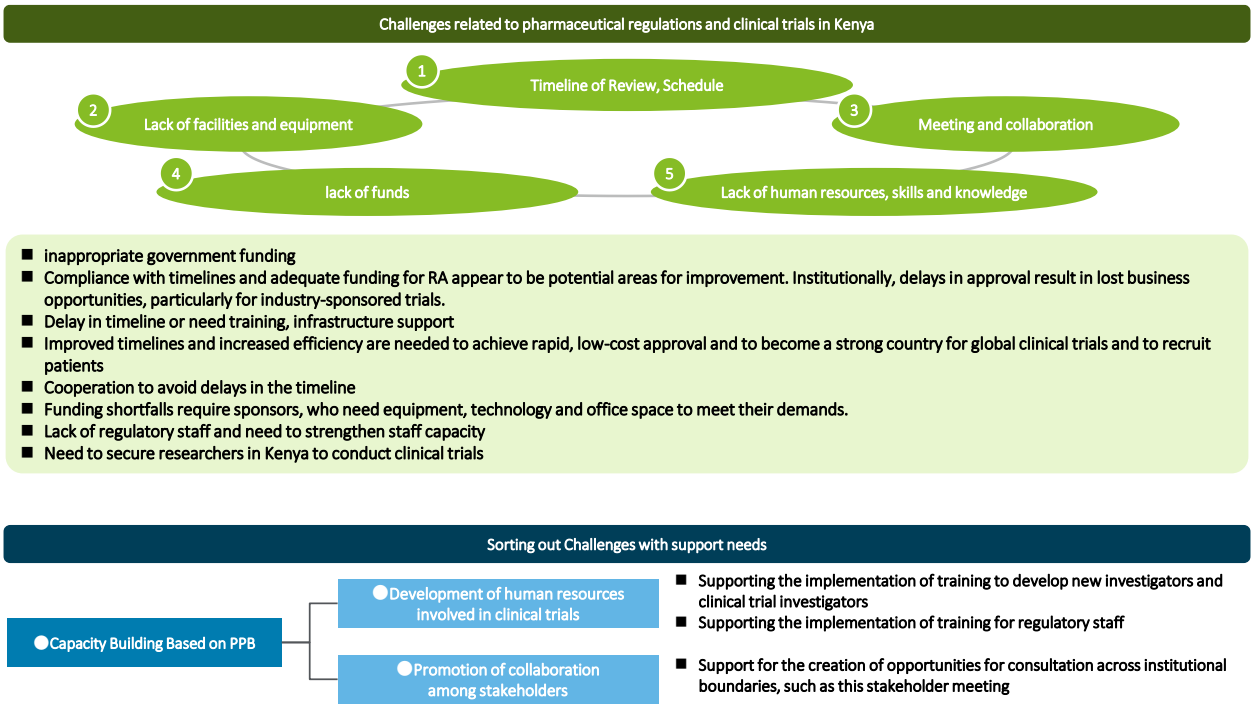


Figure 3-38 Comments related to challenges and solutions in Kenya

Many of the comments as a whole expressed a desire to continue to provide a forum for discussions involving a wide range of organizations involved in clinical trials. Specific reasons given were that involving more people from different institutions would help raise overall awareness, that discussions across institutional boundaries would contribute to building trust and cooperation, and that it would provide a opportunities for sharing information and resources. As points to keep in mind when conducting similar seminars in the future, the participants commented on the need to set specific milestones and to continue to conduct follow ups.

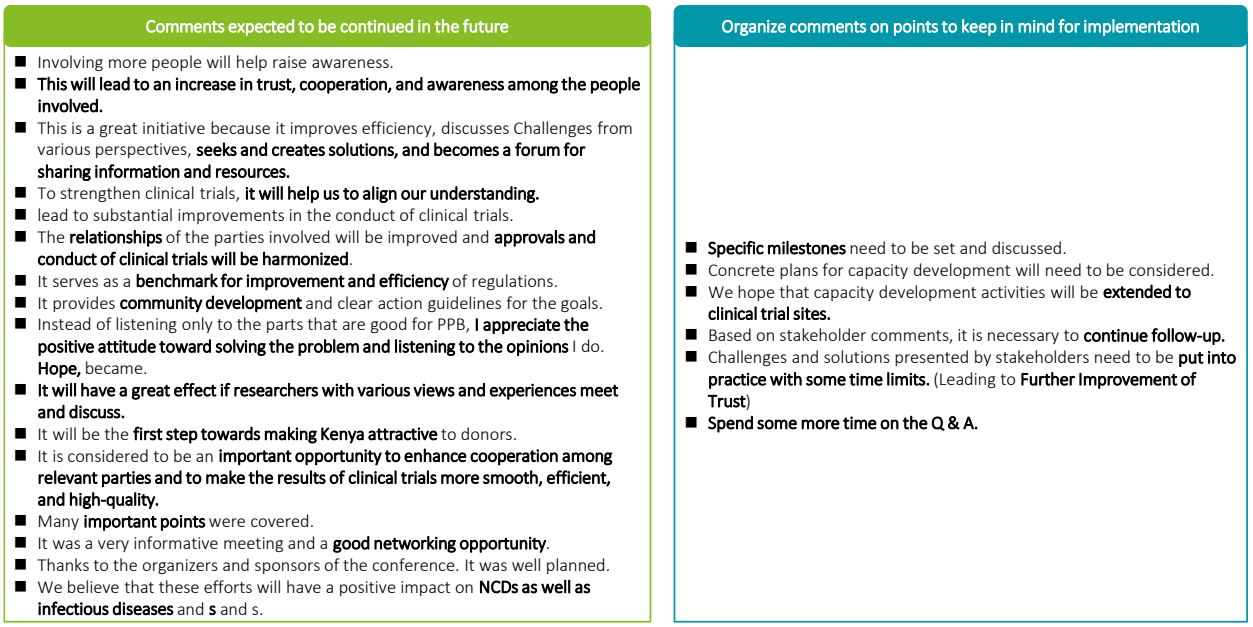


Figure 3-39 Seminar contributions and future notes

3.2.5 Visits to Vietnam and Indonesia

At the invitational training held in Japan in July 2023, the action plan for both participants from Vietnam (University of Medicine and Pharmacy at Ho Chi Minh City (UMP)) and Indonesia (Udayana University Hospital, UUH) was to establish a clinical research promotion center (in Indonesia, a clinical research unit) at their institutions.

During the invited training in Japan, Tatsuya Maruyama, Deputy Director of the Clinical Research Promotion Center, University of Tokyo Hospital, gave a lecture on the formation of the clinical research core hospital system in Japan and the role and function of the Clinical Research Promotion Center. Both participants from Vietnam (UMP) and Indonesia (UUH) expressed their desire to model the role and function of the Clinical Research Promotion Center. Under the theme of "Establishment of the Clinical Research Promotion Center (or the Clinical Research Unit)" in order to conduct a deeper assessment of the current situation and needs based on the context of the institutions in both countries, and to serve as a stepping stone for a proposal to commercialize support services, Deputy Director of the Center Maruyama was dispatched to both countries as a technical advisor to follow up the invited training in Japan.

(1) Vietnam

In December 2023, a local follow-up of UMP was conducted in the following program. The participants are as follows: Mr. Maruyama, three members of the survey team, and two members from the NCGM International Trials Division, the Director of Public Relations and the Vietnam Regional Manager.

Table 3-15 Schedule in Vietnam

DAY 1 20th December (3h30m)	9:00-9:30 (30 mins)	• Courtesy Visit to Chairman of University council and Ag. President of University
	9:30-10:00 (30 mins)	• Introduction on Clinical Research Activities by UMP
	10:00-10:30 (30 mins)	• Site visit (related to clinical trials) UMP
	10:30-11:30 (60 mins)	• Lecture by Dr Maruyama About 60 audiences
		• Q&A to Dr Maruyama
	11:30-12:00 (30 mins)	• Preparation for workshop
DAY 2 21st December (2h-3h)	10:00-11:00 (60 mins)	• Meeting with JICA office (Hanoi/Ho Chi Minh, Online)

	13:30～
	(120 mins ～180 mins)
		• Workshop 11 Participants
		  • Assessment of current situation on development of Clinical Trial Promotion Center
		  • Assessment of Action needs (Training, facility building etc)

		• Wrap up Workshop

On the first day, a courtesy visit was held to greet Mr. Ngo Quoc Dat (Deputy Dean of the Faculty of Public Health) and Mr. Nguyen Duy Phong of UMP. There was also a presentation by UMP, which introduced the facilities and efforts of clinical trials at the university. Next, the lecture on the theme of "Introduction to Clinical Research and the Sustainable Support System" by Dr. Maruyama was carried out. A total of 64 people from several faculties attended the lecture, including university management such as Dr. Ngo Quoc Dat (Vice President), Dr. Nguyen Duy Phong (Deputy Dean of the Faculty of Public Health), Dr. Dang Nguyen Trung An (Head of General Administration Department), Dr. Do Van Dung (Head of Clinical Trial Group), and Dr. Nguyen Thi Hai Lien (Main Coordinator of Clinical Trial Group).

On the second day, as shown in the table below, a workshop was held on the current status of UMP as a clinical trial institution and needs assessment. A total of 16 participants, including senior management (president and vice president), several deans, and members of the Clinical Trial Group, participated.

Table 3-16 List of workshop participants (Vietnam)

	Department	Title	Group
1	Board of Directors	Chairman	A
2	Board of Directors	Vice President	A
3	Board of Directors	Vice President	B
4	Faculty of Public Health	Former Head	C
5	Faculty of Public Health	Head	B
6	University Medical Center HCMC Branch 2	Head	D
7	Faculty of Medicine	Head	A
8	Science and Training Department, UMC	Head	C
9	Center for Molecular Biomedicine	Deputy Head	B
10	Science and Technology Department	Deputy Head	D
11	General Administration Department	Head	B
12	Inspection Legal Department	Head	B
13	Financial Planning Department	Head	D
14	Faculty of Public Health Clinical Trials Unit	Lecturer Main Coordinator	C
15	Clinical Trials Unit	Coordinator	D
16	Clinical Trials Unit	Coordinator	C

Under the theme of "What kind of clinical research promotion center (or the Clinical Research Unit) do you want to build?" the workshop aimed to conduct an assessment of the current situation of universities and the future interventions necessary for the establishment of the Clinical Research Promotion Center (or the Clinical Research Unit). As shown in the figure below, four discussion themes were set.

(1) National and UMP's policies: What is the purpose of the establishment of the Clinical Research Promotion Center (or the Clinical Research Unit) and what mission and functions would you like it to have?

(2) Functions of the Clinical Research Promotion Center (or the Clinical Research Unit): What activities would you like to focus on and promote as the Clinical Research Promotion Center?

(3) Collaboration and support by external organizations: What is the necessary cooperation and support with external organizations for the establishment of the Clinical Research Promotion Center (or the Clinical Research Unit)?

(4) Resources for the clinical research promotion center: What kind of personnel system would you like to establish and what kind of equipment is necessary for the resources and structure of the Clinical Research Promotion Center (or the Clinical Research Unit)?

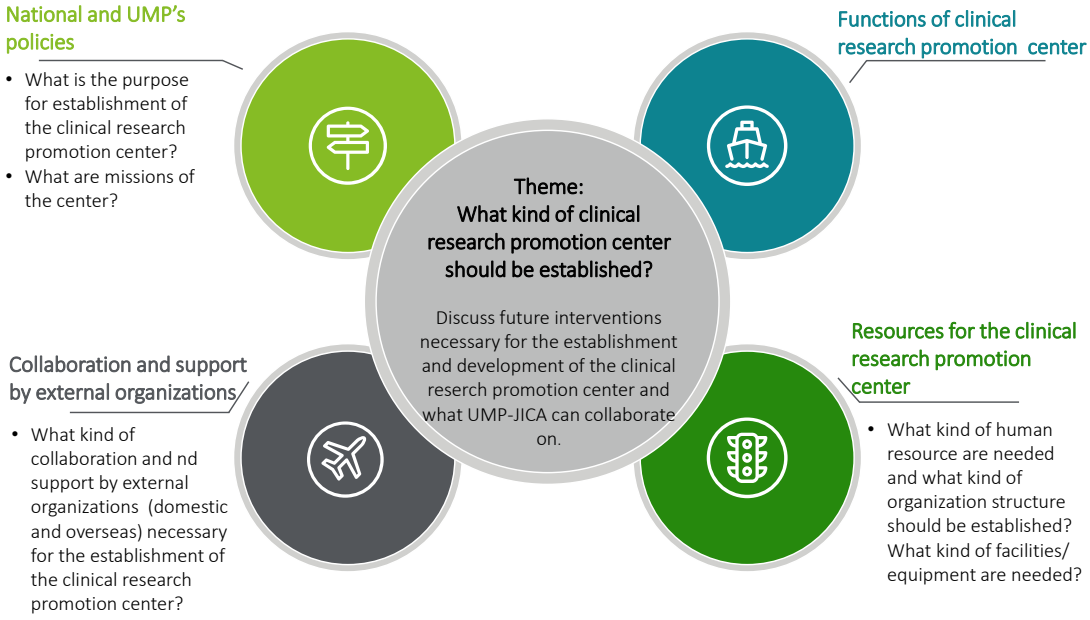


Figure 3-40 Workshop themes (Vietnam and Indonesia)

The participants were divided into four groups (A: National and UMP's policies regarding the establishment of clinical research promotion centers; B: Resources for the clinical research promotion centers (equipment and human resources); C: Functions of the clinical research promotion center; D: collaboration and support by external organizations) according to the four discussion themes shown in the figure above, and each group discussed the assessment of the current situation of the university for the establishment and improvement of the clinical research promotion center, and necessary interventions and activities for the current situation.

After the discussion, the discussions of each group were compiled into a PowerPoint document, which was presented to all participants. The flow of the workshop is as follows.

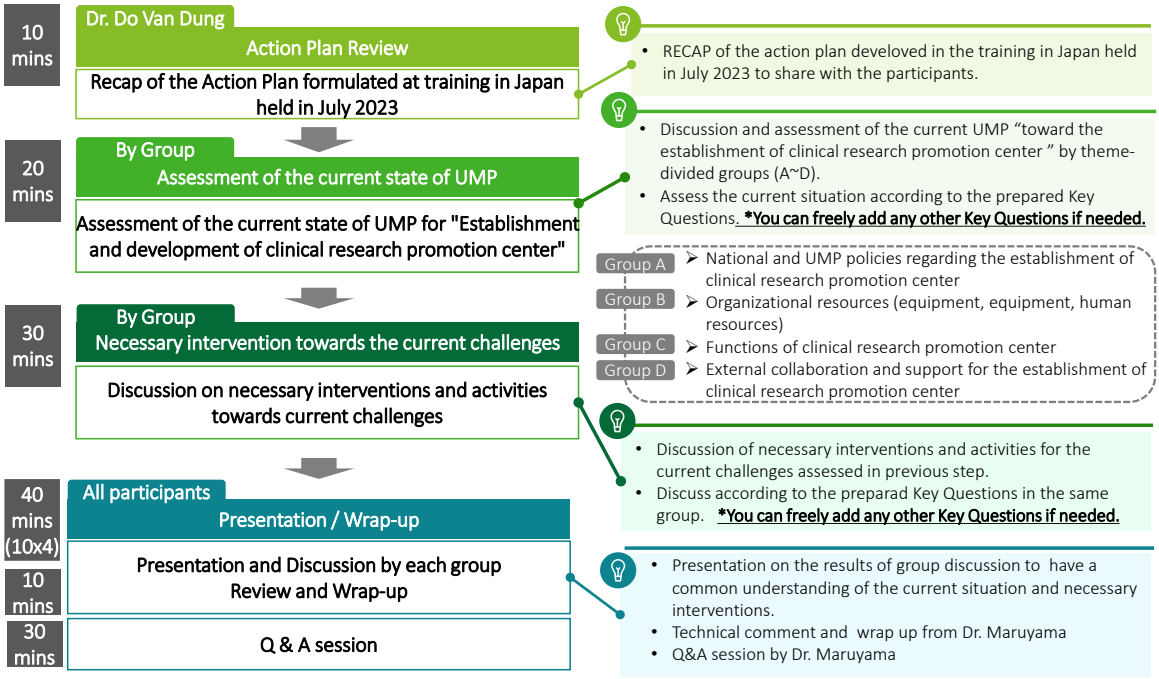


Figure 3-41 Workshop schedule (Vietnam and Indonesia)

As shown in the table below, each group discussed the "assessment of the current state of UMP" and "necessary interventions towards the current challenges" in accordance with the Key Questions that were prepared in advance to facilitate the discussion.

Table 3-17 Key Questions for each group (Vietnam and Indonesia)

		Assessment of Current Situation	Necessary Intervention
A	1	What policy have the government and the Ministry of Health proposed regarding the establishment of clinical research promotion center at national universities?	What kind of policy will University of Medicine and Pharmacy at HCMC (UMP) propose to promote clinical research in the future?
	2	What is University of Medicine and Pharmacy at HCMC (UMP)'s policy on establishing a clinical research promotion center?	What missions would you like to have in clinical research promotion center?
	3	What are the purpose and mission of establishment of the clinical trial center?	Are there any specific areas in clinical research that UMP wants to strengthen and promote?
	4	Are there any national requirements to establish clinical research promotion center? If so, what are the requirements?	What do you think about the possibility of collaboration with other faculties (Ex; Faculty of Engineering, Faculty of Science) ?
B	1	What clinical trial facilities and equipment are lacking	What kind of equipment and facilities should be reinforced to establish a clinical research promotion center?
	2	What kind of clinical trial personnels are lacking? Ex) clinical trial manager/supervisor, clinical trial coordinator, clinical trial doctors/nurse, etc.	What human resources should be strengthened to conduct more clinical trials?
	3	Where are the sources of funding for building organization and resources for clinical research promotion center?	What are the specific themes of training for human resources that should be strengthened in the future?
	4	Is it possible to exchange human resources with private companies?	
C	1	What are the current missions and roles of the Clinical Trial Group at UMP?	What kind of organizational structure is ideal for the future clinical research trial center?
	2	How is the current organizational structure of the Clinical Trial Group?	What kind of functions and roles should be equipped with clinical research promotion center in future?
	3	What are the current activities conducted by Clinical Trial Group ?	What kind of infrastructure/human resources are necessary to implement the above functions at clinical research promotion center?
D	1	Which domestic organizations are currently working with UMP and how are they collaboration together for clinical research activities? Ex) Clinical Trial Network, Collaborative Research, Human Resource Exchange/Training, etc.	What kind of collaboration would you like to promote to establish clinical research promotion center with external organizations ?
	2	Which overseas organizations are currently working with UMP and how are they collaboration together for clinical research activities? Ex) Clinical Trial Network, Collaborative Research, Human Resource Exchange/Training, etc.	What cooperation and support do you need from JICA to establish clinical research promotion center?

The table below shows the results and discussion points of each group (A-D).

Group A National and UMP's policies regarding the establishment of clinical research promotion centers

	Assessment of the current state of UMP	Necessary interventions
Key Question	What policy has the government and the Ministry of Health come up with regarding the establishment of clinical research promotion centers at national universities? What is the policy of Ho Chi Minh University of Medicine and Pharmacy regarding the establishment of the center? For what purpose do you want to create a center? Which national requirements are required for the establishment of clinical research promotion centers? If so, what are the requirements?	What kind of policy does Ho Chi Minh University of Medicine and Pharmacy want to propose to promote clinical research in the future? What functions would you like to have in a clinical research promotion center? Are there areas that you want to strengthen and promote? What do you think about the possibility of cooperation with other faculties (Faculty of Engineering and Faculty of Science)?
Group Discussion	• A clear policy direction by the national government (Ministry of Health) for the establishment of a clinical research promotion center has not been formulated. Therefore, the function of the Clinical Research Promotion Center should be clarified. • At Ho Chi Minh University of Medicine and Pharmacy, the role of the Clinical Research Promotion Center is as follows: ① Management and training in the conduct of clinical research ② Conduct a variety of clinical trials, including physician-led and company-led trials ③ Building a network for conducting international clinical trials ④ Clinical Trial Promotion Center Functions/International Standards for Clinical Trials	• Policy development at the domestic level is necessary. • Ho Chi Minh University of Medicine and Pharmacy should have a plan to pilot the establishment of a clinical research promotion center. • The functions of the Clinical Research Promotion Center are as shown in (1) - (4) below. In addition to these, (5) We would like to support the establishment of clinical research promotion centers in other academic institutions, and have functions to assess and strengthen clinical research capacity. (become a core institution in Ho Chi Minh City) • Clinical research areas to be strengthened as Ho Chi Minh University of Medicine and Pharmacy are as follows. ① Infection ② Cancer, diabetes ③ Vietnamese traditional medicine

Discussion Points

■**Commitment to the Ministry of Health**
- Although the promotion of clinical research is a national policy (In particular, UMP is very focused on the local development and production of drugs and vaccines), there are currently no specific national policies or guidelines for the establishment of clinical research promotion centers.
- In considering commercialization, it is essential to make a commitment to the Ministry of Health, but it is hoped that the proposal will be made in cooperation with JICA and not with universities alone.

■**Incorporation with Hanoi Medical University as a strategy**
- It is essential to standardize the activities for the establishment of the center in line with Hanoi Medical University, the country's top clinical trial institution.
- Japan's support comes from a desire to increase the number of international joint research networks. In order to achieve this goal, we would like to consider the incorporation of the Hanoi University of Medicine and Pharmacy, which is a top clinical trial institution in Japan and has a rich record of international collaborative research, in order to provide support.
- At present, there is no specific cooperation with Hanoi Medical University in the field of clinical research, but the university would like to cooperate with Hanoi Medical University.

Figure 3-42 Results of discussion in Group A (Vietnam)

Group B Resources for the Clinical Research Promotion Center (facilities, equipment, human resources)

	Assessment of the current state of UMP	Necessary interventions
Key Question	What is currently lacking in clinical testing equipment? What kind of clinical trial talent is lacking? Ex Investigator/supervisor, clinical trial coordinator, clinical trial physician/nurse, etc. Where are the sources of funding for building systems and resources? Is there a possibility of human resource exchange with private companies?	What kind of equipment and equipment should be reinforced to establish a clinical research promotion center? What human resources should be strengthened to conduct clinical trials? What are the specific topics of training for human resources that should be strengthened?
Group Discussion	• Current clinical trial facilities in need include the establishment of a central laboratory facility and a recruitment center (Recruitment of human resources for clinical trials and landowners). • The number of doctors and nurses involved in clinical trials is sufficient, but there is a lack of investigators/supervisors and data managers capable of clinical trial data management and analysis. • Funding sources for building systems and resources include universities, ministries of health, aid agencies, and companies. • Talent exchanges with private companies are currently difficult and unlikely.	• The necessary personnel to be strengthened are managers and supervisors who can manage clinical trial data and perform statistical analysis. • Specific training themes to be strengthened are in the areas of clinical trial data management and statistical analysis.

Discussion Points

■**Finance the independent operation of the university**
- An independent monetization perspective that would fund the Center's own operations without relying on grants from the Ministry of Health or support from international aid agencies is also important. (Even in the clinical trial core hospital in Japan, the generation of the original fund is an issue)
- Academic clinical trial centers and university hospitals in Japan face a constant shortage of funds, and it is important how to raise funds well. It is also important to secure funds in a way to further promote corporate clinical trials.

■**Need for diverse human resources**
- It's great that people recognize the need for the involvement of various human resources, such as those who manage and those who ensure safety. Many such human resources exist in companies, but academia tends to lack them. Therefore, it is advisable to consider cooperation with other faculties now.
- Collaboration with teachers at other universities is especially important during investigator-initiated clinical research. Funding is also needed to increase such human resources.

Figure 3-43 Results of discussion in Group B (Vietnam)

Group C Functions of the Clinical Research Promotion Center

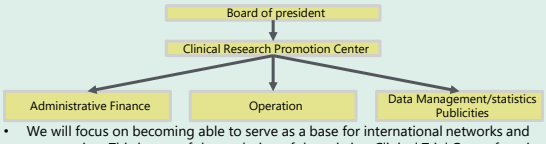
	Assessment of the current state of UMP	Necessary interventions
Key Question	What is the current mission and role of the Clinical Trial Group on campus? What is the current organizational structure of the Clinical Trial Group? What exactly is the Clinical Trial Group doing now?	What kind of organizational structure do you want the Clinical Trial Group to develop in the future? What role does the Clinical Trial Group want to focus on in the future? What resources are needed to implement the focus?
Group Discussion	• The current Clinical Trial Group is the predecessor of the Center for the Advancement of Clinical Research and was established after COVID-19 with the mission of promoting clinical trial efforts. • Individual clinical trials are conducted independently in the department, and administrative support is provided for the conduct of these trials. ① Support for project protocols such as Principal Investigators (PIs) ② Institutional Review Board (IRB) ③ Follow-up and monitoring of ongoing clinical trials ④ Finding Sponsors ⑤ Data collection and data input ⑥ Import of chemicals and equipment	• Currently, the Clinical Trial Group has a single organizational structure, but we would like to have the following organizational structure.  • We will focus on becoming able to serve as a base for international networks and cooperation. This is part of the evolution of the existing Clinical Trial Group function. • We would like to set up a center base independently in the existing building and floor.
Discussion Points	■Join ARISE • Currently, the Clinical Trial Group serves only as a support for the implementation of clinical trials on campus, but one of the functions that we would like to develop as a clinical research promotion center is to be able to serve as an international network and collaboration center. For that reason, I would like to join ARISE. • With 103 clinical trials conducted in 5 years and a good track record of industry-led clinical trials, it is considered sufficient as a requirement for membership in ARISE. The NCGM welcomes membership, and we would like to enter a concrete dialogue process for future membership. ■Increase in the number of investigator-initiated trials • Most of the clinical trials currently being conducted at universities are based on research that has largely received protocols from pharmaceutical companies. • Future investigator and physician-led clinical studies will require capacity building to enable study design. ■Role of guidance to other organizations • As one of the top medical universities in Vietnam, we feel that we also have a role in teaching other institutions.	

Figure 3-44 Results of discussion in Group C (Vietnam)

Group D Cooperation and support by external organizations (domestic and overseas)

	Assessment of the current state of UMP	Necessary interventions
Key Question	At present, which domestic organizations and how do they cooperate in clinical research activities? Ex Clinical Trial Network, Collaborative Research, Human Resource Exchange, Training, etc. At present, with which overseas organizations do clinical research activities, what kind of cooperation do they have? Ex Clinical Trial Network, Collaborative Research, Human Resource Exchange, Training, etc.	What kind of collaboration with external organizations would you like to promote to establish a clinical research promotion center? What cooperation and support do you need from JICA? What should be considered when working with external organizations?
Group Discussion	• Cooperation with domestic organizations is relatively rare, but there are more cases of cooperation with overseas organizations. For example: ① Shionogi (Medicine to treat COVID-19) ② Janssen (Dengue) ③ KOICA(Medical Education for future, academia and industry) ④ Spirokit, AstraZeneca, Takeda Pharmaceutical, Pfizer, MSD, GSK • A 5 year, $15.8 million IMPACT-MED project from USAID (Of these, the curriculum for the graduate course is provided to UMP.)*1 andcollaboration with Harvard Medical School *2	• We would like to cooperate with domestic organizations in the field of training. ① Comprehensive clinical trial training (In particular, study design and data management) ② ToT for clinical trial leaders ③ Training to become a Principal Investigator • JICA should receive support for policy advocacy and human resource development. Seed Grant to support seed-stage research • Points to consider when working with external organizations are sharing the following findings. ① Intellectual property rights ② Scope of responsibility and benefits ③ Benefit to patients
Discussion Points	*1https://www.usaid.gov/vietnam/fact-sheets/improving-access-curriculum-and-teaching-medical-education-and-emerging-diseases-impact-med-alliance *2 https://www.usaid.gov/vietnam/news/apr-28-2023-usaid-supports-locally-led-medical-education-reforms ■Overseas cooperation • In the future, researchers will be able to design their own protocols and further promote clinical research in Southeast Asia. We would like to strengthen the management and quality of clinical research promotion research. We believe that quality security will be very important not only for domestic research but also for cooperation with overseas institutions. ■Expectations for support for human resource development • We would like to receive support using JICA's scheme for the development of multifaceted human resources. It is necessary to develop diverse human resources such as human resources for clinical trial management and administration (CRC, etc.), human resources for quality control, and human resources for data management and analysis, as well as clinical personnel for physicians and researchers.	

Figure 3-45 Results of discussion in Group D (Vietnam)

The results and discussion points of each group are summarized as follows.

i. High UMP Commitment

Although the workshop was less than three hours, the members of the upper management of the university, including the president, the vice president, and the principal deans (four faculties), gathered together for a discussion with staff from the field, which showed the high level of commitment to strengthening the clinical research capacity of UMP and establishing a clinical research promotion center.

ii. Membership in ARISE

In the discussion after the lecture and workshop by Dr. Maruyama, both the President and the Vice President declared their intention to join ARISE. The NCGM also recognized the significance of UMP's membership as a base in Ho Chi Minh City, which has not been established in ARISE at present, and expressed the view that it had sufficient clinical research records for its membership. The NCGM stated that it would like to start a dialogue for membership in the future. By joining ARISE, we believe it will be easier to cooperate and collaborate with NCGM if we are to commercialize support in the future.

iii. Future challenges for commercialization

While Vietnam's national policy is to manufacture and supply its own drugs and vaccines, it has a major policy of strengthening clinical research, the workshop found that the national policy does not specifically mention the establishment of clinical research promotion centers at national universities and hospitals. Therefore, in considering the commercialization of the establishment of a clinical research promotion center, it is essential to make a commitment to the Ministry of Health, but the hope was raised that JICA would cooperate with the universities in approaching the Ministry of Health and not with the universities alone.

