Bhutan

GovTech Agency, Ministry of Health

Data Collection Survey on Developing Future Medical and Healthcare Business through Improvement of Biobanks

Final Report

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Japan International Cooperation Agency (JICA)

Mitsubishi UFJ Research and Consulting Co., Ltd.

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List of Abbreviations

Abbreviation	Formal name
ABS	Access and Benefit Sharing
ADB	Asian Development Bank
AMED	Japan Agency for Medical Research and Development
CRRH	Central Regional Referral Hospital
DHI	Druk Holding and Investment Limited
EBPM	Evidence-based Policy Making
EHR	Electronic Health Record
EMR	Electronic Medical Record
ePIS	Electronic Patient Information System
ERRH	Eastern Regional Referral Hospital
GMC	Gelephu Mindfulness City
GNH	Gross National Happiness
GoB	Government of Bhutan
GovTech	GovTech Agency
ISBER	International Society for Biological and Environmental Repositories
ISO	International Organization for Standardization
JDWNRH	Jigme Dorji Wangchuk National Referral Hospital
JICA	Japan International Cooperation Agency
KGUMSB	Khesar Gyalpo University of Medical Sciences of Bhutan
LIMS	Laboratory Information Management System
MoH	Ministry of Health
MoICE	Ministry of Industry, Commerce & Employment
NBC	National Biodiversity Centre
NCDs	Non-Communicable Diseases
NSB	National Statistics Bureau
NSSC	National Soil Services Centre
OECD	Organisation for Economic Co-operation and Development
PHR	Personal Health Record
RCDC	Royal Centre for Disease Control
SDH	Social Determinants of Health
SOE	State-owned Enterprise
SOP	Standard Operating Procedures
ToMMo	Tohoku Medical Megabank Organization
UNDP	United Nations Development Programme
UNESCO	United Nations Educational, Scientific and Cultural Organization
WHO	World Health Organization
WMA	World Medical Association

Chapter 1. Overview of the Survey

1-1. Background of the survey

In Bhutan, although its constitution guarantees free healthcare services to all citizens, most of the country is mountainous, and there are many areas where access to even basic healthcare is difficult. In addition, and the share of the healthcare sector in the country's financial expenditure is expected to rise further in the future from the current 11%[1] with the increase of non-communicable diseases (NCDs) and the aging population[2]. Regarding domestic medical human resources, although the first MBBS (Medical Bachelor of Science) course was established in 2023 to develop doctors in the country, there is still a chronic shortage of healthcare human resources, for example, the number of doctors, nurses and midwives per 10,000 population is 5.5 (doctors, in 2022), 20.5 (nurses and midwives, in 2022)[3] , which remains low compared to other countries.

Under these circumstances, the Government of Bhutan (GoB) is trying to shift to a prevention-oriented approach based on the Healthy Drukyul Program (the 13th five-year plan for the healthcare sector), and is also fundamentally reviewing its approach to healthcare issues based on the E-Health Strategy 2.0, including the use of digital technology in the medical and healthcare fields and promotion of private sector participation, in order to alleviate the aforementioned challenges.

In particular, the GoB seeks to develop four data banks in the E-Health Strategy 2.0: a medical bank[4] , to manages electric medical record (EMR) such as clinical, imaging and laboratory data of medical institutions; a health bank to manages personal health record (PHR) related to personal health; a biobank to manages biological samples such as DNA, blood, cellular tissue and genome information; and a household bank to manages data on social determinants of health (SDH) such as housing and residential and housing status, household income and expenditure; and to establish an infrastructure (hereinafter referred to as the "Digital Health Platform") that enables integrated management of the four databanks, through national IDs. The government aims to utilize the platform to improve the health of the citizens, implement evidence-based healthcare policies, foster the domestic medical and healthcare industries, promote new industries through foreign investment and loans, and create employment opportunities in Bhutan. JICA is currently supporting the establishment of the digital health platform by the government of Bhutan under the technical cooperation project "Project for Strengthening Government Capacity for Using Digital Technology and Data in Bhutan" (hereinafter referred to as the "current digital health technical cooperation project").