It was also discussed that it is essential to standardize the activities for the establishment of the center in line with Hanoi Medical University, which is the top clinical trial institution in Vietnam, if the Ministry of Health is to set policy at the domestic level. Japan's support comes from a desire to increase the number of international joint research networks. In order to do so, we would like to consider the incorporation of Hanoi Medical University, which is a top clinical trial institution in Vietnam and has experience of international collaborative research, in order to provide support. At present, there is no specific collaboration with Hanoi Medical University in the clinical research field, but the university would like to cooperate with Hanoi Medical University. In considering future cooperation programs, it should be taken into consideration that the contents of the cooperation with Hanoi Medical University by JICA and ARISE are aligned with those of Hanoi Medical University.

(2) Indonesia

In January 2024, a follow-up session was conducted at Udayana University Hospital (UUH) under the following program: the total number of traveling members was seven people, including Dr. Maruyama, Deputy Director of the Clinical Research Promotion Center, three survey team members, a Specially Appointed Researcher of Project Development and Operation and Indonesia Regional Manager of the NCGM International Trial Division, and JICA individual experts assigned to the Ministry of Health.

Table 3-18 Schedule in Indonesia

DAY 1 15th January At UUH	8:30-9:00 (30 mins)	• Courtesy Visit to Hospital Director and President of University
	9:00-9:30 (30 mins)	• Introduction on Clinical Research Activities by Udayana University
	9:30-10:00 (30 mins)	• Site visit (Udayana University) University grounds
	10:30-11:30 (60 mins)	• Lecture by Dr Maruyama 50-60 participants
		• Q&A to Dr Maruyama
	13:00-16:00 (120-180 mins)	• Workshop 15 participants
	Evening	• Dinner hosted by UUH
DAY 2 16th January	7:00~	• Flight to Jakarta
	15:00	• Meeting with Ministry of Health
	16:30-17:30	• Meeting with JICA Indonesia Office

In the field activities, in addition to a courtesy visit to the President of UUH, the President of Udayana University, the Dean of the Faculty of Medicine, etc., presentations were given on the facilities and initiatives of clinical trials at UUH, and a lecture was given by Dr. Maruyama. A total of 48 people attended the lecture. During the Q&A session, participants asked about the challenges of establishing the Clinical Research Promotion Center at the University of Tokyo Hospital and the details of funding for the center.

After Dr. Maruyama's lecture, a workshop was held on the current status of UUH as a clinical trial institution and needs assessment. Similar to the workshop conducted in Vietnam, the participants were divided into four groups (A: National and UUH's policies regarding the establishment of clinical research units; B: Resources for the clinical research promotion centers (equipment and human resources); C: Functions of the clinical research promotion center; D: collaboration and support by external organizations), and each group discussed the assessment of the current situation of the university and the necessary interventions and activities for the current situation to establish and develop a clinical research promotion unit. As shown in the table below, the total number of participants in the workshop was 15 people.

Table 3-19 List of workshop participants (Indonesia)

	Department	Title	Group
1	Public Health	Prof. dr. – MPH, Ph.D	A
2	OHCC Udayana	S.KM., MPH	A
3	Farmacology and Therapy	Dr. dr. – M.Sc	A
4	Microbiology	dr. – S.Ked, Ph.D	A
5	Anatomy Pathology	dr - SpPA	B
6	Microbiology	Ssi, Mbiotech, Ph.D	B
7	Pediatric	dr	B
8	Pediatric	dr – SpA(K)	B
9	Farmacology and Therapy	Dr. dr. – S.Ked., M.Kes	C
10	Neurology	Dr. dr. - SpN	C
11	Clinical Pathology	dr - SpPK	C
12	Pediatric	dr – M.Sc., SpA(K)	C
13	Farmacology and Therapy	Ph.D., Apt	D
14	Microbiology	Dr. dr. – M.Ked	D
15	Farmacology and Therapy	dr – M.Med.Ed., PhD	D

Each group compiled the discussion into a PowerPoint document that was presented and shared with all participants.

The table below shows the results and discussion points of each group (A-D).

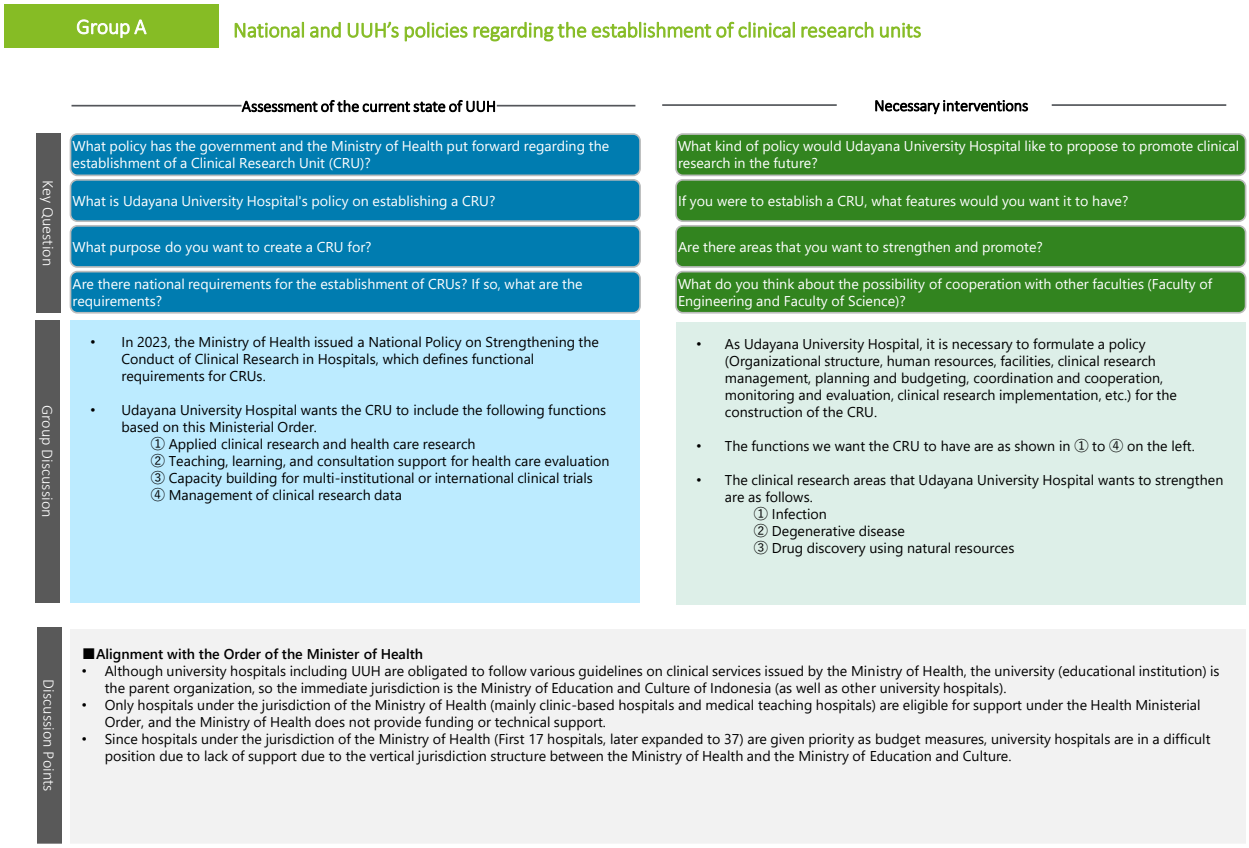


Figure 3-46 Results of discussion in Group A (Indonesia)

Group B　Resources for the Clinical Research Promotion Center (facilities, equipment, human resources)

	Assessment of the current state of UUH	Necessary interventions
Key Question	What is currently lacking in clinical testing equipment?	What kind of equipment and equipment should be reinforced to install a CRU?
	What kind of clinical trial talent is lacking? Ex Investigator/supervisor, clinical trial coordinator, clinical trial physician/nurse, etc.	What human resources should be strengthened to conduct clinical trials?
	Where are the sources of funding for building systems and resources?	What are the specific topics of training for human resources that should be strengthened?
	Is there a possibility of human resource exchange with private companies?	

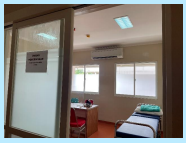
Group Discussion	• UUH has a facility, but it needs separate facilities for clinical trials because it shares the clinical trial lab and the human subjects ward with regular clinical services.
	• Equipment capable of Phase 1 trials is required.
	• There are doctors, nurses, and lab staff involved in clinical trials, but they all serve concurrently. Full-time staff for clinical trials is needed. Other staff members are also needed, including trial managers, CRCs, data management, biostatistics, information systems management, education and training, ethics, and clinical trial communications.
		• Specific training themes to be strengthened are in the areas of clinical trial data management and statistical analysis.
		  • GCP/GLP
		  • Quality control monitoring
		  • EBM
		  • Systematic review
		  • Biostatistics
		  • Protocol preparation

Discussion Points

■Need for diverse human resources
- Although there are researchers themselves, training is planned for those who are interested in GCP at university hospitals. Training in clinical trial management, monitoring, and statistics is also planned. Other human resources are needed to provide training on GCP, IT staff to put data into practical use, and human resources to manage and analyze data.
- In order to establish a CRU, the hospital is conducting its own training including GCP. In order to expand the training content and increase the number of trainees, it is considered that JICA's training scheme can be utilized.

Figure 3-47 Results of discussion in Group B (Indonesia)

Group C　Functions of the Clinical Research Promotion Center

	Assessment of the current state of UUH	Necessary interventions
Key Question	What is the current mission and role of CRU on campus?	What kind of organizational structure do you want the Clinical Trial Group to develop in the future?
	What is the current organizational structure of the CRU?	What role does the Clinical Trial Group want to focus on in the future?
	What exactly is the CRU currently doing?	What resources are needed to implement the focus?
Group Discussion	• The COVID-19 booster vaccine Phase 3 trial is underway, and the CRU is gradually being equipped. There are examination and examination rooms for subjects and information service rooms for subjects.   • The current CRU does not have a specific organizational structure or functional definition, but rather operates around the Phase3 test project described above.	• As an academic hospital, we have received many offers to conduct trials, but the facilities and other facilities are not yet in place, and the protocol is still difficult to develop. We would like to accept such offers.

Discussion Points

■Need for clinical trial administration functions
- In anticipation of an increase in the number of clinical trials, it is necessary for the management of multiple clinical trials to pre-template the administrative processes involved in conducting clinical trials, such as contracts with subjects, sponsors, and collaborating institutions.

Figure 3-48 Results of discussion in Group C (Indonesia)

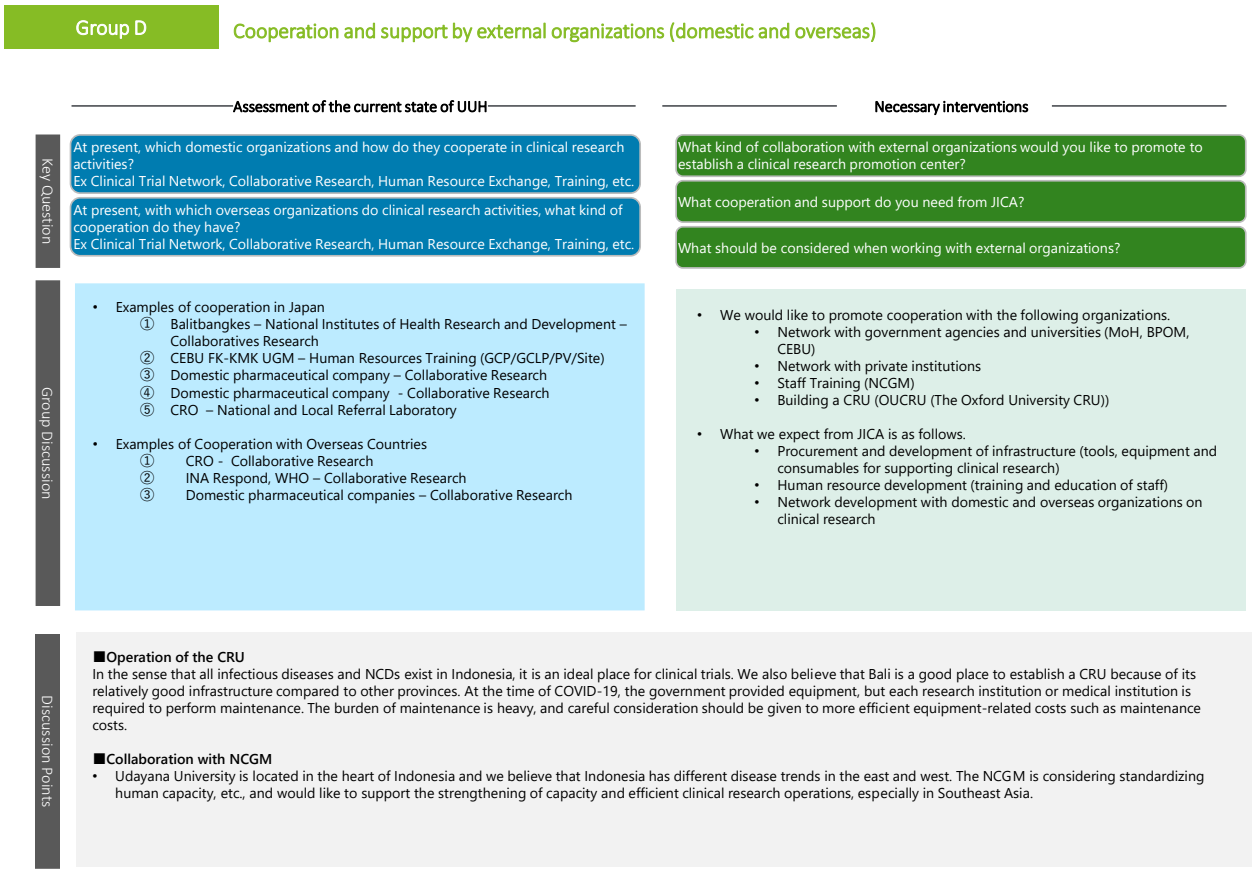


Figure 3-49 Results of discussion in Group D (Indonesia)

The results and discussion points of each group are summarized as follows.

i. Alignment with the Order of the Minister of Health of Indonesia issued in 2023

In Indonesia, the Ministry of Health issued a notification in October 2023 that clinical research units (CRU) would be established in major hospitals across the country. Since the COVID-19 pandemic, UUH is expected to strengthen its clinical research as an "academic hospital," and it has become clear that UUH has become an urgent support need throughout the hospital.

On the other hand, the parent organization of UUH is a university (educational institution), and the immediate jurisdiction is the Ministry of Education and Culture of Indonesia. The Minister of Health Order gives priority to hospitals under the direct jurisdiction of the Ministry of Health, such as clinic-based hospitals and medical teaching hospitals, and UUH is in a difficult position to receive budgetary measures and technical support from the Ministry of Health.

ii. Development of facilities and staff for smooth implementation of clinical trials

UUH shares the laboratory and human subjects wards for clinical trials with regular clinical services and does not provide independent facilities for clinical trials. During the discussion, there was a comment that there was a need for an environment in which Phase I clinical trials could be conducted, in particular. Doctors, nurses, and laboratory staff are all working concurrently with clinical services on clinical trials, and the implementation system needs to be reviewed to ensure that staff are available to conduct trials full-time.

iii. Building clinical trial administration

Although UUH has received many offers to conduct clinical trials from external organizations, it does not yet have the necessary facilities for clinical trials or the (Not only the investigators, such as doctors and nurses, but also the administrative departments that support the conduct of clinical trials) organization and

personnel system to support them. Under such circumstances, in order to accept offers from external organizations and increase the performance of joint clinical trials in the future, it is necessary to establish administrative processes for conducting clinical trials, such as contracts with subjects, sponsors, joint research institutions, etc., and to introduce and strengthen a system that enables clinical trials to be started and operated smoothly.

In addition, an interview was held with the Ministry of Health of Indonesia, where the following topics were discussed.

iv. Interview with the Indonesian Ministry of Health

Details on the implementation plan of "Order of the Minister of Health on the implementation of clinical research in hospitals" were heard. The Clinical Trial Unit (CRU) is to be established in hospitals under the direct jurisdiction of the Ministry of Health, but under the current Cabinet Order, 17 hospitals are to be given priority. However, the revision of the Ministerial Order was considered in January 2024, and it was decided that the scope of application would be expanded from 17 hospitals to 37 hospitals. However, all hospitals under the jurisdiction of the Ministry of Health are subject to support for the implementation of the Cabinet Order, and the Ministry of Health provides budget measures and technical support only to these hospitals under the Ministerial Order. University hospitals under the Ministry of Education and Culture are not supported by the Ministry of Health. In other words, the Ministry of Health and the Ministry of Education and Culture split the jurisdiction of public medical institutions vertically, so it became clear that there was an incompleteness in the fact that university hospitals such as UUH were not covered by the ministerial ordinance.

The Ministry of Health recognizes the importance of establishing CRUs at university hospitals, which are the main players in medical research activities, in order to strengthen the implementation of clinical research activities nationwide. However, due to the above-mentioned vertical structure of the two ministries, there is no direct instruction system at university hospitals. The Ministry of Health stated that it would like to resolve this incompleteness with the support of international aid agencies for hospitals outside the Ministry of Health's jurisdiction. If Japan were to support the establishment of a CRU at UUH, there were calls for cooperation with Ngoerah Hospital in Bali (included in the priority 17 hospitals) to support the establishment of a CRU at both hospitals.

3.3 Pilot activity results 2 : Matching between Indian and Japanese companies

Matching with Indian companies was not a candidate for implementation at the time of narrowing down the pilot activity proposal, but it was decided to add matching with Japanese companies since Indian officials from both the public and private sectors expressed their expectations for a win-win partnership on an equal footing during previous interviews. In addition, vaccine companies affiliated with the IVMA (Indian Vaccine Manufacturers Association) in particular strongly requested matching with Japanese companies.

Undisclosed

Undisclosed

Undisclosed

A total of six Japanese companies were mentioned by IVMA-affiliated vaccine companies in India, as potential candidates for matching. A questionnaire was sent to each of them regarding the assumed image of matching, reasons for wanting to cooperate, and the assumed cooperation method.

Indian companies listed out their various needs in the field of drug and vaccine development, but after coordinating with the Japanese companies based on the Indian companies' needs, one match was made, and the survey team decided to support and promote the matching for the influenza and hepatitis A vaccine.

An initial meeting was arranged by the survey team, and presentations on company profiles were made by both Indian and Japanese companies, followed by an exchange of views and a question-and-answer session, in which questions were asked about technical aspects of vaccines, mainly the reasons for manufacturing vaccines for each number of doses, the number of adverse reactions, and the mechanism of problems caused by vaccines.

As a follow-up to the initial meeting, an interview was held in January 2024 on the progress of communication between the two companies and future cooperation. Based on the current status of the consultations, the interviews focused on the following topics: the points to be discussed for future cooperation, the points that are considered important for promoting matching and cooperation between Indian and Japanese companies, and the expectations of JICA or Japanese public organizations in promoting matching.

As a point of discussion for future cooperation, it was mentioned that it is very important for both Indian and Japanese companies to be able to replicate the vaccine manufacturing process in India. In addition, Indian companies wanted to comprehensively check the efficiency and quality control of manufacturing processes, and the certification materials of regulatory authorities in Japan. Japanese companies also wanted to check in advance whether their partner companies would use their own funds to cover the costs of cooperation, because they were concerned that if they received government funds, there would be a risk of cash flow in the event of a change in government.

In addition to the above points, in order to promote cooperation between Indian and Japanese companies in the future, some respondents suggested that generic drugs, rather than new drugs, should be selected as the target products in order to reduce the hurdle for cooperation.

In addition, in order to promote cooperation between the private sector in India and Japan, JICA and Japanese public organizations are expected to create matching opportunities through the introduction of Japanese companies from the standpoint of Indian companies, and to introduce government officials necessary for local business development from the standpoint of Japanese companies.

Table 3-23 Comments from the follow-up interview

Discussion points	Indian companies	Japanese companies
Confirmation and discussion points toward the realization of future cooperation	✓ Reproducibility of the manufacturing process in India ✓ Efficiency of the manufacturing process ✓ Adherence to WHO guidelines for quality control (Check whether it in line with international standards guidelines because the WHO also provides vaccines to UNICEF and Gavi) ✓ Advantages over other products ✓ Confirmation of certification materials obtained from Japanese regulatory authorities	✓ Funding for cooperation ✓ Reproducibility of the manufacturing process in India (whether it can compensate for the expensive machines handled in Japan or the machines not available locally)
Important point to promote matching between Indian and Japanese companies	✓ Because of the impression that Japanese regulations are strict, whether or not Indian companies have certification from Japanese regulators can be an important point of view in deciding whether or not to cooperate ✓ As with this pilot activity, it is also important for third parties to participate in communication support leading to collaboration ✓ Generic drugs are easier to share information with and faster to match than new drugs	✓ It is important to determine whether the cooperation is realistic from the viewpoint of the funding and capacity (e.g., technical capability) of the other company ✓ It is also important to consider whether the company will cooperate with government support or whether it will cooperate with its own funds, as this will affect the company's financial position in the event of a change in government ✓ Since the Common Technical Document (CTD) and WHO Pre-Qualification may be required in many countries including India, the development of the CTD may be a barrier for Japanese companies to cooperate with overseas companies
Expectations of JICA and Japanese public institutions in regard to matching	✓ We would like you to introduce and match Japanese companies and provide opportunities to connect with Japanese companies	✓ Request advice when considering the establishment of a new local subsidiary ✓ Support the connection to local ministries and key persons

3.4 Pilot activity results 3 : Sensitive detection technology PoC by wastewate surveillance

In this PoC, surveillance of SARS-CoV-2 RNA genome in wastewater and measuring the effectiveness of reagents, and validation of monitoring process were conducted in Indonesia, using reagents with the COPMAN method, which is a Japanese technology, with the aim of making concrete proposals for future business development regarding wastewater surveillance to officials from the Indonesian Central and Provincial Governments, WHO/SEARO, other donors, Japanese relatedinstitutions, and others.

Technical training and demonstration experiments using Japanese technology were conducted based on the samples collected at four locations in Indonesia. A total of approximately 200 wastewater samples collected from the four locations includingWastewater Treatment Plant (hereinafter referred to as WWTP) were subjected to extraction, detection, and analysis. In order to ensure the reliability of the PoC in different WWTPs, the sampling sites were expanded to additional three locations, where a total of 250 wastewater samples were analyzed.

The results showed that SARS-CoV-2 was detectable in all of the WWTPs targeted in this demonstration; WWTPs was the plant that wastewater from the three areas is collected and primary, secondary, and tertiary treatment takes place, and the WWTP was confirmed to be an appropriate source of information to represent and quantify SARS-CoV-2 in the area targeted by this demonstration. On the other hand, subdivision of the area confirmed that the pattern of variation in SARS-CoV-2 differed from district to district, and it represented the infection trend in each targeted district. The correlation between wastewater surveillance and positive cases was also investigated and the results indicated that there is a correlation.

Based on the results of the trial demonstration project above, it could be said that SARS-CoV-2 detection by wastewater surveillance in Indonesia can be applied in areas under the jurisdiction of the Regional Technical Implementation Unit for Wastewater Management in Indonesia, as well as in cities and districts with different characteristics. Surveillance is effective in confirming viral trends and may provide early

warning and early detection of epidemic conditions before the next pandemic or public health risk assessment.

(For more detailed data and analysis results, refer to Appendix 2 " Final report of PoC for wastewater based epidemiology surveillance in Indonesia ".)

3.5 Verification of effectiveness of trial implementation

3.5.1 Method of verification of effectiveness

Through the invitation to Japan which is the first pilot activity, each country or institution developed an action plan to strengthen the capacity to conduct clinical trials and had better understanding about the needs of each country/institution. As described in the previous section, the six pilot activities listed in the table below were proceeded while assessing the situation according to the background and context of each country and institution.

Table 3-24 List of pilot activities (since the July 2023 Japan visit)

No.	Pilot Activity	Subject Country	Target Institution	Time
(1)	Assessment of the establishment of an academic Clinical Research Promotion Center and the strengthening of the capacity to conduct clinical trials, including the conduct of phase I trials (Follow up after Japan visit)	Vietnam	University of Medicine and Pharmacy at Ho Chi Minh City (UMP)	2023/12
(2)	Assessment of establishment of clinical research units in hospitals and human resource development for clinical trials (Follow up after Japan visit)	Indonesia	Udayana University Hospital (UUH)	2024/1
(3)	Consideration on strengthening the capacity of clinical trial examiners and inspectors and standardization of examination and inspection (Follow up after Japan visit)	Philippines	Philippine Food and Drug Administratio (PFDA)	2023/12~ 2024/1
(4)	Verification of effectiveness of IGRA to detect latent tuberculosis and consideration of collaboration with Japanese private companies (Follow up after Japan visit)	Thailand	Faculty of Medicine Siriraj Hospital, Mahidol University Siriraj Institute of Clinical Research (SiCRES)	2023/10 2023/11
(5)	Conducting sensitization meetings for clinical trial stakeholders based on regulatory agencies (Follow up after Japan visit)	Kenya	Pharmacy and Poison Board (PPB)	2023/10~ 2024/1
(6)	Matching of Indian biotech companies and Japanese companies	India	Indian Pharmaceutical and Vaccine company / Japanese Pharmaceutical company	2023/10~ 2024/1
(7)	Conducting a demonstration test	Indonesia	District Research and	2022/9~

	of highly sensitive virus detection technokogy using wastewater monitoring		Innovation Agency (BRIDA), Wastewater Treatment Plant (WWTP)	2024/1

The table below lists six indicators that should be considered when measuring the effectiveness of pilot activities. These indicators were selected to provide a basis for JICA to consider whether or not to intervene in support in the future. The details of the criteria for measuring effectiveness are also shown in the table below.

Table 3-25 Indicators for verification of effectiveness of pilot activities

Indicator	Overview
Indicator (1) Scope of Challenge Solving	・ The group of challenges that the interventionwill contribute to resolve
Indicator (2) Commitments of target institutions (implementation structure and budgetary measures)	・ The level of commitment of the target country/ institution ・ Whether if there is an implementation framework in place in the target country/ institution ・ Whether if there is a budgetary framework in place in the target country/ institution
Indicator (3) Impact on target country's policy/ urgency of needs	・ Whether if it is consistent with basic national policy ・ Whether if there is a detailed roadmap, implementation plan, guildeline, etc., as part of the national policy
Indicator (4) Collaboration and ripple effects within the target country	・ Whether if there is potential for collaboration with related institutions in the target country and for ripple effect ・ Whether if potential partners have already established a framework for collaboration or have reached an agreement on collaboration
Indicator (5) Contributions and cooperation with Japanese institutions	・ Whether if there is potential for collaboration with related institutions and for ripple effect in Japan ・ Whether if potential partners could confirm the collaboration and if there is sufficient benefit from collaboration between target country and Japan
Indicator (6) Ease of intervention	・ Whether if JICA's intervention appropriate from a financial, technical, and operational perspective

3.5.2 Verification of the effectiveness of pilot activities

Based on the above evaluation indicators and criterias, the effectiveness of the implemented 7 pilot activities was verified. The verification results are shown in the table below.

(1) Vietnam

Indicator (1)	Scope of Challenge Solving	**Capacity building contribute to solving and improving many challenges related to the capacity of clinical trials.**

The theme of the pilot activity (1), which is the establishment of a Clinical Research Promotion Center within the University of Medicine and Pharmacy at Ho Chi Minh City (hereinafter referred to as UMP) and the strengthening of clinical trial implementation capacity including the implementation of Phase I trials are initiatives that relates to solve challenges such as (1) lack of personnel, technology and knowledge for clinical trials, (2) lack of or inadequate clinical trial facilities and equipment, (3) lack of domestic policies and international assistance to promote clinical trials identified in Table 3-1.

Indicator (2)	Commitments of Target Institutios (implementation structure and budgetary measures)	**While the Clinical Trial Group established within the university in recent years and the infrastructure for implementation is in place, there are no future budgetary plans for the establishment of a Clinical Research Promotion Center in at this time.**

UMP which is the target institution of Pilot Activity (1) is establishing the Clinical Trial Group (hereinafter referred to as CTG) within the school of public health and it is the predecessor of the Clinical Research Promotion Center, which will be established after the COVID-19 pandemic with the mission of promoting clinical research activities. Dr. Do Van Dung and Dr. Nguyen Thi Hai Lien, who were participants of Japan visit, serves as the group's main coordinator and plays a central role in managing the CTG's operations. While clinical research and clinical trial activities are conducted independently by each department, the CTG's main role within the university at this time is to provide centralized administrative support for these activities. Specific CTG's tasks include (1) support to Principle Investigators on research protocols, (2) operational support to the Investigational Research Board (IRB), (3) consolidation and monitoring of information on ongoing clinical trials within the university, (4) discovering of sponsors, and (5) importation of drugs and equipment.

The fact that the CTG was established as the predecessor of the Clinical Research Promotion Center and several members are assigned to the group and key persons within the university have been identified suggests that a system for implementing support projects for the future establishment of the Clinical Research Promotion Center is in place. On the other hand, there is no concrete budget plan for the establishment of the Clinical Research Promotion Center at this point, and they are still hoping for financial support from external aid organizations such as JICA.

Indicator (3)	Impact on target country's policy/ urgency of needs	**It matches with the national policy which aims to develop and produce pharmaceuticals and vaccines in Vietnam and will contribute to resolve regional disparities of clinical trial capability, however, there are no detailed national plan to establish a Clinical Rersearch Promotion Center within major academic institutions.**

The promotion of clinical research and the strengthening of clinical trial implementation capacity are in line with Vietnam's national policy of aiming for homegrown development and manufacturing of pharmaceuticals and vaccines. In addition, as many of the respondents to the interview survey indicated, the capacity to conduct clinical trials tends to be unevenly distributed in the capital city, especially at Hanoi Medical University, and it would make sense to reduce the gap with Ho Chi Minh City, the second largest city, in order to prepare for a possible future pandemic of infectious diseases, which is the twin of Hanoi Medical University. Strengthening the capacity of the UMP makes sense and will have a positive impact on partner country policies.

On the other hand, there is no clear national policy to establish "Clinical Research Promotion Centers" at major academic institutions in Vietnam, and it is not clear what functions the Clinical Research Promotion Centers should have. Therefore, although there is a high level of need within universities, the urgency of the national need is not as great as it should be, hence it is necessary to coordinate with the Ministry of Health of Vietnam to discuss the project and to coordinate policies.

Indicator (4)	Collaboration and ripple effects within the target country	**Ripple effects on Japan's strategy to establish a multi-regional clinical trial center and the networking with Hanoi Medical University, one of the top clinical trial sites, are expected.**

During the implementation of the pilot activities, it was suggested that if a Clinical Research Promotion Center is to be established, it should follow the requirements that could serve as a national model in the future. To this end, it was also discussed that Hanoi Medical University, the top clinical trial organization

in Vietnam, should understand what kind of clinical research and trial promotion and management functions it currently possesses and align its methods with those of other institutions.

As exemplified by the fact that Shionogi has conducted clinical trials of COVID-19 vaccine and therapeutics in Vietnam and is now in concrete discussions for the transfer of the vaccine manufacturing technology, it was suggested that the establishment of an international joint clinical trial center should be considered in order to realize speedy clinical trials in a wide Asian region in the event of a future infectious disease pandemic. Vietnam is an important country for Japan in the strategy to establish a center for international joint clinical trials to realize speedy implementation of clinical trials over a wide area of Asia in the event of a future pandemic of infectious diseases. In terms of the strategy to establish a center for international joint clinical trials, it is necessary to involve Hanoi Medical University, which has an excellent track record in international joint clinical trials, in the project as a partner. Currently, there is no specific collaboration between those two universities in the field of clinical research, but the establishment of a model for the establishment of a Clinical Research Promotion Center and Japan's role as an intermediary in the networking between representative medical universities in Vietnam's two largest cities would have a ripple effect on both Japan and Vietnam.

Indicator (5)	Contributions and cooperation with Japanese institutions	**UMP's intention to join ARISE was stated clearly and it is expected to accelerate the process to join, so if UMP becomes a member, it would be easier to cooperate and collaborate with NCGM.**

During the pilot activities, both the President and Vice President of UMP expressed their intention to join ARISE. In response to this statement, the NCGM International Trial Department, which is the ARISE management secretariat, expressed its willingness to enter into a dialogue with the university regarding the possibility of joining ARISE in the future. Since the only member of ARISE in Vietnam is Bach Mai Hospital in Hanoi at this time, it would be beneficial to establish an international joint clinical research and trial network in Ho Chi Minh City as well. We believe that it is quite feasible to provide capacity strengthening support to UMP through ARISE in collaboration with NCGM.

Indicator (6)	Ease of intervention	**Since Japan has knowledge and experience in clinical research promotion and support systems and operations, including its own and other institutions, through the Core Clinical Research Hospital System launched in Japan in 2015, Japan can utilize those know-how and JICA's technical cooperation scheme.**

In Japan, in order to promote high-quality clinical research and clinical trials, the Core Clinical Research Hospital System was established in the Medical Care Act enacted in April 2015 as a hospital that plays a central role in clinical research and investigator-initiated clinical trials at the international level (ICH-GCP compliant). The functions of a core clinical research hospital include not only planning and conducting clinical research at the hospital itself, but also promoting joint clinical research with other institutions and providing necessary support for clinical research conducted by other institutions. Japan has accumulated knowledge and experience in organizational requirements and management methods that could serve as a model for a Clinical Research Promotion Center. Therefore, we believe that it is possible to apply know-how and transfer technology from establishment to operation using these centers as models in cooperation with core hospitals, including the Clinical Research Promotion Center of the University of Tokyo Hospital, where Dr. Tatsuya Maruyama, who participated in this pilot activity as an advisor, is affiliated. In addition, building and strengthening institutions through human resource development is an area where JICA's technical cooperation scheme can be utilized to its advantage.

(2) Indonesia

Indicator (1)	Scope of Challenge Solving	**Capacity building contribute to solving and improving many challenges related to the capacity of clinical trials.**

The theme of the pilot activity (2), the establishment of a Clinical Research Unit within Udayana University Hospital (hereinafter referred to as UUH) and the development of human resources for clinical trials, is similar to the theme of the pilot activity in Vietnam, are initiatives that relates to solve challenges such as 1) Insufficient human resources, technology, and knowledge for clinical trials; 2) Inadequate or insufficient clinical trial facilities and equipment; and 6) Insufficient domestic policies and international assistance to promote clinical trials described in Table 3-1.

Indicator (2)	Commitments of Target Institutios (implementation structure and budgetary measures)	**With the renovation of UUH and the expantion of hospital functions in 2018, the hospital aims to strengthen its capacity as an Academic Hospital.**

Since the hospital underwent a major expansion and renovation in 2018, UUH aims to increase the number of clinical research and clinical trials conducted as a Clinical Trial Organization and "Academic Hospital", expanding the scope of medical services provided. As of January 2024, clinical trials on the safety and prophylactic efficacy of COVID-19 booster vaccine (Sinopharm) for adults and COVID-19 vaccine (Indovac) for 12~17 year-old were underway in this building. The hospital has been now proceeded with the maintenance as shown in the pictures below. In March 2023, the Clinical Research Unit was gradually being upgraded compared to the time there was almost no equipment or materials in the building.

Examination room for subject patients

Counselling room for subject patients

The laboratory is shared with the hospital's clinical laboratories, and the maintenance and allocation of materials, equipment, and clinical trial personnel are still insufficient, but are in the process of being developed. The hospital has its own budget (budgetary measures are described below in Indicator (3)) for the development and operation of the Clinical Research Unit, and it can be said that the basic implementation system is in place.

Indicator (3)	Impact on target country's policy/ urgency of needs	**The Decree of the Ministry of Health requires the establishment of Clinical Research Unit, giving priority to hospitals under the jurisdiction of the MoH. However, UUH is out of scope of the support from MOH, so they need the one from domestic and foreign institutions.**

The Indonesian Ministry of Health has issued the "Indonesian Ministerial Decree on Health[145] regarding the strengthening of clinical research in hospitals in 2023. This Ministerial Decree requires the establishment of the Indonesian Clinical Research Center (INA-CRC) within the Ministry of Health organization, and the establishment of Clinical Research Units (CRU) within each hospital, with priority given to the following 17 hospitals under the direct jurisdiction of the Ministry of Health.

1. Dr. Cipto Mangunkusumo National Central General Hospital (Jakarta)
2. Prof. Dr. dr. Mahar Mardjono National Brain Center Hospital (Jakarta)
3. Prof. I.G.N.G Ngoerah Central General Hospital (Denpasar)
4. Dr. Sardjito Central General Hospital (Yogyakarta)
5. Dharmais Cancer Hospital (Jakarta)
6. Prof. Dr. Sulianti Saroso Infectious Disease Hospital (Jakarta)
7. Jakarta Friendship Central General Hospital (Jakarta)
8. Harapan Kita Cardiovascular Hospital (Jakarta)
9. Muhammad Hoesin Central General Hospital (Palembang)
10. Hasan Sadikin Central General Hospital (Bandung)
11. dr. Wahidin Soedirohusodo Central General Hospital (Makassar)
12. dr. Kariadi Central General Hospital (Semarang)
13. Adam Malik Central General Hospital (Medan)
14. Cicendo Eye Hospital (Bandung)
15. Children's Hospital and Our Mother of Hope (Jakarta)
16. Dr. H. Marzoeki Mahdi Mental Hospital (Bogor)
17. Prof. Dr. R. Soeharso Orthopedic Hospital (Surakarta)

The Ministerial Decree defines the functions that INA-CRC and CRU should have as shown in the figure below.

[145] Decree number HK.01.07/MENKES/1458/2023

Summary

- A range of clinical research and innovation needs to be undertaken to respond to technological developments in the field of medicine, to carry out medical transformation, and to improve health services in hospitals as health issues in the community become more complex.
- In order to conduct clinical research in hospitals, the establishment of the Indonesian Clinical Research Centre (INA-CRC) and the Clinical Research Unit (CRU) is necessary and yes.

About INA-CRC

- The INA-CRC is responsible for:
  - ✓ Formulate policies and provide technical guidance for research and development of clinical research in hospitals
  - ✓ Coordinate clinical research activities with stakeholders
  - ✓ Promote clinical research activities in Indonesia
  - ✓ Provide guidance to CRUs to conduct clinical research in accordance with Good Clinical Practice
  - ✓ Support the CRU to develop clinical trial contracts when conducting clinical research in collaboration with national and international sponsors and research institutions
  - ✓ Seek sponsorship and collaboration for international clinical research and coordinate its implementation with the CRU
  - ✓ Provide a team of experts, including statisticians and research methodologists, to assist in the conduct of clinical research

About CRUs

- The CRU is responsible for:
  - ✓ manage clinical research
  - ✓ design a program to improve clinical research and innovation in hospitals
  - ✓ Organize clinical research in hospitals
  - ✓ Develop hospital policies for the implementation of clinical research and innovation
  - ✓ Conduct clinical research activities in accordance with ICH-GCP standards
  - ✓ Coordinate, monitor, and evaluate the clinical research process in the hospital
  - ✓ Conduct dissemination activities involving hospital directors and related personnel to utilize the results of clinical research
  - ✓ submit a report on the conduct of clinical research to the hospital director
  - ✓ Work to improve the healthcare system in academia in collaboration with other hospitals, industry, clinical research sponsors, government agencies, and other relevant stakeholders

Figure 3-50 Functions for INA-CRC and CRU (1/2)

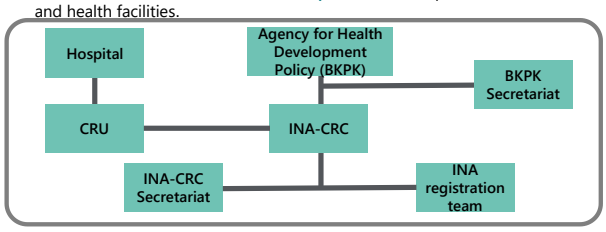
Background and Objectives

Background: Indonesia's health system has been affected by the COVID-19 pandemic, and there is an urgent need for coordination and capacity building in the conduct of clinical research

Objectives: (1) Increase in the number of clinical studies in hospitals and (2) Increase in the capacity of clinical research centers and clinical research units and Increase in the capacity to conduct clinical studies according to international standards in Indonesia.

Requirement for INA-CRC

- INA-CRC is under the Agency for Health Development Policy and has an organizational structure consisting of a coordinator, a secretariat and the Indonesia Registry Team (INA-Registry).
- The purpose of INA-CRC is to promote the conduct and registration of clinical research at the centre and hospital levels and protect researchers and health facilities.



- The INA-Registry maps the types and fields of clinical research conducted by various institutions, including hospitals, government agencies, universities, pharmaceutical companies, research institutes, contract research institutes, etc., aims to build a database of clinical research in Indonesia.

Requirement for CRU

- The specific requirements and roles of the CRU are as follows.

Item	Contents
organizational structure	• The CRU is a unit that conducts clinical research in hospitals. Manage and operate according to the clinical research needs of the hospital
Personnel	• Clinical investigators include hospital health workers and researchers • Out-of-hospital clinical research practitioners include lecturers, researchers, and students from educational institutions.
Equipment	• All sites and areas of the hospital can be used for clinical research activities with the approval of the hospital director or managing director, as long as there is no disruption to hospital services
in a hospital clinical research management	• provide details of the included studies
Planning and Budgeting	• Hospitals plan and budget clinical research to improve hospital services and develop technology
Coordination and cooperation	• The CRU coordinates with organizations and areas that play a role in the conduct of clinical research in the hospital, such as in-house research activities personnel, research teams, and other relevant stakeholders in the conduct of clinical research. • Outbound clinical research is conducted under a clinical trial agreement (CTA)
Monitoring and Evaluation	• Monitoring and evaluation of clinical studies involves the CRU, the clinical research implementation team, and/or an organization outside the hospital
Principles for conducting clinical research	• The CRU develops all operating procedures necessary for the conduct of clinical research in hospitals and refers to regulations and guidelines applicable nationally and internationally

Figure 3-51 Functions for INA-CRC and CRU (2/2)

During the pilot activity for UUH conducted locally in Indonesia in January 2024, survey team also traveled to Jakarta to conduct an interview on the said Ministerial Decree. According to the interview, the INA-CRC has already been established within the Ministry of Health, and 17 target hospitals have started working on the establishment of hospital CRUs and CRU management departments. In addition, the hearing participants were informed that the revision of the Ministerial Decree will be discussed in January 2024, and that it has been decided to expand the number of target hospitals from 17 to 37.

University hospitals, including UUH, are obligated to follow the various guidelines for clinical services issued by the Ministry of Health, but since universities (educational institutions) are the parent

organizations, the Ministry of Education and Culture of Indonesia has direct jurisdiction (the same applies to other university-affiliated hospitals). On the other hand, the Minister of Health Decree only applies to hospitals under the jurisdiction of the Ministry of Health (mainly clinical hospitals and medical teaching hospitals). Thus, because the jurisdiction of public medical institutions is vertically divided between the Ministry of Health and the Ministry of Education and Culture, university hospitals are not covered by the Ministerial Decree (they are not even included in the 37 hospitals). In the interview, the MOH recognizes the importance of establishing CRUs in university hospitals, which are the main players in medical research activities, in order to strengthen the implementation of clinical research activities, but the MOH can only provide budgetary and technical support measures to hospitals under its jurisdiction, and hospitals outside the jurisdiction of the MOH are not eligible for such assistance and would like to resolve this incompleteness by obtaining support from international aid organizations.

In light of the above, strengthening the operation of the newly organized INA-CRC and establishing a CRU is an urgent national mandate, and support for these efforts will have an impact on implementation of Indonesian policy .

Indicator (4)	Collaboration and ripple effects within the target country	**In addition to the University of Indonesia and Gadjah Mada University, which preceded UUH, Prof. I.G.N.G Ngoerah Central General Hospital, which is a priority target of the MoH Decree could be considered as collaboration partner.**

As mentioned in 1) Vietnam above, it would be possible to collaborate with University of Indonesia and Gadjah Mada University to develop domestic partnerships since those university have their own Clinical Research Supporting Unit and conduct numerous clinical trials and support for them and development of human resources. In the meeting with the Ministry of Health mentioned in the previous section, it was commented that it would be good to have support from other domestic and foreign institutions, since UUH are not eligible for budgetary measures and technical support from the Ministry of Health in the implementation of the said Ministerial Decree on Health. In addition, The Ministry of Health mentioned that it would be a good idea to support Prof. I.G.N.G Ngoerah Central General Hospital (one of the 17 priority hospitals) a public hospital located in the same province of Bali as well as UUH, to provide support to them to establish a CRU for these two hospitals since it would create ripple effects and be a good model. In light of the above, it is desirable to consider support projects in collaboration with domestic institutions, rather than targeting UUH alone, in order to spread the effects of the support.

Indicator (5)	Contributions and cooperation with Japanese institutions	**Although UHH is not yet a member of ARISE, NCGM has indicated its willingness to support Indonesia in strengthening its human capacity.**

Although UUH did not make a specific statement regarding ARISE membership during the pilot activity in Indonesia in January 2024, the NCGM International Trial Department, which participated in the activity, mentioned that the NCGM aims to standardize human capacity in the field of clinical research and would like to support Indonesia in strengthening human resource capacity and efficient clinical research operations, especially in Southeast Asia, which is a priority strategic region. Indonesia has a large population, and the capacity and level of clinical research varies within the country, and regional disparities exist. In this regard, NCGM's cooperation in standardizing human capacity in the field of clinical research will be easily obtained, and further strengthening the capacity of clinical research in a large provincial city like Bali will help to eliminate regional disparities.

Indicator (6)	Ease of intervention	**Since Japan has knowledge and experience in clinical research promotion and support systems and operations, including its own and other institutions, through the Core Clinical Research Hospital System launched in Japan in 2015, Japan can utilize those know-how and JICA's technical cooperation scheme.**

Regarding the ease of intervention, as described in indicator (6) of 1) Vietnam, Japan has knowledge and experience in clinical research promotion and support systems and operations, including its own and other institutions, through the core clinical research hospital system initiated in Japan, and we believe that this know-how and the strengths of JICA's technical cooperation scheme can be utilized.

(3) Philippines

Indicator (1)	Scope of Challenge Solving	**Capacity building contribute to solving and improving many challenges related to the capacity of clinical trials.**

The theme of the pilot activity (3), the strengthening of the capacity of PFDA clinical trial examiners and inspectors and the standardization of examinations and inspections, will contribute to the challenges such as (1) Shortage of human resources, skills, and knowledge related to clinical trials, (3) Unclear and complex regulations and guidelines for clinical trials, and delays in regulatory processes identified in Table 3-1.

Indicator (2)	Commitments of Target Institutios (implementation structure and budgetary measures)	**It is feasible to carry out the project since Philippines and institutions there have organized system and show positive stance.**

With regard to the theme of the pilot activity (3), capacity building of PFDA clinical trial examiners and inspectors and standardization of review and inspection, the Director of the Center for Drug Regulation and Research and the Head of the Clinical Research Section have been involved from the beginning of the study and have shown a high level of commitment. However, both parties are in a position to lead clinical trial-related work within the PFDA, and they are well-positioned to carry out their projects.

In addition, in discussions with the PFDA, positive statements have been made about the WHO's global benchmarks for regulators as being very timely in relation to the audit. Specifically, the PFDA has most recently undergone an audit of WHO's global benchmarks for regulators and has been given two years to reach Maturity Level 3, an indicator, and is very positive about receiving assistance to rapidly improve the capacity of its regulatory agencies and they have shown a willingness to do so.

Indicator (3)	Impact on target country's policy/ urgency of needs	**It matchs with national policy to ensure pharmaceutical security in the Philippines.**

In order to conduct local manufacturing of vaccines, it is necessary to obtain Maturity Level 3 in the WHO Global Benchmark for Regulatory Authorities, but PFDA is currently at Maturity Level 1, which is one of the most important challenges for the PFDA.

The government of the Philippines, as part of its major goal of ensuring drug security in the country, aims to be able to independently manufacture medicines and vaccines in the country[146], and the implementation of the project is in line with the national policy.

[146] Local stakeholder interview including PFDA

Indicator (4)	Collaboration and ripple effects within the target country	**Strengthening the capacity of PFDA is expected to have high ripple effects on clinical trial institutions.**

In interviews in the Philippines, several clinical trial sites commented the urgent need to resolve the shortage of PFDA personnel and to develop human resources, and it is expected that this will have a ripple effect on the clinical trial sites.

Indicator (5)	Contributions and cooperation with Japanese institutions	**It has a strong affirnity since Japanese Pharmaceutical related institution is actively working with Asia.**

Japanese regulatory authorities are actively working on cooperation with Asian countries, and there is a strong interest in the Philippines among the target countries of this survey, which is in line with the needs of the Japanese side[147]. On the Japanese side, PMDA will establish a new base in Thailand in FY2024 and aims to strengthen cooperation between Japan and Asian countries by enhancing the content of local seminars and training, to promote the entry of Japanese companies by increasing the number of simplified examinations referring to Japanese examination results, and to spread Japanese pharmaceutical regulations by expanding the number of Asian countries that refer to Japanese examination results. The project also aims to promote the penetration of Japanese regulations[148] by increasing the number of Asian countries that refer to the results of Japanese examinations.

Indicator (6)	Ease of intervention	**Certain amount of time is necessary to have involvements of Japanese stakeholders, adjust the national priorities, and coordinate the implementation of both local and Japanese intervention.**

The knowledge of Japanese pharmaceutical-related institutions is essential for the implementation of the project, and it is necessary to give due consideration to whether the Japanese side has the human resources to dispatch personnel for a certain period of time.

In addition, the PFDA and other institutions such as the Department of Health and the Department of Finance have not yet coordinated with each other, and it may take some time to formulate a project.

(4) Thailand

Indicator (1)	Scope of Challenge Solving	**Capacity building contribute to solving and improving many challenges related to the capacity of clinical trials.**

The validation of the effectiveness of IGRA to detect latent TB in Thailand and collaboration with Japanese private companies, which is the theme of the pilot activity (4), is an initiative that will contribute to solving and improving challenges such as (i) lack of and inadequate clinical trial facilities and equipment and (ii) lack of funds, as indicated in Table 3-1.

[147] Discussion with PMDA on April 7th, 2023

[148] Ministry of Health, Labour, and Welfare “Establishment of Overseas Offices of PMDA” (https://www.mhlw.go.jp/content/10601000/001184914.pdf)

Indicator (2)	Commitments of Target Institutios (implementation structure and budgetary measures)	**Although partner institutions have implementation systems in place, budgetary provisions are not sufficient.**

SiCRES, the target institution for the pilot activity (4), has already received support from the Thai Ministry of Health and the Faculty of Medicine of Siriraj Hospital and Mahidol University for the IGRA test, and has no particular concerns about the implementation system. On the other hand, SiCRES is looking for other institutions to provide funds for the IGRA test, as it requires a large amount of money, and no final budgetary provision has been set yet.

Indicator (3)	Impact on target country's policy/ urgency of needs	**There is some need, however, it is not considered as by government-wide important matters.**

Although there is a certain level of need for latent TV in recent years and interest in latent TB has been growing in many countries, it is not specifically addressed in the national plan[149].

Indicator (4)	Collaboration and ripple effects within the target country	**Collaboration and ripple effects within Thailand cannot be expected much.**

Although SiCRES is proceeding with support from the Thai Ministry of Health and the Faculty of Medicine at Sirirat Hospital and Mahidol University, there is no mention of other stakeholders, and a wide spread of effects is not expected at this time.

Indicator (5)	Contributions and cooperation with Japanese institutions	**There is possibility of joint research with Japanese universities and collaboration with Japanese companies, however, there is no specific institutions to collaborate identified at this time.**

Regarding collaboration with Japan, there is a possibility of conducting joint research with Japanese universities in the search for new markers for latent TB, or conducting clinical trials in collaboration with Japanese companies that have diagnostic pharmaceutical that could be markers for latent TB that are less expensive than IGRA. At this time, however, no Japanese institutions have been identified interest.

Indicator (6)	Ease of intervention	**Elements of collaboration with Japan are not visible at this time, and further consideration is needed for Japanese intervention.**

There is no element of collaboration with Japan, and it is difficult to provide financial support from Japan at this time, but there is a possibility of applying for the SATREPS project or AMED research funds if the research is conducted jointly with Japanese universities or research institutions.

[149] 「Thailand Operational Plan to end Tuberculosis, Phase 2 (2023-2027) 」

「TB policies in Thailand, Step Up for TB 2020 Tuberculosis Policies in 37 Countries A survey of prevention, testing, and treatment policies and practice」 (https://msfaccess.org/sites/default/files/2020-11/TB_SUFT2020_Country_Factsheet_Thailand_0.pdf)

(5) Kenya

Indicator (1)	Scope of Challenge Solving	**Capacity building contribute to solving and improving many challenges related to the capacity of clinical trials.**

The theme of the pilot activity (3) which is the sensitization meeting for clinical trial stakeholders based on the Pharmacy and Poisons Board (PPB) is an effort to address the challenges such as (1) Insufficient human resources, skills, and knowledge for clinical trials, (3) Uncertainty and complexity of regulations and guidelines for clinical trials, (4) Delays in the regulatory process, and (7) Others (lack of collaboration among clinical research organizations) listed in Table 3-1.

Indicator (2)	Commitments of Target Institutions (implementation structure and budgetary measures)	**Although the implementation system is in place at PPB, they are working on with the budgetary provisions for one implementation in 2024-2025.**

In the PPB, which is the target authority for the pilot activity (5), the future sensitization meetings are planned to be held regularly (expectedly twice a year) led by Dr. Benson Kanji (Principal Regulatory Officer), who participated in Japan visit in July 2023, Dr. Samuel Kerama (senior regulatory affairs expert) of the Clinical Trials Division of the Product Safety Department, and several other members of the same department.

As mentioned above, the PPB has already secured several members to lead the sensitization meetings, and it can be considered that a system is in place to ensure smooth implementation, from the involvement of related organizations to the day-of-meeting management. On the other hand, no specific budget plan has been presented at this time, although the PPB is aiming to obtain a budget for the next fiscal year. PPB share the reason for that no meetings were held before the sensitization meeting as a trial pilot activity although it has been few years since Strategic Plan (2020-2025) has been operated was difficulty to secure a budget for the meeting. Based on this, it is important to secure a budget to conduct the meeting continuously.

Indicator (3)	Impact on target country's policy/ urgency of needs	**This is an activity that is specified in their strategic plan and in line with the policies of PPB. It is also mentioned in many interviews with local stakeholders; therefore, it is considered to be a challenge with high needs.**

In the Strategic Plan (2020-2025) published by the PPB, it is mentioned that one of the challenges during the implementation period of the Strategic Plan (2014-2019) is "low awareness of the PPB's mandate among stakeholders," and "strengthening stakeholder engagement" as a solution of this challenge. Against this backdrop, in the implementation framework for the period 2020-2024, it is stated the plan to have sensitization meetings twice a year having stakeholders involve as an initiative plan to support public-private partnerships aimed at "improving the capacity of regulatory science to effectively evaluate healthcare products and technologies".

Interviews with research institutions conducting clinical trials and local pharmaceutical companies also indicated challenges regarding the opaqueness and complexity of the regulatory process for clinical trials and delays in the timeline for reviewing applications. In addition, as Prof. James Kimotho, a member of the Expert Committee on Clinical Trials (ECCT) and affiliated with the Kenya Medical Research Institute, mentioned in the presentation at the sensitization meeting in February, about 30% of the reasons for review delays are due to errors in the way clinical trial protocols are written. Lack of understanding of regulatory-related areas by clinical trial sites also have a significant impact on application review timeline delays.

Based on the above, conducting sensitization meetings in Kenya is clearly stated in the PPB's published strategic plan and is in line with national policy. In addition to the need by PPB as a regulatory body, the needs to promote understanding of the regulations for clinical trial application has been expressed by the clinical trial conductors and the organizations conducting the review, therefore, this is in line with the needs of both the regulatory agencies and the clinical trial sites involved in clinical trials.

Indicator (4)	Collaboration and ripple effects within the target country	**The sensitization meeting involves a wide range of stakeholders, including regulatory agencies, research institutions involved in clinical trials, pharmaceutical companies, and industry associations; therefore, high impact is expected to have in Kenya.**

For the sensitization meeting as a pilot activity, 36 stakeholders from the PPB, the regulatory authority, research institutions such as Kenya Medical Research Institute and KAVI Institute of Clinical Research, medical institutions such as Kenyatta National Hospital and Moi Teaching and Referral Hospital, industry associations such as the Clinical Research Society of Kenya, NGOs such as Amref Health Africa, and public institutions such as National Commission for Science, Technology and Innovation attanded. The PPB, as a regulatory authority, communicates with clinical trial institutions on a daily basis and has a certain level of relationship with them. Therefore, initiatives provided by PPB is considered to have a high ripple effect on the various related institutions in Kenya that PPB has already established.

Indicator (5)	Contributions and cooperation with Japanese institutions	**Although there are no urgent needs of the relevant Japanese institutions, there are high expectations for the benefits of medium- to long-term collaboration with Japan, based on the trend toward regulatory harmonization in Africa, starting with Kenya.**

Since PPB is a regulatory authority, it is thought that Japanese regulatory authorities have the greatest affinity with the PPB as candidate institutions with which Japan can collaborate.

In an interview with Japanese regulatory authorities in April 2023, prior to the initiatives of the pilot activities, it was noted that "Although Asian countries have a higher priority than African countries, to promote initiatives such as the International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH) and other global activities in Africa, we would like to collaborate with the country that is taking a leadership role in Africa".

Japanese research center has experiences of cunducting project in African countries including Kenya, and in particular, the document describing the results of the "Promotion of Understanding for the Development of Japanese Medical Devices in Africa (2018)[150]," which was conducted in Cameroon and the Democratic Republic of the Congo in collaboration with Japanese regulatory authority, mentions expectations for a opportunity to widely share information with regulatory authorities in African countries and the effectiveness of Japan's active participation in and support for the ongoing movement of regulatory harmonization in Africa.

The PPB is one of the eight members of the Steering Committee of The African Vaccine Regulatory Forum (AVAREF), a regional regulatory network established in 2006 with the support of WHO, and plays a central role in the movement to strengthen regulatory bodies and harmonize regulations in Africa.

From the above, it can not be said that there is an urgent need for collaboration from Japanese regulatory authorities and research centers in Japan, but Kenya is expected to continue to play a major role in the field of regulation in the African region, and from a medium- to long-term perspective, it would be beneficial to promote collaboration with Kenya in the African regulatory area at the earliest possible stages.

[150] NCGM “Project to promote understanding for the deployment of Japanese medical equipment in Africa” (https://kyokuhp.ncgm.go.jp/activity/open/outline/CMR_COD2018.pdf)

Indicator (6)	Ease of intervention	**it is possible to intervene by combining the experience in technical cooperation projects aimed at human resource development with our know-how in conducting subject-specific training related to pharmaceutical affairs.**

JICA has experiences of implementing projects aimed at human resource development in the past, including technical cooperation projects for regulatory authorities in Thailand. In Japan, JICA and the Ministry of Health, Labour and Welfare (MHLW) collaborate to conduct a subject-specific training course, "Pharmaceutical Administration for Appropriate Supply, Quality Control and Use of Drugs," mainly for administrative officials who are engaged in the formation of pharmaceutical-related policies and the planning and execution of pharmaceutical administrative services at government pharmaceutical regulatory authorities and related agencies. The cumulative number of participants in this training program is approximately 400 by FY2020, and the participants are from a diverse range of nationalities which is approximately 40 countries[151].

Therefore, it is considered that JICA can intervene in a way that combines its technical cooperation projects and subject-specific training know-how as described above.

(6) India

Indicator (1)	Scope of Challenge Solving	**Capacity building contribute to solving and improving many challenges related to the capacity of clinical trials.**

The theme of the pilot activity (6), matching Indian biotech companies with Japanese companies, is an initiative that contributes to solving and improving challenges such as (7) others (collaboration with academia and industry, etc.) indicated in Table 3-1.

Indicator (2)	Commitments of Target Institutions (implementation structure and budgetary measures)	**Target company in India has structural and technical capacity to implement collaboration (technology transfer).**

The Indian company, which is the target organization for the pilot activity (6), had all Whole-Time Directors, Executive Directors, and other board-level members who are in a position to decide company policy in attendance at the initial meeting with the Japanese company, so it could be considered that the Indian company is committed to promoting collaboration with the Japanese company. In addition, the company has received technology transfers from European and US companies in the past and is familiar with the practical procedures for receiving technology transfers, etc. Therefore, it is considered that the company has a certain level of technical capacity to smoothly implement the actual procedures and receive technology transfers when collaboration with Japanese companies progresses.

Indicator (3)	Impact on target country's policy/ urgency of needs	**It is consistent with several policy objectives promoted by the Indian government to promote local** manufacturing **of pharmaceuticals.**

The Indian government has implemented several policies to promote local manufacturing, including the Pharmaceutical Production Linked Incentive Scheme (PLI 2.0) to minimize dependence on imported bulk drugs from abroad and to promote local manufacturing of vaccines and other pharmaceuticals. The matching between Indian firms and Japanese firms in the pilot activity (6) aims to promote local manufacturing of pharmaceuticals in India by Indian firms through collaboration such as technology

[151] The program started in 1983 as a Ministry of Health, Labor and Welfare (MHLW) program, but was transferred to JICA in 2004 and is now being implemented as JICA's issue-specific training.

transfer triggered by the matching and is considered to be fully in line with the policy promoted by the Indian government.

Indicator (4)	Collaboration and ripple effects within the target country	**Regarding the ripple effects within the partner country, a certain amount of effectiveness are able to be expected as collaboration progresses after the matching process.**

The Indian company that was the target of the pilot activity (6) is one of the member companies of the Indian Vaccine Manufacturers Association (IVMA), an industry association of Indian vaccine biotechnology companies. We believe that the actual collaboration through the matching activities as described in the trial pilot activity (6) will generate a certain degree of ripple effect from the perspective that other companies that are members of the IVMA may also take interest and consider collaboration. It should be noted, however, that the prerequisite for the establishment of a match between companies is that the business strategies and interests of both Indian and Japanese companies must match, and that it is difficult to establish a match unless these prerequisites are in place.

Indicator (5)	Contributions and cooperation with Japanese institutions	**There are a certain number of institutions that have potential for collaboration, and we can expect beneficial collaboration with Japan from a long-term perspective, but there are areas that will require further adjustment.**

The Japanese company that the Indian company wished to be matched with was a member of the Japan Pharmaceutical Manufacturers Association (JPMA), and the survey team contacted the JPMA, and the company also expressed its desire to be matched with the Indian company. As mentioned earlier, the Indian company that is the target organization for the pilot activity (6) is a member of the IVMA, and the survey team contacted the IVMA and the Japan Pharmaceutical Manufacturers Association (which is considered to have a high affinity with the Biopharmaceuticals Committee of the Japan Pharmaceutical Manufacturers Association in particular) to match private companies in both countries. However, the possibility cannot be denied that the initiatives may be limited to the interests of individual companies, and the ripple effect may not be as high as it could be. In addition, there are several JETRO local offices in India that support the entry of Japanese companies into the Indian market, and we believe that further synergistic effects can be achieved through collaboration with such organizations and by utilizing their support schemes.

Indicator (6)	Ease of intervention	**It is largely a matter of bilateral consultation, and it is not easy for JICA or any other third party other than the partner companies to intervene.**

Regarding the creation of matching opportunities as in the pilot activity (6), it seems possible for JICA's local offices to intervene to a certain extent by acting as a contact point to connect local companies with Japanese companies. On the other hand, based on the results of the pilot activity (6), it is assumed that in many cases, a confidential non-disclosure agreement (CDA) is concluded at the initial stage of discussions to determine whether or not collaboration is possible, which may require the provision of information such as clinical trial data on vaccines. Considering that CDAs are also concluded at the stage of considering collaboration after matching has been established, it is not easy for JICA or other third parties other than the partner companies to intervene considering that the decision basically depends on discussions between the two parties.

(7) Indonesia (Wastewater Surveillance)

Indicator (1)	Scope of Challenge Solving	**Capacity building contribute to solving and improving many challenges related to the capacity of clinical trials.**

Pilot Activity (7): Demonstration of Highly Sensitive Virus Detection Technology by Wastewater Monitoring is an initiative that contributes to solving and improving challenges such as (7) others (improvement of sampling, detection, and analysis capabilities for sewage epidemiological surveys, etc.) listed in Table 3-1. This initiative will enable early identification of the spread of the target infectious disease, and at the same time, depending on the target species, will enable identification of the spread of environmental contaminants in the area, thereby contributing to the improvement of public health in a broader sense.

Indicator (2)	Commitments of Target Institutions (implementation structure and budgetary measures)	**Although implementation systems are established at some of the institutions, further cooperation and coordination with related institutions is needed for implementation systems and budgetary measures for full-scale implementation.**

The pilot activities (7) were conducted mainly with the cooperation of the relevant agencies of the Provincial Government (Provincial Health Department, Provincial Laboratory, etc). The system of cooperation and coordination among the agencies in the target province was generally solid, and strong commitments were obtained. However, since the decision makers in each of the institutions involved include the central government, the provincial government, and local research institutions, consultations and coordination are necessary to establish a framework, including applications for permits and licenses, as appropriate. In order to implement activities at the national level over the medium to long term and to ensure sustainability, strong commitment from the central government is required in terms of legal institutionalization, systematization of the implementation system, and budgetary measures.

Indicator (3)	Impact on target country's policy/ urgency of needs	**There is a high level of interest from the central government as a next-generation solution to infectious disease control, and there is a need for the technology to take root through institutionalization.**

In Indonesia, there is no de facto standard for wastewater epidemiological surveys, and protocols have not been standardized and are not reflected in policies at this time. However, there is a need from the implementing agencies to incorporate wastewater epidemiological surveys as a solution into existing health and environmental protection policies and PPR (Prevention, Preparedness and Response), and to institutionalize and adopt them as an ongoing method for the next generation of environmental protection and infectious disease control. It is considered that wastewater epidemiology is useful as a proactive post-corona countermeasure against infectious diseases, and at the same time, it will contribute to proactive improvement of the sanitation environment by visualizing and monitoring the presence of viruses and bacteria that could not be identified before. In Indonesia, wastewater epidemiological studies are required to (1) improve the water environment and sewage treatment facilities and (2) visualize the sources and spread routes of infectious diseases, thereby improving public health by improving the environment and the health and hygiene sectors. Specifically, not only was enhanced monitoring of pathogens and early detection and control of infectious diseases desired, but also environmental considerations such as water quality monitoring. On the other hand, although the provincial government is willing to implement the project, it is necessary to continue discussions with multi-stakeholders with a view to strategic nationwide development in the Indonesian government in the future.

Indicator (4)	Collaboration and ripple effects within the target country	**Standardization will be possible by sharing the activities and results of each stakeholder, and a high development effect can be aimed at.**

A wastewater epidemiological survey has being conducted, or has been conducted in the past, by three institutions in Indonesia. As of the end of January 2024, all of the three projects (1) Nationwide polio surveillance conducted by the Ministry of Health with support from WHO, (2) wastewater epidemiology study in Yogyakarta for Novel Coronavirus at Gadjah Mada University and Monash University supported by the Australian Government, and (3) PoC project conducted under this studyhave already been completed and there is no prospection for resumption due to the lack of funding. However, it will be possible to establish a surveillance network with minimal initial investment by utilizing the existing polio surveillance network and applying already established polio surveillance techniques. In addition, as mentioned above, by establishing a protocol and standards in Indonesia by combining the efforts of multiple organizations into a framework of infectious disease surveillance as a metadata set, it is expected to strategically benefit related organizations in Japan, as described in Indicator (5).

Indicator (5)	Contributions and cooperation with Japanese institutions	**Although the number of institutions conducting wastewater epidemiological studies in Japan is limited, and thus the number of institutions that will benefit from this project is limited, it will create opportunities for Shionogi and other reagent suppliers to participate in the project.**

Since wastewater epidemiological surveys in Japan are still in the demonstration stage, the number of institutions conducting wastewater epidemiological surveys is extremely limited. However, this project will enable collaboration with universities and other research institutions, voluntary administrative municipalities, and other relevant domestic institutions, and will contribute to data collection in the ASEAN region by each institution. It will also contribute to market expansion for reagent and primer supplier companies. In particular, wastewater epidemiological surveys in the ASEAN region, including Indonesia, are still in the process of development, and by using the advantages of Japan-made reagents with high sensitivity and examining their applicability, it will be possible to create a market within the ASEAN region.

Indicator (6)	Ease of intervention	**Multiple players are conducting activities independently, and barriers to entry are not high as long as capital is available. Meta involvement, such as standardization of protocols, is strategically effective.**

As mentioned above, the wastewater epidemiological survey activities by the agencies concerned are currently suspended in terms of funding, but the parties concerned are willing to resume their initiatives actively, and since the acceptance system and network are already in place, the project can aim to be effective with minimal input. In particular, it will be possible to take advantage of Japan's technological prowess by using Japanese-made reagents to detect viruses that cannot be detected with ordinary reagents, such as the applicability of reagents with high sensitivity. Starting from the virus species already detected in Indonesia, such as polio and COVID-19, the applicability of wastewater epidemiological surveys can be expanded using existing technologies and networks by expanding new target species in line with the needs of the local government, and by frame-working, protocols and standards can be established.

Chapter 4 Proposals for future business development

4.1 Support activities for target countries through JICA projects

So far, the results of the pilot activities conducted in this study have been examined using six indicators. In this section, based on the results of the examination of the effectiveness of the pilot activities presented in the preceding paragraph, we have listed out and combined intervention measures and summarized cooperation programs which are considered to be both effective and efficient for JICA to implement. Details of each proposed cooperation program (specific activity proposal, support scheme, implementation system, implementation period, etc.) are described below.

4.1.1 Prioritized support activities

The table below summarizes the examination results for each indicator with regards to the pilot activities (1) - (7) described in the preceding paragraph.

Table 4-1 Summary of examination results of pilot activities

No	Intervention Theme of Pilot Activity	Target Country	Summary of Examination Results
(1)	Strengthen the capacity to conduct clinical trials, including establishing an academic Clinical Research Promotion Center and conducting phase I trials	Vietnam	Although there is no clear government policy at present, it is an activity that contributes to the needs of the university and to the resolution of issues in Vietnam that were identified during the research process. Furthermore, while utilizing Japan's know-how in the clinical research core hospital system, JICA can take advantage of the strengths of the technical cooperation scheme for human resource development. Additionally, there is also the possibility of cooperation with Japanese national health centers, and the universities in the target country are well-equipped to accept such cooperation as well.
(2)	Establishment of a Clinical Research Unit within the hospital and human resource development for clinical trials	Indonesia	This activity aligns with the direction of the Order of the Ministry of Health in 2023, and as they are also considering cooperation with other organizations, this activity is expected to have a high ripple effect for cooperation within the country. In addition, JICA can take advantage of Japan's expertise in the clinical research core hospital system and utilize the strengths of the technical cooperation scheme for human resource development. Universities in the target country also have a foundation for accepting such cooperation as well.
(3)	Strengthen the capacity of clinical trial examiners and inspectors and standardize examinations and inspections	Philippines	This activity aligns with the major objectives of the national policy and is an activity that addresses the urgent needs of the target institutions and other national clinical trial institutions. In addition to the high level of ripple effects within the target country, cooperation needs from other organizations in Japan is expected as well.

(4)	Verification of the effectiveness of IGRA for detecting latent tuberculosis and cooperation with Japanese private companies	Thailand	Although the structure of the target organization is in place to a certain extent, the activity is not necessarily in line with important national issues, and since specific stakeholders in Japan and the target country have not yet been identified, the ripple effect is expected to be low.
(5)	Sensitization meetings for clinical trial personnel mainly from regulatory bodies	Kenya	The implementation of senisitization meetings is stated in the government's strategic plan and the budget is under adjustment. However, the implementation structure within the target institutions are in place. It is an activity that involves many stakeholders in Kenya and is likely to have a ripple effect on the movement to harmonize African regulations, in which the target organizations play a central role. JICA's expertise in technical projects and training-based workshops can be utilized as well.
(6)	Matching Indian biotechnology companies with Japanese companies	India	This activity contributes to India's national policy, and although the target companies has sufficient commitment for collaborative intiatives, it is difficult to directly utilize the knowledge and know-how of JICA, partly because it depends on consultations between two collaborating companies.
(7)	Demonstration test of highly sensitive virus detection technology by sewage monitoring	Indonesia	Although the structure and commitment of the relevant bodies of the target provincial government are in place to some extent, they are not necessarily prioritized in the Indonesian government's policy. Furthermore, the limited number of organizations conducting sewage epidemiological surveys in Japan means that the ripple effect on related organizations in Japan is limited, and it is difficult to say that this is an area where JICA can directly make the most out of its accumulated experience and know-how.

The summary of the results shown in the table above was compiled based on six indicators which were selected on the basis of whether the activity would be effective when JICA intervenes and implements the support activity. In summary of the table above, it is considered that (4) Thailand and (6) India, out of the 7 pilot activities (1) - (7) examined above, will not be able to fully utilize JICA's knowledge and know-how as support projects, and will have little ripple effects. On the other hand, the other pilot activities are in line with the priority policy of the partner countries, and considering that the target organization already has a strong foundation and high commitment, it would be effective to deploy them in future support projects.

Based on the above, the "Solutions to Resolve Issues" and the "Proposal for Programs by JICA" described below refer to (1) Vietnam, (2) Indonesia, (3) the Philippines, (5) Kenya, and (7) Indonesia (Sewage Monitoring).

Future support intervention measures are proposed based on the results of the pilot activities.

4.1.2 Solutions and support initiatives to resolve issues

In this section, based on the results of the examination of the pilot activities described in the preceding paragraph, the actions indicated by the pilot activities, proposed solutions and specific support activities for solving the issues mentioned above will be presented, in order to consider JICA’s future collaboration

programs.

(1) Vietnam

Theme	Strengthen capacity to conduct clinical trials, including establishing a Clinical Research Promotion Center and conducting phase I trials

Based on the results of the pilot activities in Vietnam, we propose support for the establishment of the Clinical Research Promotion Center in Vietnam, including support for the provision of facilities and equipment for the establishment of the Center, the design of organizational functions and operations, human resource development including clinical trial implementers and administrative departments supporting clinical research activities, and the strengthening of systems in administrative departments. The distinctive emphasis of the support includes: first, to function as a Clinical Research Promotion Center and to assess the development needs of not only clinical trial implementers but also those in charge of clinical research support and management departments, in order to respond to the increasing number of clinical research activities, and to develop diverse human resources; second, to draw up practical initiatives based on examples from the clinical research core hospital system in Japan in order to strengthen the sustainability of the Clinical Research Promotion Center (another option is to visit Japanese hospitals through country-specific and issue-specific training, and to dispatch experts from core hospitals to transfer technology for sustainable management.); and third, to strengthen the network of other academia and research institutions starting from the Clinical Research Promotion Center, and to share the center construction model and make policy recommendations to other institutions and the Ministry of Health, since the measures for the establishment of the Clinical Research Promotion Center have not been clearly established in Vietnam, although clinical research strengthening is a national policy.

Corresponding Issue	**Solution Plan**	**Details of Support Activity (specific proposals of activities)**	**Expected Target Insitution in the Target Country**
Issue② Lack of clinical trial facilities and equipment	1.Support the provision of equipment and materials to build a Clinical Research Promotion Center	• After measuring the capacity of the target institution to conduct clinical trials, a facility/equipment survey will be conducted to identify the types of facilities/equipment that are lacking. • Based on the results of the survey, the Ministry of Health, the competent ministries and agencies, and the target organizations will be consulted to provide the missing equipment and materials. • Plan and implement training tailored to the equipment and materials provided.	• In order to reduce the gap between the urban and rural clinical trial capacities, it is desirable to target clinical trial sites outside Hanoi. • On the other hand, if policy development is to be pursued at the domestic level, it is essential to collaborate in support projects to align with the standard functions of Hanoi Medical University, the country's top clinical trial institution. [Examples of Applicable Institutions] ✓ University of Pharmacy and Medicine, at Ho Chi Minh City ✓ Hanoi Medical University
Issue① Lack of human resources, skills, and knowledge for clinical trials	2.Design and build an organization to establish a Clinical Research Promotion Center	• The necessary resources (organization, human resources) for the establishment of the center will be assessed. • In accordance with the assessment results, the requirements for the organizational structure, functions, staffing, and clinical	

		research of the center to be established will be defined, and guidelines within the target institution will be developed. • Training will be conducted on organizational introduction and organizational management theory for the establishment of the center, using the core hospital of the clinical research core hospital system in Japan as a model.	
Issue①Lack of human resources, skills, and knowledge for clinical trials	3.Develop multifaceted human resources for clinical trials	• Conduct a capacity assessment of human resources for conducting clinical trials at target institutions, identify human resources that are in short supply (including clinical trial personnel and clinical research support and management personnel), and conduct a detailed assessment of training needs. • Based on the assessment results, forumulate an annual training plan and a mid-long term plan for human resource development. • Develop and implement training curricula for healthcare professionals conducting clinical trials and clinical trial implementation managers and supporters.	
Issue①Lack of human resources, skills, and knowledge for clinical trials Issue⑤ Deficiencies in data management	4.Strengthen the clinical research support system	• Develop and build systems to support the implementation of clinical trials, prepare process manuals, and create templates of relevant documents. Examples of areas include: ・ Monitoring and evaluation of clinical research projects ・ Data management ・ Safety management ・ Ethical review and conflict of interest review ・ Provisions for intellectual property management, MTA[152], and technology transfer	

[152] Short for Material Transfer Agreement

		・ Enlightenment and promotion of understanding for human subjects	
Issue①Lack of human resources, skills, and knowledge for clinical trials	5.Strengthen sustainability of the Clinical Research Promotion Center	• With regards to independent monetization leading to independent operating funds of centers that don't rely on government subsidies or support from internatianol aid agencies, learn from the example of hospitals in Japan's clinical research core hospital system, and summarize efforts that can be implemented.	
Issue⑥Lack of national policies and international assistance to promote clinical trials	6.Strengthen partnerships with other domestic and international organizations	• Meetings, networking seminars, and technical workshops with major clinical trial institutions in the country (e.g., Hanoi Medical University) will be held on a regular basis to foster multi-institutional exchanges in clinical research activities. • As a representative model of the Clinical Research Promotion Center, it will share experiences with universities and other academic institutions in Vietnam. • Establish a Clinical Research Promotion Center and make policy recommendations to the Ministry of Health on the functions and operation methods that the Center should have and its initiatives.	

(2) Indonesia (1)

Theme	Establishment of in-hospital Clinical Research Unit and human resource development for clinical trials

Similar to Vietnam, we propose support for the establishment of a Clinical Research Unit (CRU), starting with support for the provision of facilities and equipment for the establishment of the Center, design of organizational functions and operations, development of multifaceted human resources including clinical trial personnel and administrative divisions supporting clinical research activities, and strengthening of administrative divisions. In Indonesia, the Health Minister's Order on strengthening clinical research in hospitals is expected to increase the movement of hospitals nationwide to establish CRUs. In line with this, the priority of the support will be to support the construction of a CRU including a clinical hospital and a university hospital, to compile the experience and knowledge of the CRU, to materialize the CRU construction and operation model to the Ministry of Health, make policy recommendations, and to disseminate the CRU clinical research enhancement model to other hospitals.

Corresponding Challenge	Solution Plan	Details of Support Activity (specific proposals of	Expected Target Insitution in the Target

		activities)	Country
Issue② Lack of clinical trial facilities and equipment	1.Support for the provision of equipment and materials to build a Clinical Research Unit	• After measuring the capacity of the target institution to conduct clinical trials, a facility/equipment survey will be conducted to identify the types of facilities/equipment that are lacking. • Based on the results of the survey, the Ministry of Health, the competent ministries and agencies, and the target organizations will be consulted to provide the missing equipment and materilas. • Plan and implement training tailored to the equipment and materials provided.	• The Ministry of Health's Order on strengthening clinical research in hospitals, issued in 2023, states the policy implementation (in addition to public clinical hospitals under the jurisdiction of the Ministry of Health that are prioritized by the CRU, it is assumed that university hospitals that are not prioritized by the Ministry of Health's budget measures and technical support will be targeted) • Although the support needs of university hospitals that do not receive support from the Ministry of Health are high and can be assumed to be target institutions, from the viewpoint of aligning with the implementation plan of the Ministerial Order of the Ministry of Health, it is possible to implement support by combining both hospitals under the jurisdiction of the Ministry of Health, and those that are not. [Examples of Applicable Institutions] ✓ Udayana University Hospital, Denpasar, Bali ✓ Prof. I.G.N.G Ngoerah Central General Hospital, Denpasar, Bali
Issue⑤ Deficiencies in data management	2.Enhance data collection and management functions	• Develop a process for collecting and managing data on clinical research projects in the INA-Registry as required by the Order of the Ministry of Health. • Develop a data collection and management system for reporting to the INA-Registry.	
Issue①Lack of human resources, skills, and knowledge for clinical trials	3.Build a Clinical Research Unit Model aligned with the order of the Ministry of Health	• In accordance with the role requirements and functional definitions of the Clinical Research Unit as defined by the Order of the Ministry of Health, define the organizational structure, functions, staffing, and clinical research requirements of the center to be established, and develop guidelines within the target organization. • Discuss the functions that the institution wants to have on its own, and include them in the guidelines (e.g., functions to support guidance, learning, and consultation in health care evaluation, and functions to coordinate cooperation with other institutions). • Conduct training on organizational introduction and organizational management for the establishment of the center.	

		• Lesson learnt from the experience of setting up a Clinical Research Unit will be compiled and the model for building and operating a Clinical Research Unit will be fleshed out to the Ministry of Health for policy recommendations.	
Issue① Lack of human resources, skills, and knowledge for clinical trials	4.Development of human resources to conduct, support, and manage clinical trials	• Conduct a capacity assessment of human resources for conducting clinical trials at target institutions, identify human resources that are in short supply (including clinical trial personnel and clinical research support and management personnel), and conduct a detailed assessment of training needs. • Based on the assessment results, formulate an annual training plan and a mid-long term plan for human resource development. • Develop and implement training curricula for healthcare professionals conducting clinical trials and clinical trial implementation managers and supporters.	
Issue⑥Lack of national policies and international assistance to promote clinical trials	5. Launch clinical research enhancement model through the established Clinical Research Unit	• The organization and management model of the Clinical Research Unit will be disseminated to other hospitals within the country.	

(3) Philippines

Theme	Strengthen the capacity of clinical trial examiners and inspectors and standardize examinations and inspections

For regulatory agency administrators involved in clinical trial review, we plan to conduct an assessment of administrative capabilities and business processes for pharmaceutical and clinical trial regulations and intervene from the perspectives of human resource development and improvement of business processes to resolve problems caused by human resource shortages and delays in regulatory processes. The overall organizational effort also includes a master plan for identifying and implementing the interventions needed to upgrade the PFDA to achieve WHO Maturity Level 3, future project proposals, and recommendations for ways to promote recruitment of regulatory personnel.

Corresponding Challenge	Solution Plan	Details of Support Activity (specific proposals of	Expected Target Insitution in the Target

		activities)	Country
Issue①Lack of human resources, skills, and knowledge for clinical trials Issue③ Uncertainty, complexity, and delay in the regulatory process of clinical trial regulations and guidelines	1.Development of human resources for pharmaceutical regulation	• Conduct an assessment of the regulatory administrative capacity of pharmaceutical and clinical trials at target institutions, identify human resources in short supply, and conduct a detailed assessment of training needs. High-need training topics for clinical trial examiners and inspectors are as follows: ・Clinical Study Regulations, Safety and Efficacy Review ・New Drug Approval ・GCP • Based on the assessment results, forumulate an annual training plan and a mid-long term plan for human resource development • Develop and implement training curricula for training subjects.	• PFDA
Issue③ Uncertainty, complexity, and delay in the regulatory process of clinical trial regulations and guidelines	2.Standardization of regulatory review and inspection processes	• Conduct an operation process analysis of the current inspections and reviews (in particular, analysis of the application review process at the clinical trial application stage, GCP inspection, etc.) to identify issues such as waste, lack of human resources, and uneven workload at each stage of the operation process. • Design new operation processes and develop guidelines in line with identified issues. • Training will be provided to the examiners and inspectors concerned with the content of the developed guidelines. • Verify the efficiency improvement of the operation processes after the introduction of the guidelines.	
Issue①Lack of human resources, skills, and knowledge for	3.Maturity Level Upgrade in WHO Benchmark Tool	• Assess unmet requirements for the Maturity Level (currently Level 1) upgrade	

clinical trials Issue③ Uncertainty, complexity, and delay in the regulatory process of clinical trial regulations and guidelines		(aiming for Lelve 3) in the WHO Benchmark tool. • Based on the results of the assessment, the actions required for the upgrade are identified and organized, and a master plan for implementation is developed. • Formulate a short-term, mid-long-term business plan based on the master plan.	
Issue① Lack of human resources, skills, and knowledge for clinical trials	4.Promote recruitment of personnel from regulatory agencies	• Analyze the causes of poor recruitment activities. • Propose measures to promote new recruitment.	

(4) Kenya

Theme	Strengthening the capacity of pharmaceutical administrators in regulatory bodies and implementing sensitization meetings involving personnel conducting clinical trials

For regulatory agency administrators involved in clinical trial review, we will conduct an assessment of administrative capabilities and business processes for pharmaceutical and clinical trial regulation. We will attempt to resolve issues such as the shortage of human resources and delays in the regulatory approval process at PPB, mainly from the perspective of human resource development and improvement of operation processes. In addition, the implementation component of the PPB's Strategic Plan (2020-2025) includes the implementation of a sensitization meeting involving personnel involved in the conduct of clinical trials, with the aim of improving the regulatory process based on the opinions of clinical trial institutions (applicants for clinical trial protocols, etc.). In addition, the PPB will promote understanding of the regulations of clinical trial institutions through communication from PPB administrators to applicants and will seek to mitigate delays in the regulatory process from both sides.

The urgent priority of the PPB is to increase the Maturity Level of the WHO Benchmark Tool from 1 to 3, and it is hoped that the above initiatives will be designed in a way that can achieve synergy with these priorities.

Corresponding Challenge	Solution Plan	Details of Support Activity (specific proposals of activities)	Expected Target Insitution in the Target Country
Issue① Lack of human resources, skills, and knowledge for clinical trials Issue③ Uncertainty, complexity, and delay in the regulatory process of clinical trial regulations and guidelines	1.Develop human resources for pharmaceutical regulations	• Conduct an assessment of the regulatory administrative capacity for pharmaceutical and clinical trials at target institutions, identify missing human resources and knowledge, and conduct a detailed assessment of training needs. • Based on the assessment results, formulate an annual training plan and a mid- long term plan for human resource development	• PPB

		• Develop and implement training curricula for training subjects.	
Issue③ Uncertainty, complexity, and delay in the regulatory process of clinical trial regulations and guidelines	2.Standardization and unification of regulatory review and inspection processes	• Conduct a operation process analysis of the current reviews and inspections (analysis of the application review process, especially at the clinical trial application stage, GCP inspections, etc.) to identify issues such as waste, lack of human resources, and uneven workload at each stage of the operation process. • Design new operation processes and develop guidelines in line with identified issues. • Training will be provided to the examiners and inspectors concerned with the content of the developed guidelines. • Verify the efficiency improvement of operation processes after the introduction of guidelines.	
Issue①Lack of human resources, skills, and knowledge for clinical trials Issue③ Uncertainty, complexity, and delay in the regulatory process of clinical trial regulations and guidelines	3.Maturity Level Upgrade in WHO Benchmark Tool	• Assess unmet requirements for the Maturity Level (currently Level 1) upgrade (aiming for Lelve 3) in the WHO Benchmark tool. • Based on the results of the assessment, the actions required for the upgrade are identified and organized, and a master plan for implementation is developed. • Formulate short-term, mid-long-term business plans based on the master plan.	
Issue①Lack of human resources, skills, and knowledge for clinical trials Issue③ Uncertainty, complexity, and	4.Conduct a sensitization meeting	• Make presentations that help promote understanding of the regulatory processes of clinical trial institutions. • Identify and assess any ambiguities or lack of understanding in the current regulatory process from clinical trial protocol applicants.	• PPB • Research institutions: Kenya Medical Research Institute and KAVI Institute of Clinical Research. • Medical institutions: Kenyatta National Hospital and Moi Teaching and Referral Hospital, etc.

delay in the regulatory process of clinical trial regulations and guidelines Issue⑦ Others (lack of cooperation among clinical research institutions)		• In accordance with the assessment results above, formulate measures to improve the regulatory process.	• Industry groups: Clinical Research Society of Kenya • NGOs: Amref Health Africa • Public Sector: National Commission for Science, Technology and Innovation

(5) Indonesia (2)

Theme	Demonstration and dissemination of highly sensitive virus detection operations through sewage monitoring

In response to the needs of Indonesian related organizations, who want to institutionalize and adopt it as a continuous method for the next generation of environmental conservation and infectious disease control measures, the activity will conduct the prediction of infectious diseases by visualizing and monitoring viruses using methods of sewage epidemiology, formulating operation protocols for infectious disease prevention measures, and transferring technology to local related organizations (in priority areas) involved in sewage surveillance. The goal of the activities is to standardize the operation protocol based on the results of sewage surveillance in priority areas, and to propose to the central government a solution for virus detection and monitoring by sewage surveillance that is optimal for post- COVID-19 Indonesian infectious disease control.

Corresponding Challenge	Solution Plan	Details of Support Activity (specific proposals of activities)	Expected Target Insitution in the Target Country
Issue⑦Others (improvement of sampling, detection, and analysis capabilities for sewage epidemiological surveys, etc.)	1.Development of operational protocols for sewage surveillance	• Select priority areas for sewage surveillance. • Identify the organizations (ministries, municipalities, research institutions, medical institutions, government related institutions, etc.) involved in sewage treatment and public health services in priority areas and analyze the functions and roles of each. • Develop operational protocols for sewage surveillance operations. • Define roles among the agencies in the focus areas in line with the established operational processes.	• Provincial government agencies(Provincial Department of Health, Provincial Inspection Agency , UPTD-PAL, etc.) • National Research and Innovation Agency(BRIN, Indonesia's National Research and Innovation Agency) • Regional Research and Innovation Agency(BRIDA, Regional Research and Innovation Agency) • Waterwater Treatment Plants (WWTP) • Local research institute such as national university faculty of medicine
	2.Technology transfer for sewage surveillance	• Develop training plans for the institutions in each role in accordance with the established operational protocols.	

		• In line with the technology transfer plan, training will be conducted on topics such as sewage sampling (sample collection), laboratory testing and inspection, data analysis, data accuracy management, and database construction and management. • Periodically monitor post-training operations to analyse issues and measures in line with local conditions and the normal business processes of relevant agencies and brush up on operational protocols.	
	3.Policy recommendations for Indonesia	• The results of sewage monitoring activities in the priority areas and standardized operation protocols based on local conditions will be compiled, and a solution for virus detection and monitoring through sewage surveillance that is optimal for Indonesia will be proposed to the central government.	

4.1.3 Proposal for programs by JICA

In this section, preconditions, points to keep in mind, and the possibility of cooperation with Japanese related organizations will be described, which will be necessary to keep in mind when formulating a program based on the proposed solutions and support activities described in the previous sections.

(1) Vietnam

Solution Plan	Preconditions and Points to Keep in Mind	Possibility of Cooperation with Relevant Organizations in Japan
1.Support the provision of equipment and materials to build a Clinical Research Promotion Center 2.Design and develop an organisation to build a Clinical Research Promotion Center 3.Develop human resources for clinical trials 4.Strengthen the clinical	[Preconditions] • Policy direction of the Clinical Research Promotion Center needs to be aligned with the Vietnamese Ministry of Health. [Points to keep in mind] • For the selection of clinical trial institutions, it is necessary to consider the clinical research collaboration partnership and the strategy of establishment of a base by Japanese institutions in	• Human resources and echnology exchange through the ARISE Network • Transfer of clinical research center management and clinical trial technology from a clinical trial core hospital in Japan

research support system	Vietnam, in accordance with the needs of the partner country and the level of commitment of the clinical trial institutions.	
5.Strengthen the sustainability of the Clinical Research Promotion Center		
6.Strengthen partnerships with other domestic and international organizations		

(2) Indonesia (1)

Solution Plan	Preconditions and Points to Keep in Mind	Possibility of Cooperation with Relevant Organizations in Japan
1.Support the provision of equipment and materials to build a Clinical Research Unit	[Preconditions] • Eligible clinical trial sites should be coordinated with both the Ministry of Health and the Ministry of Education and Culture, which oversees university hospitals. [Points to keep in mind] • The selection of medical institutions should take into consideration the direction of strengthening clinical research in Indonesia.	• Human resources and technology exchange through the ARISE Network. • Transfer of clinical research center management and clinical trial technology from a clinical trial core hospital in Japan.
2.Enhance data collection and management functions		
3.Build a Clinical Research Unit Model aligned with the order of the Minister of Health		
4.Develop human resources for clinical trials		
5.Launch the clinical research enhancement model through the established Clinical Research Unit		

(3) Philippines

Solution Plan	Preconditions and Points to Keep in Mind	Possibility of Cooperation with Relevant Organizations in Japan
1.Develop human resources for pharmaceutical regulation	[Preconditions] • It is necessary to utilize the cooperation system with Japanese pharmaceutical regulatory bodies and make use of the support of technical cooperation, and training resources.	• The knowledge of pharmaceutical regulatory bodies in Japan is essential. In addition to dispatch of long-term individual experts, dispatch of short-term experts, utilization of workshop contents of Japanese regulatory bodies can be considered as future cooperation programs. • The implementation of country-specific training in cooperation with the support scheme of the Asian Drug and Medical
2.Standardize and unify regulatory review and inspection processes		
3.Maturity Level Upgrade in WHO Benchmark Tool		
4.Promote recruitment of personnel from regulatory agencies		

		Device Training Center may also be considered.

(4) Kenya

Solution Plan	Preconditions and Points to Keep in Mind	Possibility of Cooperation with Relevant Organizations in Japan
1.Develop human resources for pharmaceutical regulation 2.Standardize and unify regulatory review and inspection processes 3.Maturity Level Upgrade in WHO Benchmark Tool	[Preconditions] • Knowledge from the Japanese pharmaceutical regulatory bodies are necessary, and cooperation from those institutions are a precondition.	• Possibilities include dispatching short-term experts to Kenya, participating in training programs in Japan, and conducting projects in cooperation with Japanese pharmaceutical regulatory bodies.
4.Conduct a sensitization meeting	[Preconditions] • As a commitment to implementing meetings, it is important to clarify not only the PPB implementation structure but also future budgetary arrangements. [Points to keep in mind] • The Clinical Research Society of Kenya, a trade association for clinical research in Kenya, also held a meeting for clinical trial personnel in November 2023. Differences and objectives between the existing meeting and the sensitization meeting held by the PPB need to be sorted out in advance.	• In addition to cooperation with Japanese pharmaceutical regulatory bodies, human resources and technology exchanges may be possible through joint research with Kenya, as well as the participation of pharmaceutical companies and research institutions that are considering clinical trials in Kenya.

(5) Indonesia (2)

Solution Plan	Preconditions and Points to Keep in Mind	Possibility of Cooperation with Relevant Organizations in Japan
1.Develop operational processes for sewage surveillance	[Preconditions] • Since the decision makers of each relevant institution span from the central and state governmentsto the local research institutions, appropriate consultation and coordination are necessary in the establishment of the system, including the application for licensing. [Points to keep in mind]	• Since sewage epidemiological surveys are at the demonstration stage in Japan, the number of organizations conducting sewage epidemiological surveys is extremely limited, but it is possible to collaborate with research institutions such as universities and related domestic organizations such as voluntary administrative municipalities.

	• A strong commitment from the central government, including legal institutionalization, systematization of the implementation system, and budgetary measures, is necessary to ensure the implementation of activities at the national level in the mid- long term and to ensure sustainability.	• Since several Japanese companies are developing testing technologies and reagents to detect viruses from sewage, cooperation with Japanese companies is highly desirable in terms of actively utilizing Japanese technologies and expanding overseas. • In Indonesia, the WHO and the Ministry of Health have conducted national polio surveillance, and the Australian Government has recently conducted a sewage epidemiology survey in Yogyakarta for the COVID-19 of the University of Gadjah Mada and Monash University, and there is considerable potential to use the know-how gained from these projects and to collaborate on subsequent projects.

Chapter 5 Summary of the survey and recommendations

5.1 Issues in Japan and government initiatives

At the G7 Hiroshima Summit chaired by Japan, the current state of health and medical care faced by the international community was discussed, and Japan's contribution and JICA’s role through the international framework is expected, for tackling future issues.

5.1.1 Initiatives by the government of Japan and relevance of this study

During the COVID-19 pandemic, effective vaccines and drugs were developed and put into practical use at an early stage in Europe, the United States, China, and India, while in Japan, where the level of basic research is considered to be very high, practical use was delayed. Based on these issues, the Government of Japan formulated the "Strategy for Strengthening the Vaccine Development and Production System" in 2021. The Strategy also mentions the development of the infrastructure for conducting clinical trials overseas and the consideration of the use of ODA for vaccine delivery. In addition, a rapid vaccine development system is being developed through the establishment of SCARDA. In 2022, the Global Health Strategy was developed, taking into account the lessons learned from the COVID-19 pandemic. The strategy describes the contribution to building and strengthening the global health architecture and strengthening prevention, preparedness and response to public health crises. Japan's efforts and the importance of cooperation in the international framework were also communicated at the G7 in 2023.

As this survey examined the direction of future cooperation, upon extracting the current situation and issues related to clinical research and pharmaceutical regulation of vaccines and other pharmaceuticals, through research and pilot implementation, this survey is said to be consistent with the policies and initiatives of the Japanese government mentioned above. In this study, we also collaborated with ARISE, which is promoted by NCGM, through co-hosting seminars and cooperating in pilot activities (exchange of views during visits to each partner country on the proposed establishment of clinical trial promotion centers in Vietnam and Indonesia). The possibility of the Kenya PPB being added to the issue-specific training jointly promoted by JICA and PMDA, and proposing the establishment of a Clinical Research Promotion Center by the University of Udayana (Indonesia) and the Ho Chi Minh University of Medicine and Pharmacy (Vietnam), together with the NCGM and the Clinical Research Promotion Center of the University of Tokyo Hospital, were effective in expanding connections with domestic and international institutions.

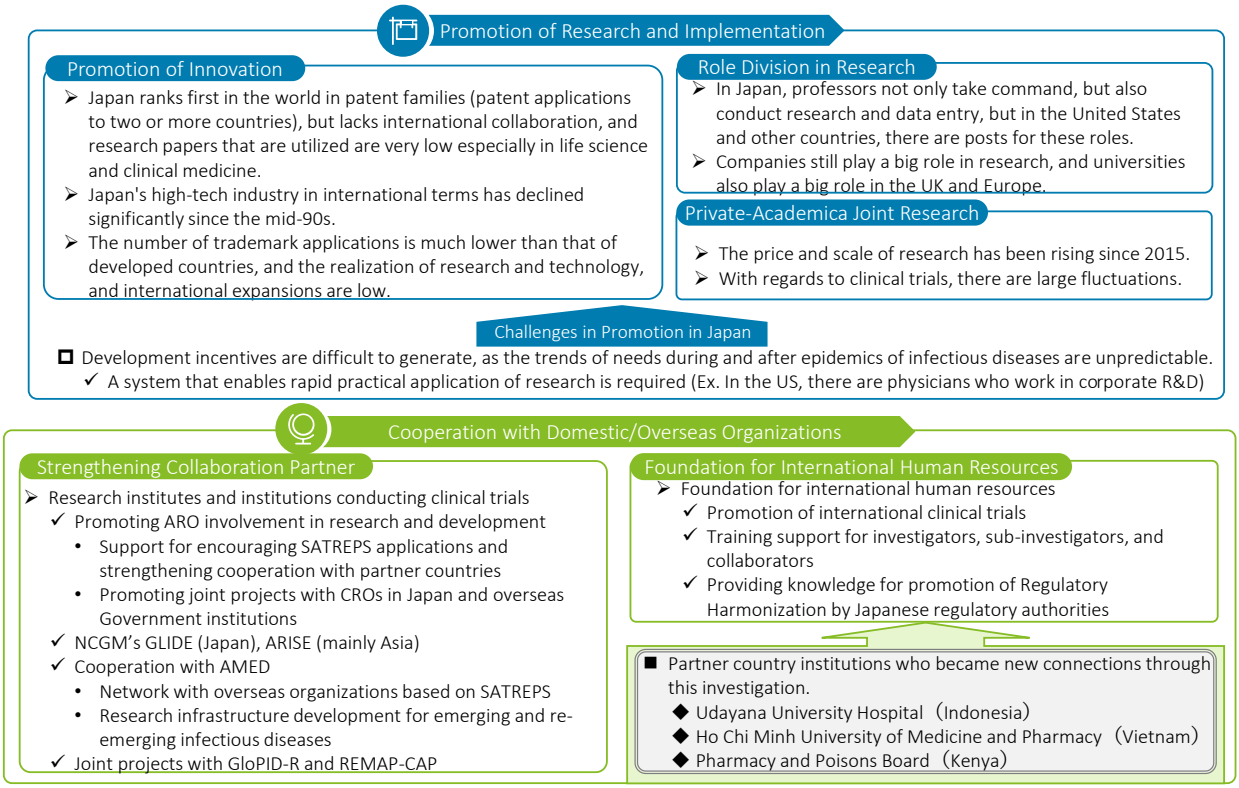


Figure 5-1 Current status of clinical research in Japan and further cooperation

5.1.2 Coordinated development by the public and private sectors

"The Grand Design and Implementation Plan of the New Capitalism," developed in 2022 and revised in response to the G7, also mentions cooperation with international organizations and public-private partnerships in the field of global health, which is based on the G7 agreement on the importance of the private sector's role in global health.

(1) Intergovernmental partnership

In the formulation of the Global Health Strategy, it was also discussed how to realize a system for effective business formation under the Global Health Architecture with the Japanese government as the control tower. In the Global Health Strategy, building a sustainable health system by strengthening cooperation between national finance and health authorities and strengthening cooperation between relevant international organizations and public-private partnership funds are essential for building an architecture. With regards to the system considered in the Global Health Strategy, the Japanese government acting as a control tower, will gather opinions from ministries and agencies, academia, private companies, civil society and industry groups, and share them with JICA field offices and diplomatic missions. It will also strategically send managerial and working-level personnel to international organizations and coordinate information with JICA field offices and diplomatic missions. By collecting and analyzing issues and needs from relevant organizations in partner countries, through JICA field offices and diplomatic missions that are in charge of on-site coordination, it becomes possible to accurately match needs with seeds and form businesses.

The expected role of JICA is to further strengthen the relationships with the parties involved in the partner countries built on the previous projects, and to bridge them to Japanese companies and academias. In addition to collecting information on technologies and services that can respond to the needs of partner countries through JICA, it would also be effective to share such information with AMED and NCGM. In addition, it is expected that the activities of Japanese stakeholders will be eased, by sharing SATREPS

counterparts who conducts international joint research with research institutions in other countries, led by Japanese academia, as well as potential partners for demonstration projects of Japanese private companies. With regards to SATREPS, it is also possible to encourage the participation of Japanese companies that are suitable for research applications. Research projects such as SATREPS can provide continuous support for demonstration projects such as private sector collaboration projects, as well as support for implementation and standardization such as technical and financial cooperation.

One of the pillars of the JICA Global Health Initiative, launched in 2020, is the establishment of core hospitals and infectious disease research centers in each country. In addition to business formation and implementation, they can also serve as a recipient for demonstration and joint research.

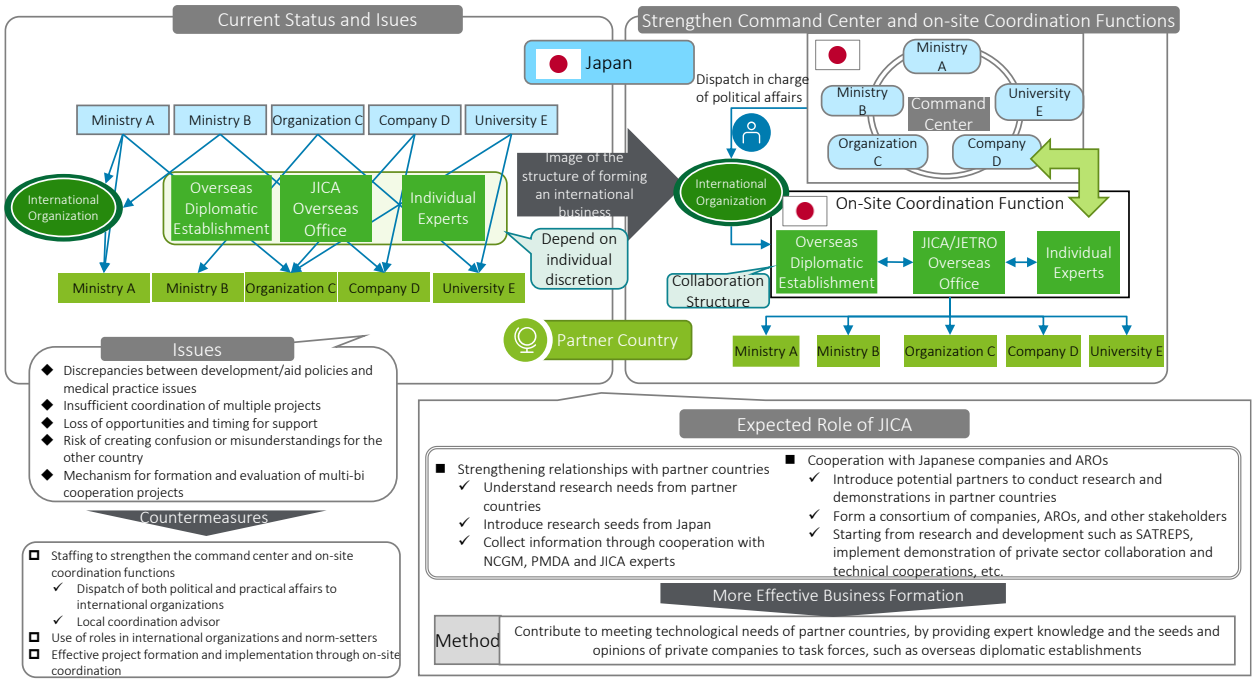


Figure 5-2 Structure for overseas business formation of Japanese government agencies

In the past, when considering responses to social issues in partner countries, it has often been attempted to solve individual issues faced by the target organization, by applying the unique technology and know-how of the company. For companies, the partnership with ODA schemes enabled them to create opportunities for deployment and direct sales to partner governments. Some argue that COVID-19's enormous impact has been a "syndemic," an interplay of environmental factors, including climate change and biodiversity loss; health factors, such as obesity and the spread of non-communicable diseases; health system vulnerabilities; and social and economic factors, such as urbanization and rising inequality[153].

In the next pandemic, it will be necessary to address issues other than those related to health and medical care. Therefore, it may be more important to form a combined program than to solve individual issues through the provision of technology by individual companies, and to use funds and networks from international organizations to form development projects involving local companies. This combined approach to problem solving by linking individual technologies, as well as the cooperation of companies and industry associations in partner countries as business partners, will enable Japanese industry, government and academia to tackle social problem solving with the same objectives, rather than the relationship between the target country government and international organizations, or ODA of bilateral governments. For example, the partnership for Access and Delivery of Novel Medical Technologies (ADP), led by the UNDP involving the government of Japan, develops and implements tools for monitoring adverse

[153] UHC Day Homepage "Addressing COVID-19 with Universal Health Coverage" (https://uhcday.jp/2021/06/11/1742/)

drug reactions in partnership with startups. In addition, the use of ICT and transport technologies is also progressing, including the introduction of refrigerated vehicles for vaccine delivery. Ajinomoto, which promotes improved nutrition in Ghanaian countries, works with Sysmex, which produces diagnostic equipment to measure the effectiveness of improved nutrition in preventing malaria transmission, and with NEC for useful data storage. Such combined approach can be an effective method for infectious disease control. In terms of clinical research, there were some CROs operating with multinational pharmaceutical companies in the target countries of this study and some local CROs, but the lack of human resource skills was stated as an issue. Currently, only a limited number of CROs from Japan can be deployed overseas, but it is possible that Japanese CROs, together with international joint research and Japanese pharmaceutical companies, can be deployed overseas to form a cooperative system, and transfer technology to local CROs.

In past interviews that were conducted, it was stated that by properly protecting intellectual property and promoting regulations, on the businesss side, it would be possible to look ahead to the standardization of technology in the target country, and would also be possible to develop the Japanese system as a package for solving social issues.

Despite the unprecedented speed of research and development into vaccines and therapeutics during the COVID-19 pandemic, the WHO General Assembly in May 2020 adopted a resolution calling for voluntary sharing through the use of patent pools and for international coordination with the World Trade Organization (WTO) Trade-Related Aspects of Intellectual Property Rights (TRIPS Agreement) and the Special Declaration on TRIPS and Public Health (Doha Declaration) to remove barriers to ensure equitable and affordable access. Subsequently, WHO established the mRNA Vaccine Technology Transfer Hub in 2021 as a scheme to facilitate the sharing of mRNA-based technologies. It was sparked by Indian and South African proposals for exemptions from the TRIPS Agreement to prevent, contain and treat COVID-19, which led to an international debate. Many developing countries indicated that the pandemic, with its huge public resources, should not link intellectual property with the recovery of investments such as research and development, thereby creating barriers to affordable and timely access. Pharmaceutical and biotechnology industry groups in Japan, the United States and Europe oppose the move, arguing that it would create barriers to rapid research and development. At the corporate hearings, it was also mentioned that although the company had succeeded in developing a drug for specific diseases, it was not easy to gain shareholders' understanding of the situation in which it was difficult to generate profits by deploying the drug in developing countries.

In addition, by continuing to standardize in other countries, technical recommendations from specific countries necessary for certification by international organizations can be obtained, and international standardization can be considered by developing countries through certification.

This is in line with the idea of "establishing a system and framework," which is considered as a package of measures in the "Harmonized Grand Design for Regulations on Pharmaceuticals and Medical Devices in Asia" compiled by the Japanese government in 2019.

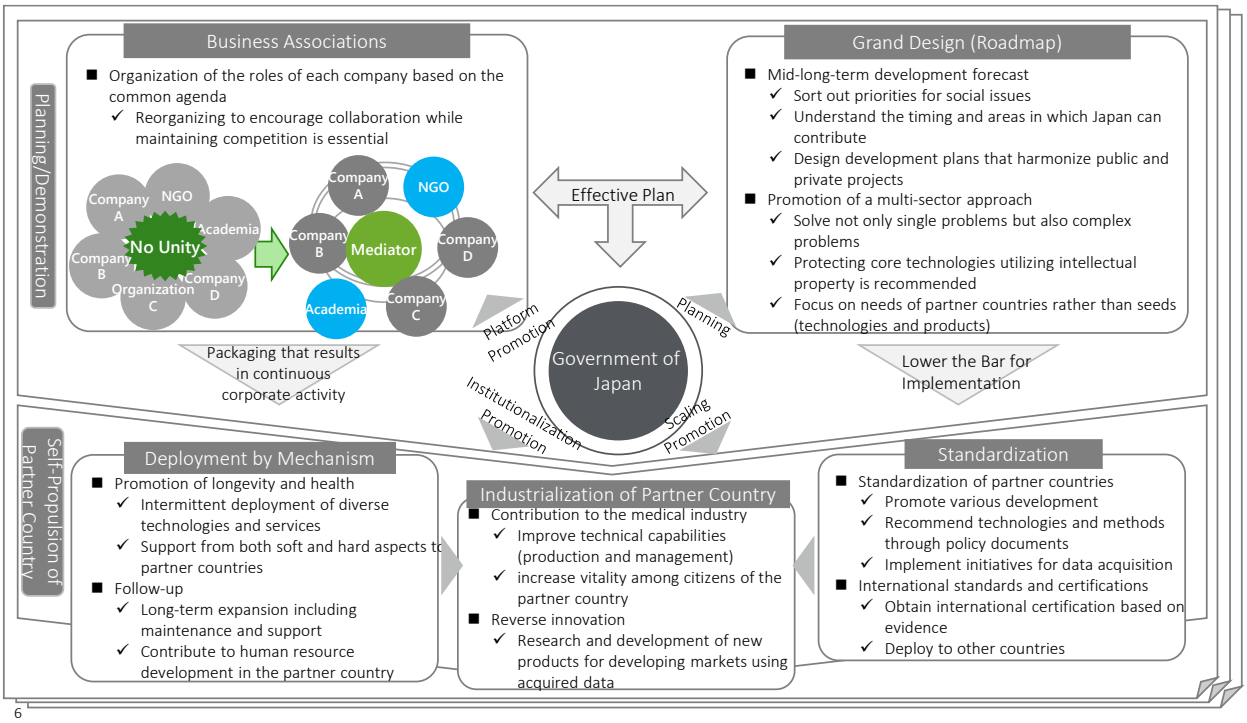


Figure 5-3 Roadmap for the development of companies

5.1.3 Roadmap of the target countries

Following the COVID-19 pandemic, it was argued that the health crisis response should not only protect the health of people in developed countries, but also target governments and communities in low- and middle-income countries and prepare for new crises by utilizing existing disease control mechanisms, systems, and organizations[154]. Advancing the health crisis response will require both "compensating for inequalities" and strengthening the health system[155].

The figure below shows how the health system built on existing measures against infectious diseases was useful during the COVID-19 pandemic, and how the added functions during the pandemic can be used to further prepare for infectious diseases. In addition to building a resilient health system and achieving national security, it is important to promote joint research and clinical trials with partner countries, as well as networking. From this point of view, support for the establishment of clinical research promotion centers (or clinical research units) proposed by Vietnam and Indonesia in this study may be useful.

[154] Global Fund "Re-thinking Global Health Security" (https://www.theglobalfund.org/en/blog/2020-03-27-re-thinking-global-health-security/)

[155] Global Fund "WHO and Global Fund Warn Inequalities Block Progress Towards Ending AIDS, TB and Malaria" (https://www.theglobalfund.org/en/news/2021/2021-12-08-who-and-global-fund-warn-inequalities-block-progress-towards-ending-aids-tb-and-malaria/)

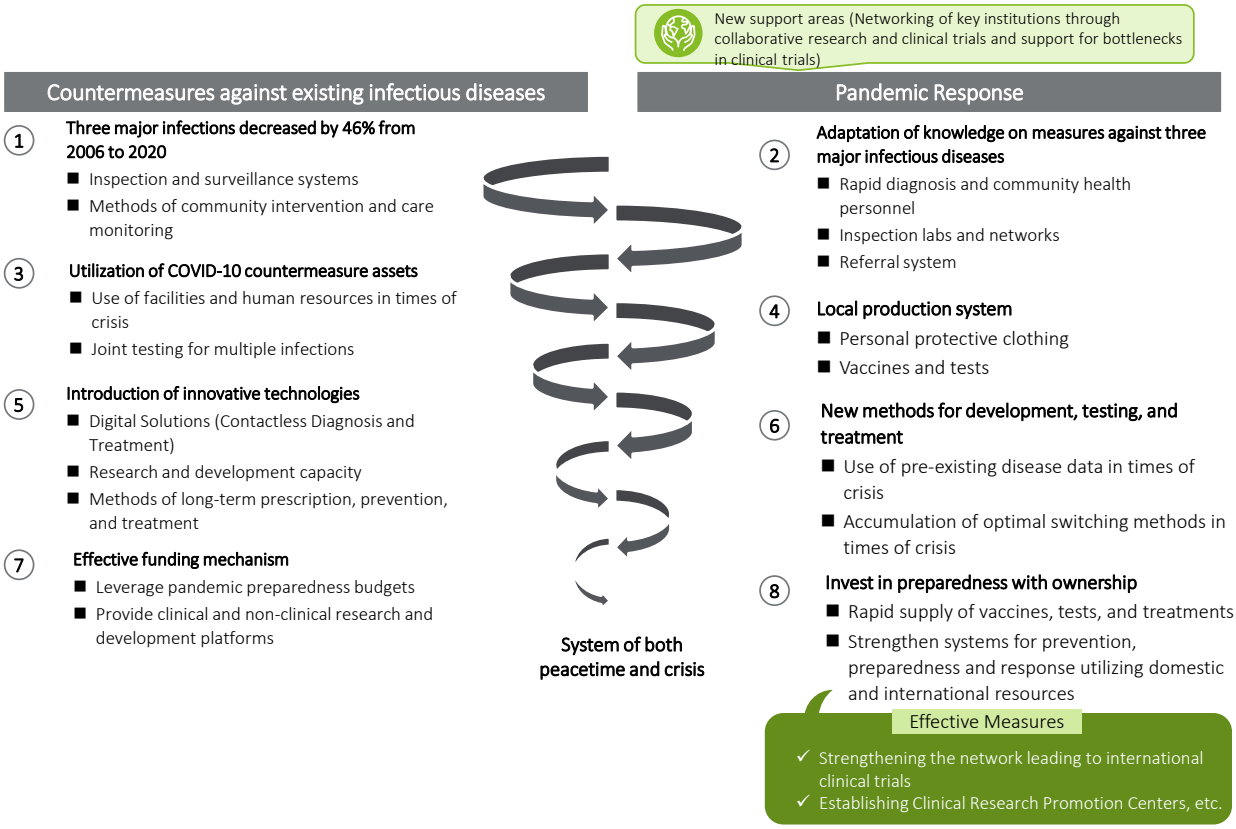


Figure 5-4 Health system strengthening and pandemic preparedness

With regards to the roadmap described in the previous section, private companies and industry associations whom we conducted interviews with expressed their preference for creating a "roadmap" between the partner countries and Japan and the international community. For example, by creating a road map to establish the SDGs goal by 2030, by listing necessary issues and solutions and have priorities sorted by issue and year, this would make it easier for each relevant party to make mid-long-term commitments and would enable ODA to be used in the overall planning in a manner consistent with the Global Health Strategy. It is also important for such planning to take a long-term perspective and establish visible targets for achieving the short-mid term goal and analyze the current situation for this purpose. For example, even in a five-year mid-term plan, it is important to have a blueprint for the next five years after the achievement of that goal.

Based on interviews with countries in this study, the following figure generalizes the anticipated challenges and responses to the promotion of clinical trials and the intensification of manufacturing of vaccines and other pharmaceuticals over the next 10 years. During COVID-19, existing medical laboratories (JICA has supported Vietnam National Institute of Hygiene and Epidemiology (NIHAE), Philippine Institute of Tropical Medicine (RITM), Kenya KEMRI, etc.) played a central role in the autonomous movement of developing countries, as shown in the figure below. The ability to respond to emergencies in the mid- long term by strengthening such functions from peacetime (a step toward achieving UHC) is important as a core capacity against infectious diseases. Based on this, how to smoothly transition from normal times to emergency situations (for example, using existing facilities for vaccine research and development or to convert them into infectious disease control wards) is required as a core capacity.

As all of the institutions included in this survey provide clinical trial sites for vaccines and drugs in Western countries, some of the institutions aimed to form their own clinical trial platforms by enabling the implementation of Phase I clinical trials and research and development in their own countries. The figure below shows the steps needed to strengthen the health system in the short to medium term and the preparedness for infectious diseases in the long term, divided into material measures, use of digital technology, and systems (human resources, technology standardization, and collaboration with each field),

and the corresponding ODA responses. As cited by research institutions such as universities and CROs in various countries, the soft side of short-term clinical trial promotion is human resources capable of quality control and data management. There are many cases in which data management is performed by hand or by stand-alone terminals, and IT utilization such as systematization and networking is required. In addition, attempts to digitize medical data of patients (linking with national IDs, etc.) are also considered. For human resource development by combining these IT, it is possible to utilize private technology and, in a good case, to standardize in the partner country. In parallel with this move, joint research and international clinical trials through SATREPS, etc. should be promoted, so that academia and the private sector can develop in a unified sense.

In the short to medium term up to around 2030, it is important to strengthen the health system and core capacity to improve the ability to respond in normal times. With the aim of achieving the UHC that is resilient to previous pandemics, we are examining the human resource development required for clinical trials from the perspectives of research institutions, regulators, and manufacturers. The ability to conduct clinical trials based on international standards will enable more foreign investment and human resources to be strengthened. In ICT, it is also important to promote remote diagnosis and strengthen capabilities such as medical data handling. In line with this, cooperation with relevant domestic and international organizations will be promoted. This is expected to increase even in countries with few clinical trial promotion centers.

From 2030 onward, the transition from core capacity to surge capacity is expected. In terms of facilities, the establishment of biobanks and other facilities, and in ICT, the development of policies based on infection spread prediction models and data will become important. In the long term, it will also be necessary to establish a disease control center, such as the CDC, and to provide training in the initial response to emergencies.

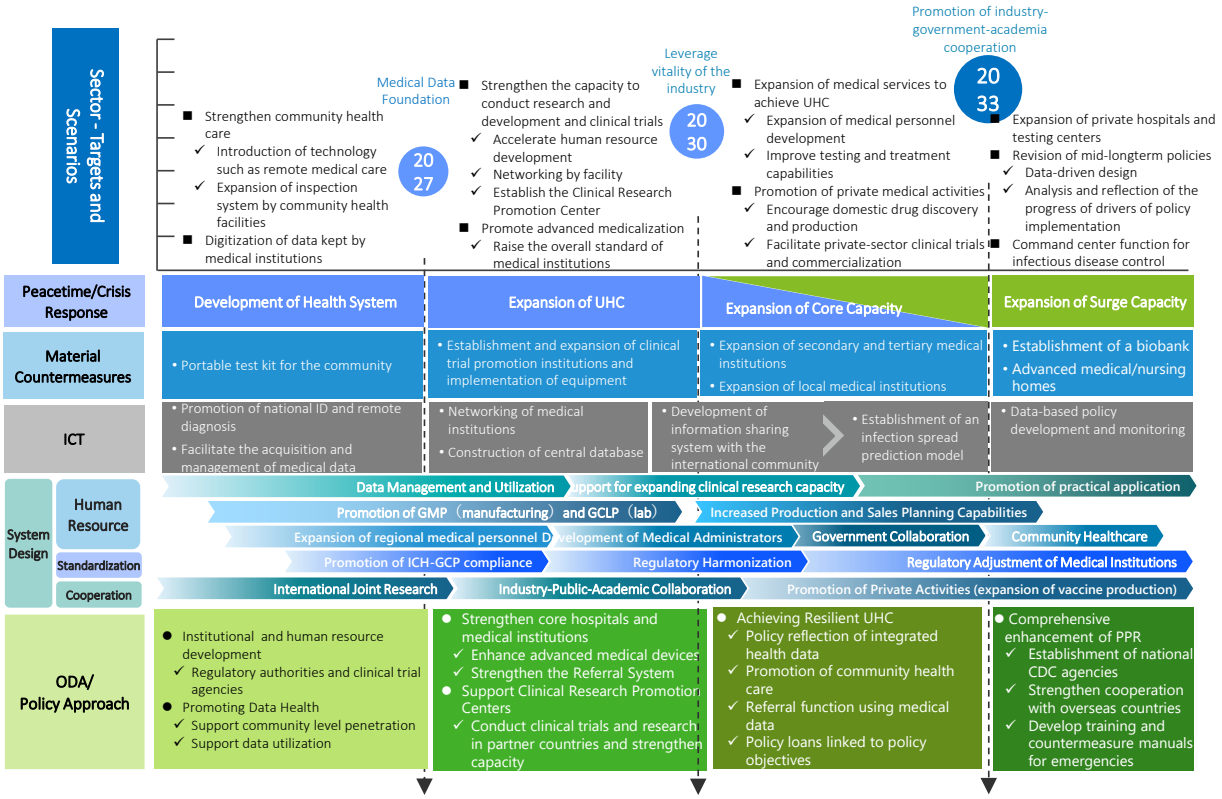


Figure 5-5 Roadmap image for the partner country

5.2 JICA’s expected role in the mid-long term

Chapter 4 covered the most recent issues and needs of the target countries in this study through the implementation of pilot activities and examination of their effects, and proposed support projects that JICA could implement in the short term. This section describes JICA's mid-long-term initiatives in line with JICA's Global Agenda for Health and Medicine, based on the Government of Japan's policy on vaccine and drug development, and the contents of the roadmap for 10 years ahead, as outlined in the previous section.

5.2.1 Relevance to the JICA Global Agenda

JICA has set up three pillars of strengthening its efforts: strengthening the diagnosis and treatment system, strengthening the research and surveillance (inspection) system, and strengthening prevention and mainstreaming health crisis preparedness. In response to each of these three pillars, JICA has established four clusters as its global agenda in the field of health and medical care that it will focus on: strengthening diagnosis and treatment at core hospitals, strengthening infectious disease control and testing sites, strengthening high-quality maternal and child care continuity including the use of the Maternal and Child Health Handbook, and strengthening the medical security system.

The main topic of this study, "Support for R&D and manufacturing of vaccines and drugs for infectious disease control," is related to the "Strengthening of infectious disease control and testing sites" cluster among the above four clusters. Under the cluster, the following activity policies are established:

- Enhancement of testing and diagnostic technology
- New and expanded infectious disease testing and research sites, and training of specialized human resources
- Strengthen contact tracing and early detection of infected people through the development of COVID-19's testing system
- Strengthen border measures
- Expansion of new cooperative partnerships utilizing the network of infectious disease testing and research centers cultivated through previous cooperation

5.2.2 Proposal for mid-long term support and cooperation by JICA

Based on the information on the issues and needs of each country obtained through the literature study and interviews with the target countries, the figure below shows proposals for assistance and cooperation that JICA can undertake in the mid-long term in each of the following four categories: policy strategy and system development, implementation of support platform, human resource and organizational development, and infrastructure strengthening through the development of facilities and equipment. In addition, the horizontal axis shows the steps in the process from vaccine and drug development to delivery to the community (basic research, non-clinical testing, development, clinical testing, manufacturing, distribution, and delivery) at which these efforts can spread their effects. In addition, a support scheme (loan and grant aid, technical assistance (including SATREPS), dispatch of individual experts, training projects, overseas investment and loans, research projects, private sector collaboration projects) that JICA can utilize for each proposed support cooperation is also shown.

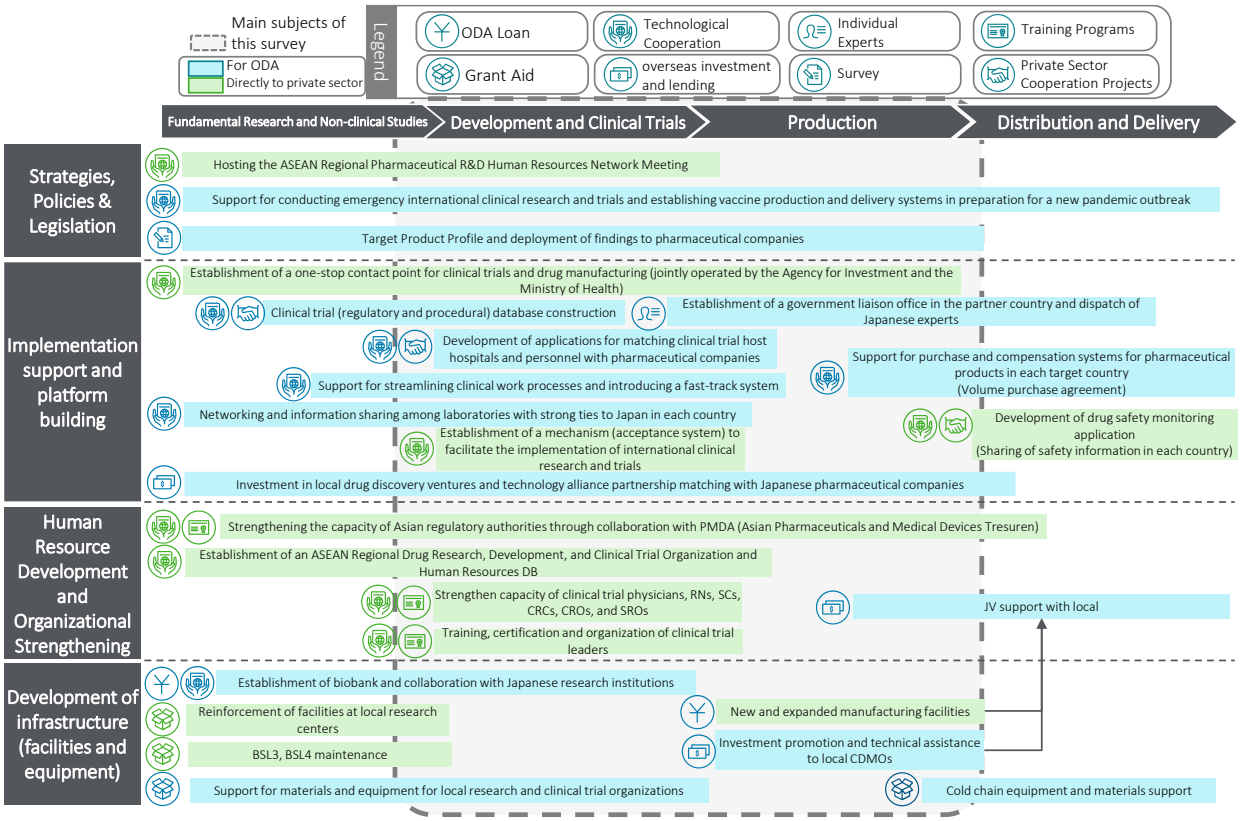


Figure 5-6 Examples of JICA's mid- long-term cooperation initiatives

(1) Development of strategies, policies and legislation

Initiatives (example)	Summary	Issues to be Addressed	Relations with GA*
Support for organizing the ASEAN Regional Human Resources Network for Pharmaceutical Research and Development meeting	Collaborate with existing clinical research networks originating in Japan (ARISE, ATLAS, etc.) to identify key personnel in pharmaceutical R&D in the ASEAN region through international conferences and seminars, and support the establishment of relationships	① Lack of human resources, skills, and knowledge for clinical trials	New and expanded infectious disease testing and research sites Development of specialized human resources at research sites Expansion of new cooperative partnerships
Support for the implementation of international clinical research and trials in emergencies, and the establishment of operations	Support the development of work and operational procedures to facilitate the smooth and rapid implementation of international clinical trials, and the establishment of vaccine and	③Uncertainty and complexity of clinical trial regulations and guidelines, and delays in	Enhancement of testing and diagnostic technology

for vaccine and drug manufacturing and delivery systems	drug delivery systems in the event of a global pandemic emergency	regulatory processes	
Expansion of the “Target Product Profile” and the study results	Conduct a comprehensive study of the pharmaceutical needs of countries around the world, and priority diseases and priority modalities in vaccine and drug development, identify global needs and trends in the field of vaccine and drug development, and share the survey to relevant organizations in Japan (pharmaceutical companies, research institutions, clinical research networks, etc.) to support the formulation of respective action strategies	⑥Lack of national policies and international aid to promote clinical trials	Enhancement of testing and diagnostic technology Expansion of new cooperative partnerships

*GA: JICA Global Agenda

(2) Implementation support and platform development

Initiatives (example)	Summary	Issues to be Addressed	Relations with GA*
One-stop point of contact for clinical trials and pharmaceutical manufacturing Establishment of liaison offices (liaison bases) and dispatch of Japanese experts	In order to create an environment in which relevant Japanese institutions (research institutions, pharmaceutical companies, etc.) can conduct international joint clinical research smoothly and quickly in other countries, establish one-stop contact points and liaison bases in priority countries and assign human resources who can collect and disseminate information.	① Lack of human resources, skills, and knowledge for clinical trials ⑥ Lack of national policies and international aid to promote clinical trials	New and expanded infectious disease testing and research sites
Network and information sharing of laboratories with strong ties to Japan in various countries Development of applications for matching clinical trial acceptance hospitals and human resources with pharmaceutical companies	Establish a network among infectious disease laboratories (Vietnamese, Filipinos, Ghanaians, Kenyans, Zambians, Nigerians, Congolese citizens, etc.) based in each country, which Japan has been providing intensive support for, and strengthen the matching function of these bases as a site for collecting information on clinical trial hospitals in other countries, and clinical trial personnel	① Lack of human resources, skills, and knowledge for clinical trials ⑥ Lack of national policies and international aid to promote clinical trials	Enhancement of testing and diagnostic technology New and expanded infectious disease testing and research sites

	affiliated with them.		
Support for streamlining regulatory processes and the introduction of a fast-track system	Support the development of regulatory processes and manuals and the implementation of fast-track systems for pharmaceutical regulatory bodies in response to pandemic emergencies	③Uncertainty and complexity of clinical trial regulations and guidelines, and delays in regulatory processes	Strengthening border measures Development of specialized human resources at research sites
Development of a pharmacovigilance system (sharing of safety information in each country)	Strengthen the ability to collect and analyze real-time information by establishing a monitoring system and database for the presence of adverse events associated with the use of drugs in Asia, in cooperation with the WHO International Drug Monitoring System. In addition, establish a framework for utilizing Real World Data (RWD) in Asia, in terms of ensuring database quality and establishing rules for collecting and managing information.	⑥ Lack of domestic pharmaceutical companies and international aid to promote local manufactruing	—
Invest in local drug discovery ventures and partner with Japanese pharmaceutical companies	Promote international technology alliances, international joint research, and human resource exchanges through support for matching local drug discovery ventures with Japanese pharmaceutical companies	⑦ Lack of collaboration between academia and industry	Expansion of new cooperative partnerships

*GA: JICA Global Agenda

(3) Human resource and organizational development

Initiatives (example)	Summary	Issues to be Addressed	Relations with GA*
Strengthen the capacity of Asian regulatory authorities in collaboration with the PMDA	In anticipation of possible regional and global pandemics in the future, work with the PMDA to strengthen the capacity of the Asian regulatory authorities as a whole, and support the establishment and regulatory	① Lack of human resources, skills, and knowledge for clinical trials ③ Uncertainty	Development of specialized human resources at research sites

	harmonization of the regulatory process for Asian countries	and complexity of clinical trial regulations and guidelines, and delays in regulatory processes	
Establish the ASEAN Regional Drug Research, Development, Clinical Trial Organization and Human Resource Database	Establish a common database that integrates information on medical needs/seeds, clinical trial regulations and procedures, clinical trial data, laboratories, national and regional platforms, clinical trial personnel, etc., and use the information in the database to support the strategic development of clinical trial institutions, strengthen capacity, and promote strategic human resource exchange and knowledge/technology transfer	① Lack of human resources, skills, and knowledge for clinical trials	Expansion of new cooperative partnerships Development of specialized human resources at research sites
Training, certification, and organization of clinical trial instructors Strengthen the capacity of clinical trial-related personnel such as clinical trial physicians, nurses, and trial coordinators	In order to expand human resources for clinical trials in the partner country, establish a certification system and provide training for clinical trial instructors, establish an education system for human resources related to clinical trials, focusing on trained instructors, and support the expansion of human resources.	① Lack of human resources, skills, and knowledge for clinical trials	Development of specialized human resources at research sites

*GA: JICA Global Agenda

(4) Infrastructure development

Initiatives (example)	Summary	Issues to be Addressed	Relations with GA*
Establish a biobank and cooperate with Japanese research institutes	Build biobanks that store DNA data and data on specific diseases, and design strategies for utilizing biobank data in clinical research, as well as use cases.	⑤ Weak data management	Network with infectious disease testing and research sites
Reinforce facilities and laboratories at local research centers Support materials and	(Thailand, Indonesia, Vietnam, etc.) Develop clinical research facilities and equipment and provide equipment training to research institutions in regions where	② Insufficient or inadequate clinical testing facilities and equipment	New and expanded infectious disease testing and research sites

equipment of local research and clinical trial institutions	there is a high need for research institutions and pharmaceutical companies to strategically base their research.		
Establish and expand manufacturing sites Promote investment and technical support to local contract development and manufacturing institutions (CDMO)	Establish a core research and manufacturing base where CDMOs gather around the organizations that JICA has supported in the past, such as POLYVAC and IVAC in Vietnam, as a base for vaccine and pharmaceutical manufacturing, and support the development of functions such as research and development of vaccines and biologics, international joint research for infectious diseases, secretariat functions for CDC initiatives, and clinical trial facilities.	② Lack of manufacturing facilities and equipment ②Insufficient or inadequate clinical testing facilities and equipment	New and expanded infectious disease testing and research sites

*GA: JICA Global Agenda

5.2.3 Recommendations for the role expected of JICA in the future

(1) Further expansion of the broader approach

JICA's mid-long-term support and cooperation proposals, as exemplified in 5.2.2 above, include initiatives that will be more effective by working on a broad-area basis.

For example, 1) "Support for the operation of the ASEAN Regional Pharmaceutical Research and Development Human Resources Network" proposed in the area of strategy, policy, and legislation development, and 3) "Construction of an ASEAN Regional Pharmaceutical Research and Development, Clinical Trial Organization, and Human Resource Database" proposed in the area of human resource and organizational development are areas of activity where Japan can lead a synergistic effect in the wider region of Asia, focusing on ASEAN countries, by implmeneting them in parallel.

The figure below shows an example of expanding the network with related institutions such as academia, medical institutions, and research institutes in the wider Asia region through two broad-area approaches. In addition to expanding the network, a common database that accumulates various types of data[156] obtained through the use of the network will be constructed to support the strategic formulation of clinical trial institutions in Asia using the data, strengthen capacity, and promote strategic human resource exchange and knowledge technology transfer.

[156] Examples of various types of data include medical needs/seeds across Asia, updates on clinical trial regulations and procedures, clinical trial data, information on laboratories, national and regional platforms, and data on human resources for clinical trials.

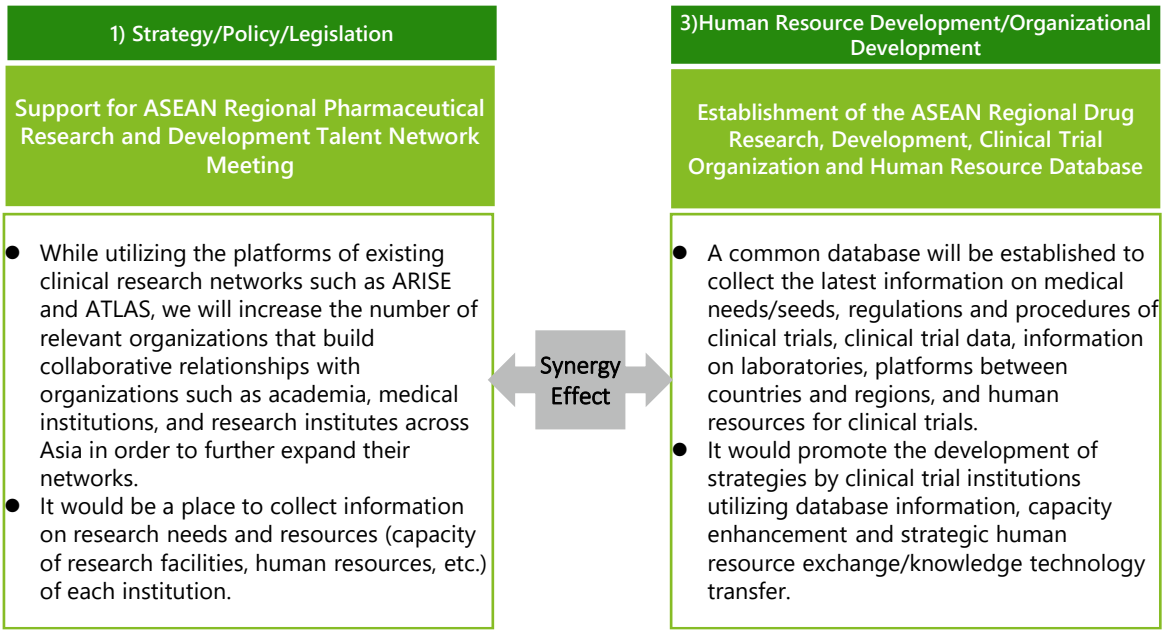


Figure 5-7 Example of a broad-area approach

It is effective to utilize and cooperate with existing Asian clinical research network platforms such as ARISE and ATLAS for this broad-area approach. By utilizing JICA's support schemes, project methods, funding, connections with relevant organizations and specialized human resources that have been established through ODA projects, etc., JICA is expected to play a role in further expanding the scope of activities, funding scale, approach methods, etc. for the formation of the Asia broad-area platform promoted by ARISE and ATLAS.

(2) Initiatives of digital transformation (DX)

The incorporation of digital technology is essential when establishing a database that integrates data obtained from the Asia broad area network mentioned in the preceding paragraph, and when working on the "establishment of a biobank and cooperation with Japanese research institutes" exemplified in 5.2.2. JICA has accumulated knowledge and experience in the field of healthcare in developing countries from the past projects, including the utilization of digital health and digitalization of businesse processes. In addition, JICA is able to bring together not only health and medical professionals, but also specialized human resources in areas of system development, network infrastructure, data analysis, and data security, of whom that have been pooled through past projects in various fields. JICA has a foundation that enables intersectoral collaboration in developing countries. From this point of view, when incorporating DX into support projects for the development and manufacturing of vaccines and pharmaceuticals in the future, JICA is required to play a leading role by actively mobilizing knowledge of specialized human resources and utilizing know-how gained from past projects.

(3) Environmental development and business matching for private companies

For the development and dissemination of vaccines and drugs, it is essential to actively involve the private sector at all stages, and it is necessary to seek the active use of innovative modalities and technologies originating in Japan in cooperation with the private sector. In recent years, JICA has been mobilizing private sector technology and funds to solve problems in developing countries through private sector collaboration projects. However, there are still limited examples of collaboration projects with private companies related to the development and dissemination of vaccines and drugs (or reagents). As described in 5.1.1, what JICA is expected to do in the mid-long term, is to strengthen its role as a bridge between the partner country institutions and Japanese companies, in order to further strengthen the relationships with relevant organizations and parties in partner countries. For example, with regards to SATREPS, it is possible to not only collaborate between universities and research institutes in Japan and

the partner country, but also promote partnerships with private companies, strengthen demonstration of the technology of private companies, and recruit specialized human resources from private companies for SATREPS and other technical cooperation. It is also conceivable for Japan and its partner countries to intiate a collaboration with private-secotor technology, similar to the mid-long term support project, "Investing in local drug discovery ventures and partnering with Japanese pharmaceutical companies" which was previous proposed, as well as development of new support schemes developed to support the development of an environment for private companies to easily enter the market, similar to the “Target Product Profile.”

Appendix 1: Interview Questions

Government Institutions

■ Current Situation and Issues

- What are the bottlenecks in conducting clinical trials?
- What are the bottlenecks in strengthening the production system for vaccines and drugs?
- Is there cooperation between medical ministries and agencies, and if so, what role does each organization play?
- Are there opportunities for stakeholders to share knowledge and concerns (For example, are there networks between public/private institutions and pharmaceutical companies where they can share each other's needs)?
- Is there a support system in which public and private institutions can receive assistance to create innovative new drugs?
- Are there concerns raised by private institutions and pharmaceutical companies about clinical trials and the manufacture of drugs, and are appropriate actions taken?

■ Future Outlook

- What is your outlook for the acceleration of clinical trial processes and pharmaceutical manufacturing in the future (e.g., networking)?
- Japan is developing its own technology for high-precision sewage epidemiology. Is there any interest in cooperation in such related fields?
- What do you expect from the Japanese public and private sectors (short-term pilot activities and mid-long term collaboration)?

Medical Research Institutions/Academia's

■ Current Situation and Issues

- What are the bottlenecks in conducting clinical trials?
- What are the bottlenecks in strengthening the production system for vaccines and drugs?
- Is there cooperation between medical ministries, and if so, what role does each organization play?
- Are there opportunities for stakeholders to share knowledge and concerns (For example, are there networks between public/private institutions and pharmaceutical companies where they can share each other's needs)?
- Is there a support system in which public and private institutions can receive assistance to create innovative new drugs?
- Are there any successful cases of cooperation with overseas medical institutions and pharmaceutical companies?

■ Future Outlook

- What is your outlook for the acceleration of clinical trial processes and pharmaceutical manufacturing in the future (e.g., networking)?
- Are there any needs or strategies for implementing new methods for clinical trials, such as adaptive design or real world data?Japan is developing its own technology for high-precision sewage epidemiology. Is there any interest in cooperation in such related fields?
- What do you expect from the Japanese public and private sectors (short-term pilot activities and mid-long term collaboration)?

CROs/Clinical trial sites

■ **Common questions (Challenges and future prospects)**

- Have there been measures to implement new methods such as adaptive design and real world data? Are there barriers in regards to implementing these methods?
- Which phase of a clinical trial does your organization take part in the most? Do you prioritize specific research areas or phases?
- Is the professional quality sufficient to conduct clinical trials? If not, what is the reason for the lack of expertise?
- What are the main barriers affecting relevant organizations and shortage of human resources? Is there an effective incentive to increase the number of staff?
- Are there efforts to share knowledge and data on clinical trials with other organizations in Japan and abroad?
- Do you feel there is not enough data sharing or collaboration between relevant organizations and the government? If so, what would be the solution to fix this issue?
- What technological innovations are important in promoting the efficiency and quality of clinical trials?

■ **Individual questions (Challenges and future prospects)**

- Is there a mechanism for efficient collaboration and a network for global communication within your organization?
- What are the challenges in clinical trial management? Does your organization have an adequate supply of tools and technologies?
- How can inconsistencies in conducting trials be resolved due to differences in the expertise of each clinical trial site?
- How do you feel about the use of AI and other technologies in larger clinical trials? Do you already have the infrastructure/platform for clinical data management?

Private Companies/Industry Associations

■ Current Situation and Issues

- Are there operational or structural problems with the manufacturing process?
- Has the uncertainty of pharmaceutical demand from the pandemic affected the manufacturing and distribution processes? What kind of operation is planned?
- Are there issues such as supply delays due to supply chain disruptions or supply shortages, from the impact of COVID-19?
- What is needed to maintain a transparent and efficient supply chain (e.g. digital solutions)?
- Is collaboration with academia important for R&D and what are the barriers?
- Do you feel that CSR activities generate shareholder value and increase the profitability of pharmaceutical companies in your country?
- What initiatives do you think will help get more pharmaceutical companies into the market for vaccine production in your country?

■ Future Outlook

- What are the barriers for pharmaceutical collaboration with foreign companies and is it worthwhile to create a platform for drug development in collaboration with foreign companies?
- Are there any needs or requests to your local government or the Japanese public and private sectors regarding manufacturing or clinical trials (e.g., the possibility of joint development)?
- Do you think the use of technological advances in related fields, such as cooperation between sewage epidemiology and drug discovery, is in demand in your country?
- How do you shorten the launch timeline from drug discovery (what can be done not only by government, by pharmaceutical companies)?
- There is a need to improve the efficiency of data collection and management for medical needs that are difficult to predict. Are there major challenges in data collection and analysis? What data collection and management technologies are used?

Appendix 2: Final report of PoC for wasterwater based epidemiology surveillance in Bali

Republic of Indonesia

Proof of Concept for Wastewater Based Epidemiology (WBE) Surveillance in Bali

Final Report （Public Version）

Feb 2024.

Japan International Cooperation Agency (JICA)
Yachiyo Engineering Co., LTD.

ABBREVIATIONS

No.	Abbreviations/Acronyms.	Explanation
1	Asia-Pacific Economic Cooperation	Asia-Pacific Economic Corporation
2	COPMAN	Coagulation and Proteolysis method using Magnetic beads for the detection of Nucleic acids in wastewater).
3	COVID-19.	Coronavirus Disease of 2019
4	JSWE	Japan Society on Water Environment
5	Lab-Kes (UPTD Balai Laboratorium Kesehatan Kerthi Sadhajiwa)	UPTD Bali Health Laboratory Centre, Bali Province
6	MICE	Meeting Incentive Conference and Exhibition
7	N1 gene	Nucleocapsid Protien-1
8	NaCl	Sodium Chloride
9	PEG	Polyethylene Glycol
10	PMMoV	Pepper Mild Mottle Virus
11	POC	Proof of Concept
12	PB buffer	Phosphate Buffer
13	RNA	ribonucleic acid
14	RT-PCR	Reverse Transcription-Polymerase Chain Reaction
15	RT-qPCR	Real-Time Quantitative Polymerase Chain Reaction
16	SARS-CoV-2	Severe Acute Respiratory Syndrome Coronavirus 2
17	UPTD-PAL (Unit Pelaksana Teknis Daerah Pengelola Air Limbah)	Regional Technical Implementation Unit for Waste Water Management
18	UN	United Nations
19	**WBE**	Wastewater Based Epidemiology
20	WTP	Wastewater Treatment Plant

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Chapter1 Report on the results of the demonstration survey.

1.1 Developing a research plan

1.1.1 Background to the study.

Since the early cases of novel coronavirus infection (hereinafter referred to as COVID-19) were reported as pneumonia of unknown cause at the end of 2019, the disease has spread rapidly around the world, causing enormous impact on people's lives and health, society and economy. Studies and initiatives on Wastewater based Epidemiology (hereinafter refer to as WBE) are being conducted in Japan and abroad as a means of understanding the trends of infection, and in Japan, studies and initiatives on WBE are being conducted in some regions under the leadership of the Cabinet Office and others.

The idea of using WBE (testing and monitoring viruses in sewage) for infectious disease control dates back to the 1930s for polio control, and similar attempts have been made against COVID-19. The fact that WBE correctly reflect the infection situation at the local or facility level has been described in many research reports carried out over the past decades, and recent studies have shown that SARS-CoV-2 concentrations in sewage have a strong relationship with the actual number of confirmed cases. Testing for the virus in sewage may be useful in situations where the number of clinical cases is difficult to ascertain accurately, such as in areas where testing systems are weak or where there is a shift towards self-testing rather than testing in healthcare facilities during epidemics (as is the case with tests using nasopharyngeal swabs, saliva or nasal swabs, such as COVID19 , which do not require specimens to be collected from each person). It is expected that self-testing may enable a more rapid assessment of the infection status.

Against this background, Yachiyo Engineering Corporation ("YEC") (hereinafter referred to as 'YEC') has developed a technology that has improved the detection sensitivity of viruses including SARS-CoV-2 in sewage samples in Denpasar, Bali Province, Republic of Indonesia, as a result of the '2021 Smart JAMP (Feasibility Study on the Introduction of Sewerage Management System in ASEAN)' project of the Ministry of Land, Infrastructure and Transport (“MLIT”). The company has been conducting COVID-19 WBE as its own project since 2021, using reagents and other products from a Japanese company that has developed a technology that has improved the detection sensitivity of viruses including SARS-CoV-2 in sewage samples. In addition, the Department of Earth and Social Infrastructure Science, Kanazawa University (hereafter referred to as “Kanazawa University”) has been conducting COVID-19 WBE since 2021 as an in-house project. YEC is expanding the area covered by the sewage epidemiological survey demonstration in Denpasar and confirming the capacity (sampling, detection and analysis capacity) of relevant personnel in the target area. YEC will also identify and study measures to implement **WBE** (e.g. strengthening data analysis and evaluation capacity, response capacity, monitoring capacity, sample collection and transport capacity, etc.) in the target areas, with the aim of further utilising these results by the relevant central ministries and other provinces, thereby strengthening **WBE** in Indonesia. The aim is to strengthen the Indonesian Sewage Epidemiology Survey by further utilising the results by the central ministries and other provinces.

In this context, JICA's 'Information Collection and Verification Study to Promote the Development of R&D and Production Infrastructure for Vaccines and Other Medicinal Products (September 2022 - March 2024)'

(hereinafter referred to as the 'Information Collection and Verification Study') is collecting and analysing information on legal systems, local implementation systems, etc. related to clinical trials and production of medicinal products, with the aim of identifying issues for conducting multinational clinical trials and local production of medicinal products (including performance testing of test drugs and kits) in a timely manner, and presenting project activity plans for the issues identified. The purpose of the survey is to identify issues for speeding up multinational clinical trials and local production of medicinal products (including performance testing of test drugs and kits) and to present business activity proposals to address the issues identified. The demonstration of **WBE** in Indonesia, which YEC is undertaking, is highly significant as a demonstration activity that contributes to pandemic countermeasures using Japanese technology. The possibility of collaboration and cooperation as a pilot activity in information collection and confirmation surveys is to be considered.

1.1.2 Purpose of the survey.

In relation to the demonstration project of sewage epidemiology research being implemented by YEC, the following tasks will be undertaken: (1) Collection and compilation of basic information on the legal system, capacity and implementation systems of related facilities and personnel, and trends in initiatives by donor organisations, research institutions and companies, etc., related to sewage epidemiology, and examination of issues for the expansion of the project; (2) Proposal and implementation of a trial demonstration project in the target area (Denpasar). (3) Based on the results of the trial demonstration project, concrete proposals for future project development will be made to the Indonesian central government, provincial government officials, WHO/SEARO, other donors and relevant Japanese institutions.

1.1.3 Planning of investigations

(1) Investigation.

After compiling the results of technical training and demonstration experiments using Japanese technology (COPMAN method) based on sampling samples collected by YEC at four locations in Denpasar, the necessary information for the expansion of the sewage epidemiological survey project will be collected and organised. Based on the exchange of opinions with YEC, JICA, relevant consultants, Kanazawa University and other relevant parties, the demonstration project will be expanded and the direction of future project development, international cooperation support, etc. will be discussed.

(2) Areas covered.

The target area shall be the city of Denpasar, Bali and surrounding areas.Denpasar and its surrounding areas are characterised by a distinctive industrial structure (tourism and agriculture), the impact of the Corona disaster on the tourism industry (cessation of human flow), and an industrial economic structure consisting of three layers ((1) a foreign currency inflow market formed by foreign tourists, (2) a traditional economic market formed by local residents, and (3) a three-layer rural economic market). The impact of implementing the projects considered in this work will be significant. It is also an area where sewerage systems have been developed with the help of yen loans.

The initial target areas for sewage surveillance are.Fig. 1-1 shows the initial coverage area. The total area

of the sewerage service area is 1,145 hectares with a population of 104,286 people and was initially sampled at the four sites shown below.

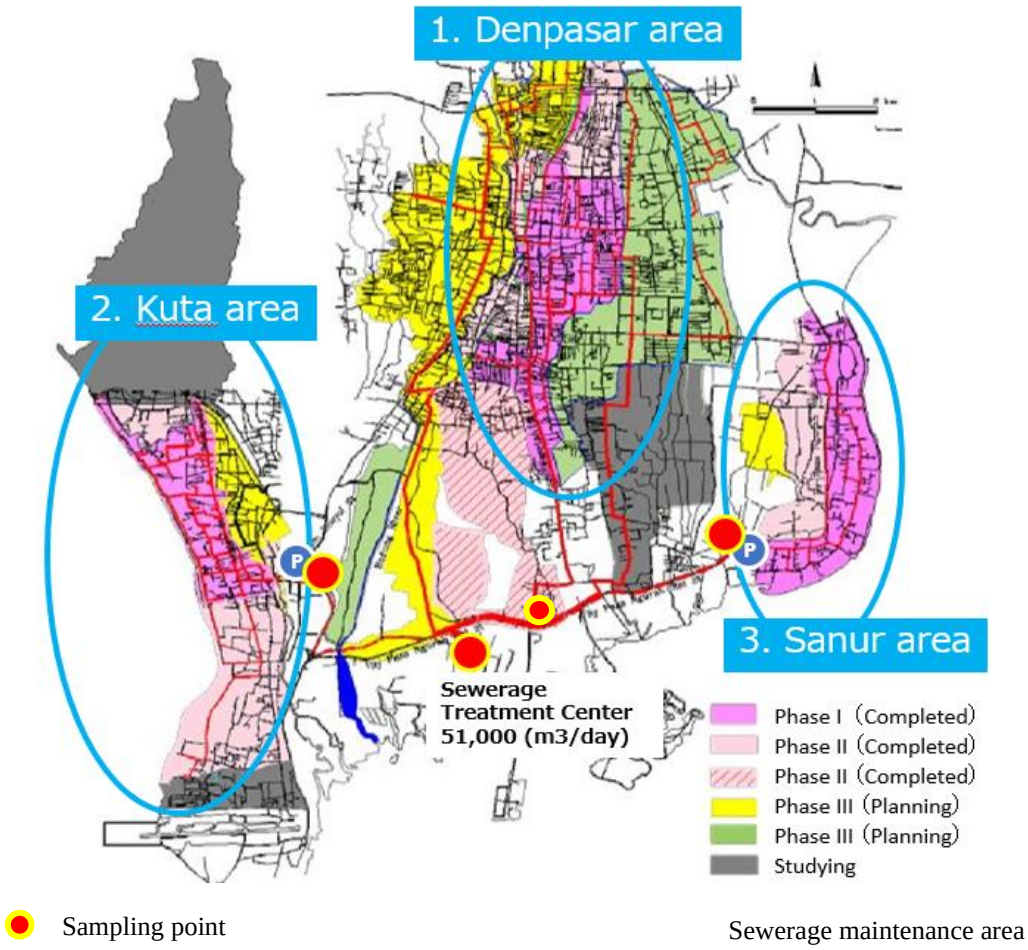
The characteristics of each district are briefly described below:

① The Denpasar Sewerage Service Area is 520 ha and the wastewater sampling point is a major manhole where sewage from upstream collects. This manhole has a gravity rapid transfer system that transfers sewage to its final destination (sewage treatment plant).

② The Sanur Sewerage Service Area is 330 ha. The Sanur pumping station, where sewage from Sanur collects, was chosen as the sampling point. Sewage from this pumping station is pumped daily to the WWTP.

③ The Kuta service area covers 295 ha. The Kuta pumping station was the main collection point and sampling point for sewage from the Kuta area.

④ Wastewater Treatment Plant (WWTP): this is the central location where sewage from the above locations is collected and treated. Sampling was carried out at the location where sewage collects from all three of the above locations. Primary inflow sewage samples were collected for analysis.



Source: Yachiyo Engineering Co., Ltd.

Fig. 1-1 Areas initially covered by sewage surveillance

In addition, in order to increase the objectivity of the PoC and to identify trends in SARS-CoV-2 in different districts and sewage discharge facilities, the sampling sites in this demonstration wereFig. 1-2 expanded to Tabana, Bangli and Nusa Dua, as shown in Figure 2.

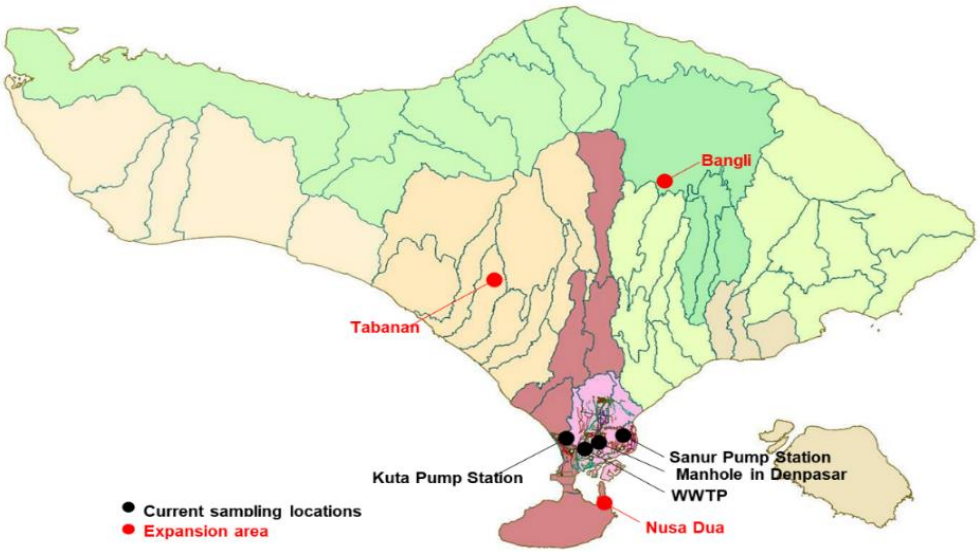
The characteristics of each district and its sewage treatment works are briefly described below:

① Tabanan District: the Dauh Pala sewage treatment plant is located in western Tabanan and serves two villages, Dauh Peken and Dajan Peken. Sewage service users include residential, commercial, office and schools. There are approximately 350 connections and the capacity is relatively large (Residential Sanitation Development, Tabanan, 2023). Sewage sampling was carried out at the treatment works at the main collection points from influent sewage between 13 October and 28 December 2023.

② **Bangli** district: the village of Surahan is one of the oldest villages in **Bangli** district. Most of the population are farmers and it is a rural residential area.

③ Thesewage communal treatment plant, built in 2014, is very small and only used by about 107 households of local residents (Surahan Village official website, 2023). Sewage sampling was carried out from 2 November to 28 December 2023 at the treatment plant at the main collection point from incoming sewage.

④ Nusa Dua District: the Nusa Dua tourist area is one of the world's best developed tourist destinations to date, with 19 star hotels with over 5,000 rooms, shopping centres, museums, cultural facilities, golf courses, hospitals and other tourism businesses, and two international MICE (Meetings, incentive, conference and exhibition) facilities, and the district has been host to various international-scale events, including UN Climate Change 2007, APEC 2013, Bali Democratic Forum and Miss World 2013. The district's sewage treatment plant mainly treats wastewater from hotels, villas, spas, restaurants and other tourist facilities, with a capacity of 10 000 m3 per day (Indonesia Tourism Development Corporation, 2023). Sewage sampling was carried out at WWTPs collected from three different pumping stations. Sampling was conducted with influent sewage at the WWTP's main collection points between 13 November and 28 December 2023.



Source: Yachiyo Engineering Co., Ltd.

Fig. 1-2 Expansion of areas covered by sewage surveillance

(3) Virus to be detected

The virus to be detected in this demonstration is SARS-CoV-2.

1.2 Basic information in sewage epidemiological studies.

1.2.1 Current status of sewage epidemiology in Indonesia.

WBE are being conducted, or have been conducted in the past, by three institutions in Indonesia. These are (i) a nationwide polio surveillance conducted by the Ministry of Health with support from the World Health Organisation (WHO), (ii) a sewage epidemiology survey in Yogyakarta for new coronaviruses conducted by Gadjah Mada University and Monash University with support from the Australian Government, and (iii) this demonstration project conducted in the province of Bali. As of the end of January 2024, all activities from (i) to (iii) have already been completed and there is no prospect of resuming them as funding is not yet available. In addition, there is no de facto standard for sewage epidemiological studies in Indonesia, and protocols have not been standardised and are not reflected in policy at this time. However, there is a high demand from implementing organisations to incorporate **WBE** as a solution into existing health and environmental protection policies and PPR (Prevention, Preparedness and Response), and to institutionalise and adopt them as an ongoing method for the next generation of environmental protection and infectious disease control. There is a high need for the

1.2.2 Indonesian government agencies involved in sewage epidemiological studies in Bali Province.

The relevant bodies for the sewage epidemiological study in Bali Province are the Bali Provincial Health Department, the Bali Provincial Laboratory Lab-kes and UPTD-PAL, with strong support and cooperation from these bodies for this pilot project. The system of cooperation and coordination among the organisations concerned in Bali in this pilot project is generally solid and strong commitments have been obtained. At the same time, as the decision-makers in each of the organisations involved include the central and provincial governments and local research organisations, it is necessary to consult and coordinate as necessary in establishing the system, including applications for licences and approvals. Although this demonstration experiment was a short-term initiative, lasting from 2022 to one year, and started during the Corona Disaster, the results were achieved thanks to the cooperation of the organisations involved and the flexible response of the people involved.

1.2.3 Overseas expansion of Japanese companies in sewage epidemiology.

In Japan, **WBE** are at the demonstration stage and are carried out by a very limited number of institutions, in collaboration with universities and other research institutions, voluntary administrative authorities and other relevant domestic organisations. In addition, efforts are being made by some universities and other research institutions to develop the project in the ASEAN region.

Looking at Japanese companies, Shionogi, Takara Bio and other suppliers of reagents and primers are looking to expand overseas, and for these companies, overseas expansion will contribute to market expansion. In particular, **WBE** are still in their infancy in the ASEAN region, including Indonesia, and by using the advantages of Japan-made reagents with high sensitivity and examining their applicability, it will be possible to create a market within the ASEAN region.

1.3 Study of issues related to sewage epidemiological studies.

The general challenges that exist in the implementation of sewage surveillance in Indonesia are summarised below.

① Variability of data through sampling

The variability of data from sampling is due to the complexity and variability of the sewage environment. As is evident in the analysed data in this demonstration, sewage is subject to sampling and environmental variables, the characteristics of which vary from place to place and time, and therefore an appropriate sampling plan based on existing data is necessary.

② Impact of regional differences and complexity of data interpretation.

As confirmed by the analysis results of this demonstration, the concentration of viruses in sewage varies even in neighbouring areas. It is necessary to understand the characteristics and social situation in each area, and other complementary data are needed to analyse the relationship between the detection of viruses in sewage and the infection situation.

③ Identification of viruses for detection.

Although COVID-19 was the only target species in this demonstration, there are cases, such as hepatitis and drug-resistant bacteria, where different analytical methods from existing sewage epidemiological survey methods and testing instruments are required. In addition, it is necessary to identify target species based on the social environment and trends while analysing data at all times, such as identifying mutant strains during the spread of infection.

Indonesia is a geographically and culturally diverse country, with rural and urban areas having different living conditions and sewerage facilities. Sewerage facilities have been prioritised in some metropolitan areas, while rural areas still use combined septic tanks, which poses a challenge for metadata sets.

In addition, sewage surveillance is currently being implemented in several relevant institutions and local cities, and information sharing and coordination between actors is insufficient. The future social implementation of sewage surveillance as a national infection control measure and PPR will require the establishment of criteria standards at the central government level. In order to address these issues, it is important to establish and promote the diffusion of the technology through cooperation between national and international experts and initiating organisations, in addition to cooperation between government and local authorities.

1.4 Implementation of trial demonstrations in the target sites

1.4.1 Methods of demonstration

The basic flow of sewage surveillance is shown in Figure 1-5 and consists of sampling and logistics, laboratory testing, data analysis and interpretation.

Source: Yachiyo Engineering Co., Ltd.

Fig. 1-3 General flow of sewage surveillance

An overview of each activity and the methods implemented in the demonstrations is summarised below:

(1) Sampling and logistics

Sewage surveillance can use the concentration of infectious disease markers in wastewater not only to track disease outbreaks in contributing communities, but also to identify disease trends in individual districts/cities In the case of SARS-CoV-2, over a given period of time, it is It is important to know how patient trends and disease severity have changed over a given period of time. Sampling frequency is therefore a very important factor. The higher the frequency, the more accurate the outbreak trends.

In this demonstration, a minimum weekly sampling frequency was adopted from September 2022 to August 2023, taking into account several constraints such as limited capacity of kits/reagents, laboratories and technicians; from September 2023, in order to more accurately track viral trends, the sampling frequency in the original target areas (Denpasar, Kuta, Sanur and WWTP), the sampling frequency was increased from once a week to twice a week and implemented. Similarly, in the extension areas, twice-weekly sampling was conducted from October to December in Tabanan and from November to December 2023 in Bangli and Nusa Dua.

1) Sampling procedure

Sampling was conducted in accordance with the Manual for Detection of SARS-CoV-2 RNA in Wastewater (December 2022) of the COVID-19 Task Force of the Japanese JSWE, taking into account the sampling conditions, water quality testing methods and materials and equipment for sampling and water quality testing held by UPTD-PAL, with Slight modifications were made to suit the situation in the field.Table. 1-1 shows the procedure.

Table. 1-1 Sampling procedure

Step	Contents
1. preparation	① Wastewater sampling tools ・ 500 ml sampling glass bottles for wastewater sampling ・ Plastic centrifuge tubes ・ Fill in the sampling tube with the date, place and time of sampling. ② Bucket, rope, funnel. ・ Plastic bucket (~300 ml), rope, plastic funnel ③ Prepare protective equipment ・ Waterproof gloves, masks, if necessary, protective glasses, protective shields, protective clothing, etc.

	④ Transport tools ・ Styrofoam (ice boxes): Styrofoam (ice boxes): ice boxes with Styrofoam lids ・ Zip bags, cushioning materials
2. sampling	① Pretreatment of sampling tools by sewage ・ Pre-treat the inside of drainage containers and other sampling tools (buckets, funnels) two or three times with drainage samples. ② sampling ・ Depending on the sampling location, grab sampling during peak hours (9:00-11:00). ・ Sampling date collection days in this demonstration: every Thursday (September 2022 - August 2023),Mondays and Thursdays (September-November 2023). ・ Collect approximately 100 ml (50 ml x 2 bottles) of influent sewage at each sampling point. ③ cleaning ・ After sampling, container surfaces should be rinsed with tap water, wiped with clean paper and sprayed with disinfectant ethanol.
3. transport	・ Tightly close the tube lid and place the two tubes in a zipped bag with cushioning material (e.g. kitchen paper). ・ The bagged containers are placed in Styrofoam (iceboxes) together with a refrigerant. ・ Moulded styrofoam caps are secured with packing tape and transported (refrigerated or frozen transport recommended).
4. storage	・ All samples are transported to the UPTD Lab-Kes in Denpasar. (a) For analysis after 24 hours:Freeze in a standard freezer (0°C). (b) Analysis exceeding 24 hours:Freeze in an ultra-low temperature freezer (-80°C).

Source: Yachiyo Engineering Co., Ltd.

It also includes a step-by-step sampling procedure, including equipment preparation, sampling, disinfection, labelling, storage in ice boxes and transport to the laboratory.Fig. 1-2 shows the following.

Source: Yachiyo Engineering Co., Ltd.

Fig. 1-4 Sampling procedure

2) Sampling frequency and duration

Sampling was conducted every Thursday during peak drainage hours (9:00-11:00) from September 2022 to August 2023, covering the first target areas (Kuta, Sanur, Denpasar and WWTP) From September 2023, sampling frequency was increased from once a week to twice a week (Monday and Thursday). The frequency of sampling was increased from once a week to twice a week (Monday and Thursday). Furthermore, the sampling area was expanded from four to seven sampling sites, including Tabanan, Bangli and Nusa Dua, and sampling in the expanded area was conducted from October to November 2023. The sampling sites and frequency are organised into.

Table. 1-2 Sampling sites and frequencies

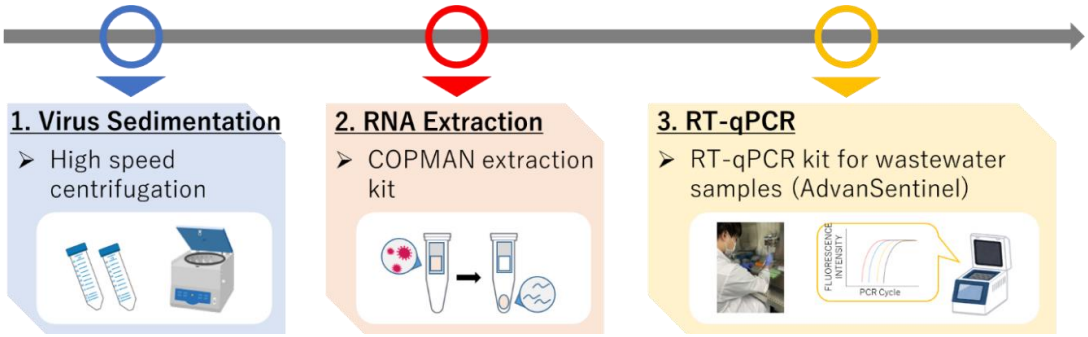
Location		Initial Sampling (22 September, 2022 to 25 September, 2023)				Expansion Area & Frequency Increase (October, 2023 to December, 2023)			
		Samples/ week	Samples/ month	Duration/ month	Total	Samples/ week	Samples/ month	Duration/ month	Total
Denpasar City	Sanur	1	4	12	48	2	8	3	24
	Denpasar	1	4	12	48	2	8	3	24
	WWTP	1	4	12	48	2	8	3	24
	Kuta	1	4	12	48	2	8	3	24
Kabupaten Tabanan	Tabanan	0	0	0	0	2	8	3	24
Bangli	Bangli	0	0	0	0	2	8	2	16
Kabupaten Badung	Nusa Dua	0	0	0	0	2	8	2	16
Sub-total		**4**	**16**		**192**	**14**	**56**		**152**
Total					**344**				

Initial target location
Expansion area

Source: Yachiyo Engineering Co., Ltd.

3) Clinical examination and detection

The testing and detection procedure is shown in Figure 1-7. It involves three main steps: viral sedimentation, RNA extraction and RT-qPCR analysis.



Source: Yachiyo Engineering Co., Ltd.

Fig. 1-5 Laboratory testing and detection procedures

The protocols for each step are organised below.

i. virus sedimentation protocol

① Thaw frozen samples (-80° C) in 50 ml tubes and shuck well.

② Transfer 10 ml of the sewage sample into a new sterile 15 ml tube.

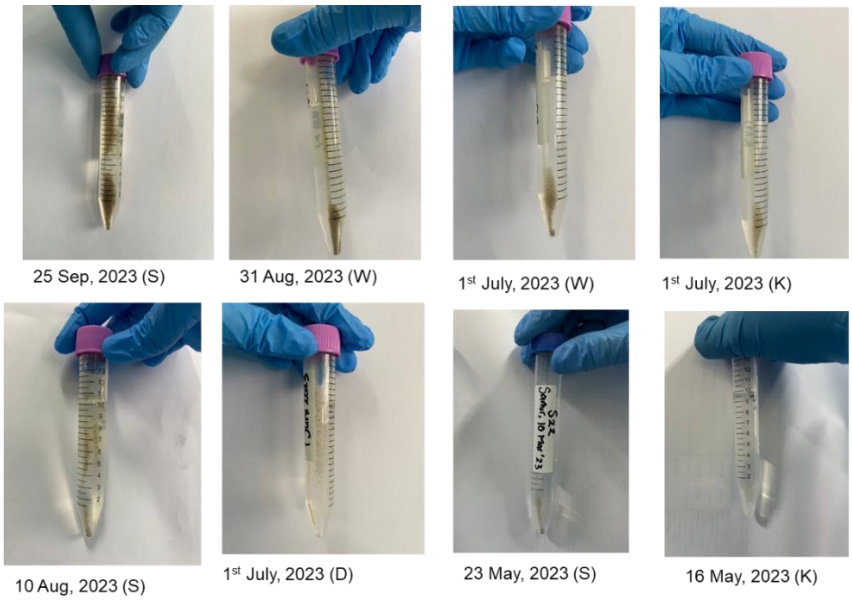
③ The sample is then centrifuged at high speed (6000-10000 g) for 10 minutes.

The amount of solids collected after centrifugation varies from sample to sample, depending on the type of collection point, manhole, pumping station, treatment plant, etc., the time of year, date of collection, wet weather, etc. (Fig. 1-6). During the early stages of the analysis, there was concern that such samples could adversely affect the detection and quantification of target viruses. Therefore, a trial sampling method was used to find a suitable method and, as a result, two 50 ml tubes were collected during the morning peak period when the pumps were running. Although there is a large variation in the amount of solids in the samples, the results are not significantly affected by this difference in solids content, except for those with no apparent sedimentation or abnormal effluent quality.

ii. RT-qPCR protocol

① RT-PCR, pre-amplification and qPCR were performed using the AdvanSentinel RT-qPCR kit for wastewater samples according to the kit manufacturer's protocol.

② A minimum of two replications were performed for each sample and PMMoV, which is naturally abundant in wastewater, was used as the process control.



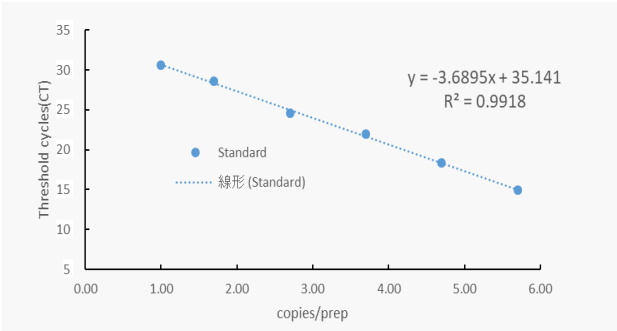
Source: Yachiyo Engineering Co., Ltd.

Fig. 1-6 Differences in sedimentation volume after centrifugation

(2) Data analysis and visualisation

Absolute quantification of SARS-CoV-2 from unknown effluent samples was performed. Standard curves were prepared for both target (SARS-CoV-2) and endogenous/internal reference (PMMoV) and the amount of target and endogenous reference in each experimental sample was determined from the appropriate standard curve by making a series of separate dilutions from both the target sample and endogenous reference in known amounts, as determined. An example of the preparation of a standard curve and absolute

quantitation of an unknown sample is shown inFig. 1-7 Shown are.



Sample Name	Ct values		Original Concentration of sample	Original Concentration of sample
	#1	#2		
NTC	*Undetermined*	*Undetermined*	gc/L	log10 gc/L
K-52	26.38	26.39	240250	5.38
S-52	27.54	27.85	97125	4.99
D-52	27.00	26.06	217375	5.34
W-52	31.55	31.82	6125	3.79

Source: Yachiyo Engineering Co., Ltd.

Fig. 1-7 Example of a standard curve and absolute quantification of an unknown sample by RT-qPCR.

Pepper mild mottle virus (PMMoV), a type of plant virus, is also very common in wastewater. To evaluate and assure the virus detection method, PMMoV copy number was quantified as an internal control using an RT-qPCR assay.

1.4.2 Analysis results and discussion

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1.5 Consideration of the standard protocol for the use of detection reagents.

1.5.1 Objectives of the study

To ensure the sustainability of sewage surveillance in Indonesia, it is necessary to identify standardised protocols that are applicable at the regional level and sustainable, including economically, while based on standard protocols specified by reagents and analytical methods for each process, such as extraction and detection. .

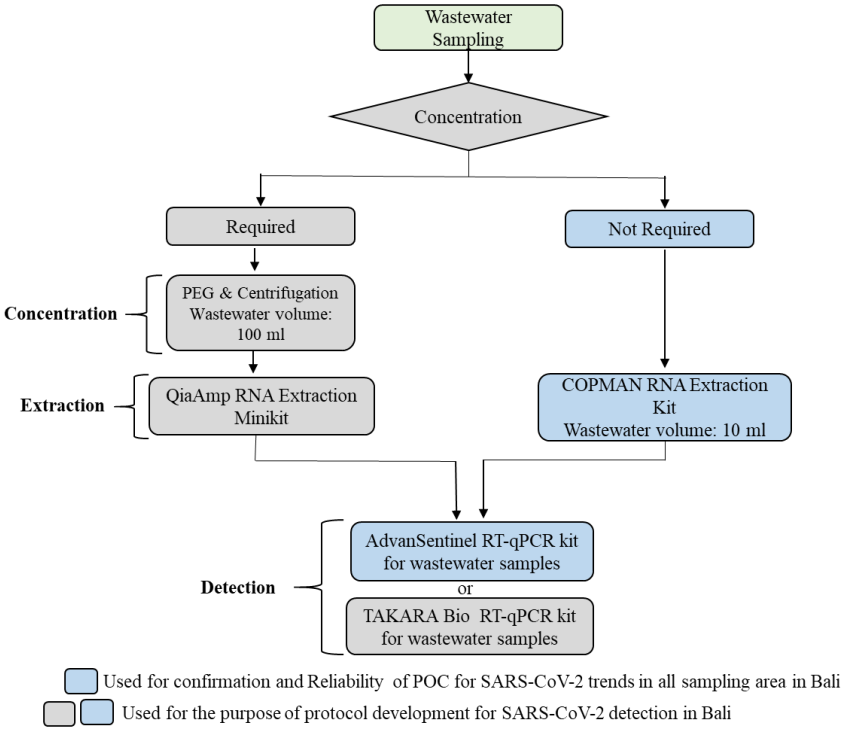
In sewage surveillance, various factors such as the sewerage system, sewage quality, regional and social characteristics and peak sewage discharge times influence sampling and analysis procedures and methods. In order to optimise the overall operating procedures, it is therefore necessary to test and compare the various available analytical methods and techniques under field conditions for a given period of time.

Therefore, with the aim of developing a protocol that is applicable and affordable to the Indonesian context in this demonstration, the validity and applicability of different reagents/kits used in this country and abroad was confirmed, and the advantages and disadvantages of different reagent combinations were identified and the appropriate A review of protocols was conducted.

1.5.2 Method of examination

Standard protocols were examined for the extraction/detection process and validated by comparing different reagents and kits used in Japan and other countries, and by examining combinations of reagents and

kits. Reagents and kits commonly used in Japan and other countries were used locally. The flow of the study and the list of reagents and kits used in this study are shown in Figure 2-1.



Source: Yachiyo Engineering Co., Ltd.

Fig. 1-8 Standard protocol study flow in extraction/detection and reagents/kits used

In this study.Fig. 1-8 using the reagents/kits shown in,Table. 1-3 Protocol-1 was conducted to study the applicability of highly sensitive reagents, while Protocol-2 to 5 was conducted to compare methods and reagents/kits in the enrichment and extraction/detection processes.

Table. 1-3 Different analysis methods and combinations considered in this demonstration

Method/Protocol		Sweage sample volume	Concentration Step	RNA Extraction	RT-qPCR
Protocol-1	Protocol 1-1	10 ml	Note required	COPMAN RNA kit	AdvanSentinel RT-qPCR kit for wastewater
	Protocol 1-2	10 ml	Note required	COPMAN RNA kit	TAKARA Bio RT-qPCR kit for wastewater
Protocol-2	Protocol 2-1	80 ml	PEG	QiaAmp RNA mini kit	AdvanSentinel RT-qPCR kit for wastewater
	Protocol 2-2	80 ml	PEG	QiaAmp RNA mini kit	TAKARA Bio RT-qPCR kit for wastewater
Protocol-3	Protocol 3-1	80 ml	Centrifugation	QiaAmp RNA mini kit	AdvanSentinel RT-qPCR kit for wastewater
	Protocol 3-2	80 ml	Centrifugation	QiaAmp RNA mini kit	TAKARA Bio RT-qPCR kit for wastewater
Protocol-4		80 ml	PEG	QiaAmp RNA mini kit	TAKARA RT-Master Mix & Probe qPCR
Protocol-5		10 ml	Note required	COPMAN RNA kit	Vazyme Triplex RT-qPCR kit

Source: Yachiyo Engineering Co., Ltd.

(1) Enrichment and RNA extraction

Because sewage samples are diluted with a very low copy number of viral RNA compared to clinical (human) samples, an enrichment process is required when extracting SARS-CoV-2 from sewage samples. There are several methods to enrich the virus, but considering the availability of reagents and equipment,

PEG and centrifugal enrichment methods were used here, followed by RNA extraction using the QiaAmp RNA mini kit . On the other hand, the COPMAN extraction kit (Advansentinel, Japan) does not require a concentration step and allows samples to be directly subjected to RNA extraction.

(2) RT-qPCR

Two RT-qPCR kits, the AdvanSentinel RT-qPCR kit (AdvanSentinel, Japan) and the TAKARA Bio RT-qPCR kit (TAKARA Bio, Japan), were used to detect SARS-CoV-2 in sewage samples (RT-qPCR).

1.5.3 Feasibility study on the application of highly sensitive reagents (Protoco l)

In this comparative study, RT-qPCR was performed on five samples (K-32, S-32, D-32 and W-32) after RNA extraction with COPMAN using two different kits (AdvanSentinel RT-qPCR kit and TAKARA Bio RT-qPCR kit). The main objective was to compare two RT-qPCR kits with different sensitivities: the AdvanSentinel RT-qPCR kit is a kit touted as highly sensitive by the manufacturer.

The results of the comparative analysis.Fig. 1-9 in Figure 1. As a result, SARS-CoV-2 was detected in both kits, but differences in the analysis results were identified as follows. In addition,Fig. 1-9 shows the analysis results of protocol studies 2 and 3 (Protocol 2 and 3) other than this study (Protocol 1-1 and 2). The contents of Protocol Studies 2 and 3 (Protocol 2 and 3) are1.5.4 and onwards. The details of the studies are described below.

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Fig. 1-9 Comparative results of analysis of two RT-qPCR kits for detection of SATS-CoV-2 in sewage.

i. AdvanSentinel RT-qPCR kit (Protocol 1-1).

- Fig. 1-9 shows the higher amount of viral genome copies (gc) per litre (higher detection concentration) when compared to the Takara Bio RT-qPCR kit. An average increase of 5000-10000 gc/L was observed in each sample. This is due to the AdvanSentinel having a pre-amplification step, which resulted in a higher copy number.
- On the other hand, viral RNA was detected in all four samples of K-32, S-32, D,32 and W-32 .
- There are three steps - RT-PCR, pre-amplification and qPCR - which take at least one day.
- Price: ¥ 12,800/sample (purchase price at time of demonstration)

ii. TAKARA Bio RT-qPCR kit (Protocol 1-2)

- Viral RNA was also detected in this kit from in all four samples, K-32, S-32, D,32 and W-32.
- Because it does not have a pre-amplification step, the number of viral genome copies per sample is lower than the AdvanSentinel RT-qPCR kit, but is sufficient to investigate SARS-CoV-2 sewage surveillance.
- Very time-efficient as it is only a one-step RT-qPCR; the experiment can be completed in 2 hours.

- Price: 8900 yen/sample (purchase price at time of demonstration)

Based on the results of the above analysis, the TAKARA Bio RT-qPCR kit, which is highly sensitive, time-efficient and economical (low cost compared to the two target groups), should be applied in the implementation of sewage surveillance for constant monitoring and understanding of infection trends. The AdvanSentinel RT-qPCR kit may be applied to situations where detection is necessary even in trace amounts of virus, e.g. to confirm the presence or absence of viruses (zero detection), to confirm the presence or absence of infection in hospital-related facilities, or for pathogens with very low concentrations in sewage such as influenza viruses. It is conceivable that this could be applied. However, further verification is needed to confirm this applicability.

1.5.4 Comparative study of extraction/detection reagents (Protocol -2)

In this protocol study, RNA extraction was performed using the QiaAmp viral RNA mini kit after the PEG-enrichment method and then compared using two RT-qPCR kits, AdvanSentinel RT-qPCR and Takara Bio RT-qPCR.

(1) Protocol 2-1 (PEG + QiaAmp + AdvanSentinel RT-qPCR).

Viral RNA enrichment was performed using the PEG enrichment method, followed by RNA extraction using the QiaAmp viral RNA mini kit and RT-qPCR using the AdvanSentinel kit. Results are as follows.

- Viral RNA was detected in all four samples (K-32, S-32, D-32 and W-32).
- Fig. 1-9 shows that the amount of viral genome per litre was 4.91, 4.55, 4.56 and 4.81 Log10 copies/L, respectively.Although the amount of viral genomic RNA was lower compared to Protocol-1, the quantification of genomic copies of SARS-CoV-2 and viral in sewage sufficient and efficient to confirm surveillance.
- The cost of analysis is slightly lower than Protocol 1-1 (11,758) but higher than Protocol 1-2.
- A disadvantage is that PEG precipitation requires overnight incubation, which increases the total time required for RNA extraction and AdvanSentinel RT-qPCR, taking on average three days.

(2) Protocol 2-2 (PEG + QiaAmp + Takara Bio RT-qPCR).

Viral RNA enrichment was performed using the PEG enrichment method, followed by RNA extraction using the QiaAmp viral RNA mini kit and RT-qPCR using the TAKARA BIO kit. Results are as follows.

- Viral RNA was detected in all samples (K-32, S-32, D-32 and W-32), with viral genome copy numbers of 4.40, 4.11, 4.14 and 4.26 Log10 copies/L per litre respectively.
- Although the viral genome copies per litre are lower than the three aforementioned protocols, the amount of virus detected is above the average amount of SARS-CoV-2 detected throughout the year.
- The cost of analysis per sample is the cheapest of the three aforementioned protocols.
- The analysis takes two days, including the concentration process and viral RNA extraction.

1.5.5 Comparative study of extraction/detection reagents (Protocol -3)

For this protocol study, sewage sediment after centrifugation was extracted with the QiaAmp Viral RNA Mini Kit and compared using two RT-qPCR kits, AdvanSentinel RT-qPCR and Takara Bio RT-qPCR.

(1) Protocol 3-1 (centrifugation + QiaAmp + AdvanSentinel RT-qPCR)

RNA extraction was performed from the PEG-enriched sediment using the QiaAmp viral RNA minikit and RNA extraction using the AdvanSentinel RT-qPCR kit. Results are as follows.

- Viral RNA was detected in all four samples (K-32, S-32, D-32 and W-32), with viral genome copies per litre of 4.97, 3.84, 4.18 and 4.37 Log10 copies/L respectively.
- The centrifugation speed for collecting the PEG precipitate was 3000 x g. When the centrifugation speed was increased to 6000 x g, larger amounts of viral RNA were detected.
- The amount of virus detected in sewage samples is slightly higher than the average detection of SARS-CoV-2 over the year.
- Quantitation and efficiency are moderate, while the cost of analysis is high (11,540/ sample).
- Total analysis time is long, requiring an average of three days.

(2) Protocol 3-2 (centrifugation + QiaAmp + TAKARA Bio RT-qPCR)

RNA extraction was performed from the precipitate by the PEG enrichment method using the QiaAmp Viral RNA Mini Kit and RT-qPCR was performed using the TAKARA BIO kit. Results are as follows.

- Viral RNA was detected in all four samples (K-32, S-32, D-32 and W-32), with viral genome levels of 4.33, 3.80, 3.31 and 3.35 Log10 copies/L per litre respectively.
- The amount of virus detected in sewage samples is lower than the average amount of SARS-CoV-2 detected throughout the year.
- Quantitation and efficiency are moderate, while the cost of analysis is high (7,680 yen/sample).

1.5.6 Comparative study of extraction/detection reagents (Protocol -4)

In this protocol study, RNA enrichment was performed by PEG enrichment followed by RNA extraction with the QiaAmp viral RNA mini kit. rT-qPCR was performed using two-step RT-qPCR (RT TAKARA RT Master Mix and Probe qPCR) and results are shown below andFigure 1-10 The results are shown in Figure 1 below and in Figure 1 at 19.

As the TAKARA BIO RT Master Mix and Probe qPCR were not available at the target site, Protocol-4 was conducted at Kanazawa University using sewage samples dated 29 May 2023 from Sengakuji, Osaka, Japan.

- Viral RNA was detected in sewage samples and the amounts were significantly higher (6.32 Log10 copies/L from PEG extracts and 5.85 Log10 copies/L from sediment of PEG samples).
- The advantage is that the analysis price is the cheapest of the protocols up to the aforementioned (4,120 yen).
- The time required for analysis is comparable to other protocols and takes two days.

- This protocol is highly ideal in terms of both efficiency and cost, but for practical comparisons, confirmatory experiments are needed on sewage samples at the target sites.

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Figure 1-10 TAKARA BIO RT Master Mix and probe qPCR kit efficiency comparison

1.5.7 Comparative study of extraction/detection reagents (Protocol -5)

As RT-qPCR kits for sewage samples are not yet commercially available, commercially available RT-qPCR kits for clinical samples (human samples) were used to confirm their relevance to sewage samples.

There are some differences between RT-qPCR kits for clinical specimens and RT-qPCR kits for sewage samples. RT-qPCR kits for clinical specimens are usually designed to detect two viral genes (N1 and ORF 1ab), whereas RT-qPCR kits for sewage samples are designed to detect the N1 gene only. Another difference is that the clinical RT-qPCR kit uses the housekeeping gene as an internal control, whereas the RT-qPCR kit for sewage samples uses the PMMoV virus as a positive control.

Based on the differences described above, RT-qPCR kits for clinical samples were tested against sewage samples. Specifically, RNA extraction was performed using the COPMAN RNA kit and Vazyme Triplex Clinical RT-qPCR. The results are presented below and in Figure 1-20.

- Viral RNA was detected in all target samples (K-32, S-32, D-32 and W-32), but the amounts detected for clinical samples were significantly lower at 2.75, 2.65, 2.88 and 2.48 Log10 copies/L, respectively.
- The amount of viral genome copies per letter is significantly lower than the AdvanSentinel RT-qPCR kit and the amount of virus detected is below the average amount of SARS-CoV-2 detected throughout the year.
- The Vazyme RT-qPCR kit does not contain PMMoV probes and primers, so the quality of the RNA extraction cannot be checked.
- Cost is lower than RT-qPCR kits for sewage samples (¥ 5,542/sample).
- The time required for analysis is comparable to Protocol-2, requiring two days.
- Low quantification rate, not suitable for sewage surveillance of SARS-CoV-2.

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Figure 1-11 RT-qPCR of sewage samples (left) vs RT-qPCR of clinical samples (right) in SARS-CoV-2 detection

1.5.8 Summary of protocol review

A table comparing the advantages and disadvantages of each protocol considered in this demonstration is shown in Table 1-4 shows the advantages and disadvantages of the protocols considered in this demonstration.

Considering various factors in Indonesia, efficiency, price and availability of kits, etc., all combinations of

protocols -1 to protocol -3 are applicable for SARS-CoV-2 sewage surveillance in Bali and other similar cities in Indonesia, but the following four protocols are particularly recommended in Indonesia.

(1) Protocol 1-2 (COPMAN + Takara Bio RT-qPCR).

Protocol 1-2 proved to be cheaper than protocol 1-1 (COPMAN + AdvanSentinel RT-qPCR), yet had the second highest amount of viral RNA in sewage after protocol 1-1. Protocol 1-2 also requires less time for analysis compared to protocol 1-1. Protocol 1-1, the AdvanSentinel RT-qPCR kit for sewage, is a three-step RT-qPCR and requires two days for detection including RNA extraction, while protocol 1-2, the Takara Bio RT-qPCR kit for sewage, is a compact one-step RT-qPCR and It takes only one day for detection, including RNA extraction. Therefore, it is highly applicable for constant monitoring as it can detect a certain concentration in a short period of time and at a low cost.

(2) Protocol 2-2 (PEG + QiaAmp + TAKARA Bio RT-qPCR)

This protocol is cheaper than Protocol 1-2, but is capable of detecting SARS-CoV-2 in a range comparable to the range of average amounts of SARS-CoV-2 detected during one year of sewage surveillance (Log10≥3.9). Therefore, like Protocol 1-2 above, it has high applicability for constant monitoring. On the other hand, compared to Protocol 1-2, it takes two days for detection, which is inferior to Protocol 1-2 in terms of early detection.

(3) Protocol 4 (PEG + QiaAmp + TAKARA RT Master Mix and Probe qPCR)

Although this is the cheapest protocol, the quantification rate and efficiency remain high. Therefore, this is the most promising protocol that can be used for SARS-CoV-2 sewage surveillance in Indonesia. However, it requires two days for detection. In addition, field results need to be confirmed using local sewage samples.

(4) Protocol 1-1 (COPMAN + AdvanSentinel RT-qPCR).

Although this protocol was the best in terms of SRAS-CoV-2 detection rate in sewage in Bali, it was the most expensive of the other protocols used in this demonstration and required a number of days for detection. Therefore, as mentioned above, it is not suitable for constant sewage surveillance surveys, but this protocol may be applied in specific situations where the amount of viral RNA in sewage is below average and the presence of SARS-CoV-2 cannot be detected by the other protocols.

Table 1-4 Comparison of SARS-CoV-2 detection protocols for sewage surveillance in this demonstration (◎ predominant, ○ medium, △ low)

No.	Methode	Evaluation Parameters		No.	Methode	Evaluation Parameters	
P 1-1	COPMAN+ AdvanSentinel RT-qPCR	Quantitification rate: **Very High**	◎	P 3-1	(Centrifugation+QiaAmp)+ AdvanSentinel RT-qPCR	Quantitifications rate: **Medium**	○
		Effeciency: **High**	◎			Effeciency: **Medium**	○
		Price: **JPY 12800/Sample***	△			Price: **JPY 11540/sample**	○
		Time required: **2 days**	△			Time required: **2 days**	△
		Accessibility: **Import from Japan**	△			Accessibility: **QiaAmp from local market RT-qPCR Import from Japan**	△
P 1-2	COPMAN+ TAKARA Bio RT-qPCR	Quantitification rate: **High**	◎	P 3-2	(Centrifugation+QiaAmp)+ TAKARA Bio RT-qPCR	Quantitifications rate: **Low-Medium**	○
		Effeciency: **Very High**	◎			Effeciency: **Medium**	○
		Price: **JPY 8900/Sample**	△			Price: **JPY 7680**	○
		Time required: **1 day**	◎			Time required: **1 day**	◎
		Accessibility: **Import from Japan**	△			Accessibility: **QiaAmp from local market RT-qPCR Import from Japan**	△
P 2-1	(PEG+QiaAmp)+ AdvanSentinel RT-qPCR	Quantitification rate: **High**	○	P-4	(PEG+QiaAmp)+ TAKARA Bio RT-qPCR (2 step)[2]	Quantitifications rate: **High**	○
		Effeciency: **Medium-High**	○			Effeciency: **Medium to high**	○
		Price: **JPY 11758/Sample**	△			Price: **JPY 4120**	◎
		Time required: **2-3 days**	△			Time required: **2 days**	○
		Accessibility: **PEG and QiaAmp from Local market RT-qPCR Import from Japan**	△			Accessibility: **QiaAmp from local market RT-qPCR Import from Japan**	△
P 2-2	(PEG+QiaAmp)+ TAKARA Bio RT-qPCR	Quantitification rate: **Medium-High**	○	P-5	COPMAN+Vazyme RT-qPCR[1]	Quantitifications rate: **Low**	△
		Effeciency: **Medium-High**	○			Effeciency: **Low**	△
		Price: **JPY 7860**	○			Price: **JPY 5542/Sample**	○
		Time required: **2 days**	△			Time required: 1 **days**	○
		Accessibility: **PEG and QiaAmp from Local market RT-qPCR Import from Japan**	△			Accessibility: **COPMAN Import from Japan Vazyme from local market**	△

* Reagents/Kits` price calculation per sample was carried out in accordance to qoutations provided during 2023, and the shipment cost for Japanese reagents are not included.

[1] Vazyme is a clinical RT-qPCR kit which is designed and mainly used for human samples and is not relevant for wastewater samples.

[2] Due to unavailiblity of TAKARA BIO RT-qPCR (2 step) in Bali, this protocol was only used at Kanazawa university with wastewater samples from Japan.

1.6 Summary of demonstration results

Sewage surveillance is a useful tool that has the potential to serve as a complementary approach to monitoring the presence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in the community and as an early warning system for COVID-19 outbreaks. The COVID-19 pandemic has increased attention to WBEs, which are now being used globally for monitoring COVID-19; COVID-19-infected individuals may shed the viral genome in faeces even in the absence of symptoms, and the virus can be detected in sewage. This demonstration was conducted to provide a proof of concept (POC) for sewage surveillance in Bali, Indonesia, and to develop a protocol that can be applied in Indonesia.

To achieve this objective, untreated sewage samples were collected from Kuta, Sanur, Denpasar and WWTP from September 2022 to August 2023 (once a week), increasing the collection frequency to twice a week in the second half of the demonstration, and to confirm the reliability of POCs at different sewage treatment facilities, Tabanan and expanded to Tabanan, Bangli and Nusa Dua to carry out sampling (n=350). Sampling was essentially conducted according to the JSWE COVID-19 Task Force Manual for the Detection of SARS-CoV-2 RNA in Effluents, with minor modifications to suit the field situation. The COPMAN RNA kit was used to extract the viral RNA genome and the AdvanSentinel RT-qPCR kit for sewage was used for reverse transcription polymerase chain reaction (RT-PCR) and real-time quantitative reverse transcription PCR (RT-qPCR).

The results showed that SARS-CoV-2 was detectable in all types of sewage treatment plants targeted in this demonstration, including WWTPs, where sewage from the three districts mentioned above - Kuta, Denpasar and Sanur - is collected and treated in primary, secondary and tertiary treatment. It was confirmed that the WWTP could be an appropriate source of information to represent and quantify SARS-CoV-2 in the areas targeted in this demonstration. However, when the area was subdivided, it was confirmed that the pattern of SARS-CoV-2 variation differed from district to district, and that in each district it represented the infection trends in the targeted area. In some cases, a sudden drop in viral RNA concentration was observed, but this phenomenon did not necessarily mean that the viral RNA copy number had dropped to zero, suggesting that the kit was not able to detect a decrease in viral counts due to insufficient capacity. The correlation between sewage surveillance and positive cases was also investigated, and the results indicated a correspondence between sewage surveillance and positive cases.

To develop protocols for sewage surveillance, kits and reagents commonly used in Japan and other countries were examined, taking into account various local conditions such as various factors, efficiency, price and availability in Indonesia. The results confirmed that several protocols could be recommended for SARS-CoV-2 sewage surveillance in Bali and other similar cities in Indonesia. However, further validation is needed to confirm this applicability.

In summary, the SARS-CoV-2 detection by sewage surveillance in Indonesia, in areas under the jurisdiction of the Regional Technical Implementation Unit for Sewage Management (Indonesian acronym: UPTD-PAL) in Bali, Indonesia, and in areas with conventional sewage treatment facilities, including cities/districts with different characteristics The system was found to be applicable and to be compatible with

clinical cases and outbreaks of viral infections. Taken together, these results suggest that SARS-CoV-2 sewage surveillance is effective in confirming viral trends and can provide early warning to the health sector before actual infections occur.

Chapter2 Future business development, support for international cooperation, etc.

2.1 Proposals for future business development, international cooperation support, etc.

Based on the consideration of the current status and challenges of sewage surveillance in Indonesia through this demonstration, it is considered that (i) maintenance and improvement of sewerage facilities and (ii) technology transfer of sewage surveillance will be useful for its continuation and social implementation in the future. Firstly, the country of Indonesia is still underdeveloped in terms of economy and society, and it is difficult to implement sewerage system improvement only with own funds and domestic technology. By providing advanced sewage treatment technology from Japan, a sustainable sewage surveillance situation can be established. It is also possible to build capacity for sustainability in the soft aspects by providing training programmes for sewage surveillance experts and technicians and implementing capacity development in the country after the sewerage infrastructure is in place (or in parallel in areas where it is already in place).

Furthermore, in future implementation of sewage surveillance throughout the country, sewage surveillance as an infection control measure will become more effective if priority areas are defined from which an inter-regional network can be expanded. In establishing regional networks, the data collected from sewage surveillance can be used to generate a metadata set of infection risks, which can be used to identify areas at high risk of infection.

In terms of specific projects, the "Information Collection and Confirmation Survey on Strengthening the Network of Infectious Disease Control Centres for Global Pathogen Genome Surveillance" is already scheduled to be implemented, assuming Japan's international cooperation support scheme. It will be necessary to understand in detail the current status and challenges of sewage surveillance in the country, and to make proposals for future projects.

2.2 Baseline survey results for regional expansion, expansion of target viruses, etc.

In Indonesia, although there are some well-developed sewage treatment facilities in urban areas such as Jakarta, Yogyakarta and Bali, they are also inadequately maintained. While recognising the need for continued infrastructure development through sewerage improvement projects funded by yen loans and other means, sewage surveillance makes it possible to ascertain the sanitary conditions in targeted areas and can be a tool that contributes to improving public health. However, as there are no relevant engineers and researchers in the country, there is an urgent need for human resource development.

In addition, the Australian Government and several international donor agencies, such as the Bill & Melinda Gates Foundation, have also conducted or will conduct sewage surveillance in the country in the past, which could lead to multiple sewage surveillance standards being disrupted, not only by the types of viruses to be detected. For this reason, there is an urgent need to establish an infectious disease control platform by strengthening inter-regional cooperation and collaboration with relevant organisations.

Furthermore, as there are differences in the spread of infectious diseases between geographical and social

regions in the country, it is necessary to analyse the data in combination with social conditions and other data, and to establish an agile sewage surveillance method through these.