In general, a biobank is an initiative to collect and store biological samples and related data for research, and its utilization can promote medical, epidemiological, and pharmaceutical research (e.g., clarification of pathological conditions), promote personalized medicine (e.g., provision of treatment based on patients' genetic information), develop preventive medicine (e.g., strengthening preventive measures by identifying risk factors for diseases), and promote the development of new drugs and technologies (e.g., development of new treatments and diagnostics and streamlining the process). In Bhutan, the integrated use of data from the biobank and data accumulated in other banks is expected to contribute to the development of the medical and healthcare fields and, as a result, to the improvement of the health and well-being of the people. On the other hand, the value proposition for users of biological samples and analytical data collected in a biobank, and the feasibility of

[1] Ministry of Finance of Bhutan. National Budget Financial Year 2024-25. https://www.mof.gov.bt/wp-content/uploads/2024/06/Budget-Report-2024-25-English.pdf

[2] According to the Annual Health Bulletin published by the Ministry of Health of Bhutan, the number of hypertension patients per 10,000 population increased from 301.2 (2019) to 362.4 (2023), and similarly, the number of diabetics increased from 73.8 (2019) to 224.6 (2023).

[3] WHO. The Global Health Observatory

[4] It is a so-called electronic medical record system, called ePIS (Electronic Patient Information System) in Bhutan.

designing and operating a cost-effective biobank for the country have not been sufficiently verified yet. Fundraising for the sustainable operation is also a big challenge in other countries. For example, the UK Biobank, a representative example of a population-based biobank, operates based on funding from the government and private foundations. There are also biobanks that are partially self-financing by collecting fees for the use of biobank data from users, but it is reported that it is difficult to cover all costs and operate autonomously. Other challenges for many biobanks include ethical issues related to the use of biospecimens and its complicated reviewing procedures, quality control of stored samples, and clarification and standardization of procedures for transfer and collaborative research[5], which are barriers to effective use of data. In establishing a biobank, it is essential to develop a regulatory and governance system that reflects the opinions of various stakeholders, including sample and information providers, users, and administrators, and to ensure a system that enables highly transparent operations from the very beginning of its establishment.

1-2. Outline of the survey (purpose and policies)

The purpose of this survey is to collect information necessary to verify the feasibility of further developing a health and industrial promotion strategy through establishing a biobank in conjunction with the Digital Health Platform in Bhutan (effects of utilization, cost-effectiveness, business models, identification of potential partners, etc.), and to conduct a needs assessment of the GoB regarding the utilization of the biobank. In addition, information that will be helpful in considering the development impact of biobanks in developing countries will also be collected.

1-3. Structure and process of the survey

This survey was conducted by a survey team consisting of the following five members. In addition, a local consultant deployed in Bhutan provided a necessary support, including information collection, coordination and follow-up of meetings with relevant organizations.

Figure1-1 Survey team members

Category	Areas of responsibility	Name	Organization
Survey team	Chief/Healthcare Data Utilization/Digital Health	Yu Hasegawa	Mitsubishi UFJ Research and Consulting Co., Ltd.
	Biobank Strategy and Planning	Fuji Nagami	Tohoku University Tohoku Medical Megabank Organization
	Business Model Study / Business Creation (1)	Tomoko Kunimitsu	Mitsubishi UFJ Research and Consulting Co., Ltd.
	Invitation Program / Business Creation (2)	Atsushi Morisawa	Mitsubishi UFJ Research and Consulting Co.
	Biobank Strategy and Planning (Assistant)	Takahiro Nobukuni	Tohoku University Tohoku Medical Megabank Organization
Local consultant	Support for information collection, coordination and follow-up of meetings in Bhutan	Green E Solutions	

This survey was performed over an eight-month period from April 2024 to December 2024. The details are shown in the table of the work process below.

[5] Biobanks generally use biospecimens and related information in two forms: “transfer” and “collaborative research.” In the case of transfer, samples and information are provided to a user, and the samples, data, research outcomes, and its intellectual property belong to the user. In the case of “collaborative research,” on the other hand, the biobank and the user share the samples, data, research outcomes, and its intellectual property. Many biobanks set the available information and fees for each of these types of use.

Figure1-2 Work process

	Work Items		April ~ December 2024								
			4	5	6	7	8	9	10	11	12
(1) Exploring business models for industrial promotion in the area of health promotion through the development of a population-based biobank in Bhutan											
1	Data collection and analysis	Exploring and identification of business areas with potential for biobank utilization by Japanese research institutions and companies									
		Examining effects and impacts of biobank on health promotion and economic benefits in Bhutan									
2	Data collection and analysis	Understanding the system and environment for the development of medical and healthcare products and services in Bhutan									
3	Data collection and analysis	Baseline survey and GAP analysis for the development of a population-based biobank									
4	Discussion and consultation	Collaboration and consultation with a technical cooperation project for the Digital Health Platform									
5	Discussion and consultation	Hypothesizing and testing the impact of population-based biobank development on GNH/well-being									
6	Discussion and consultation	Business model consideration for industrial promotion									
		(0) [Operating body] Biobank management, operation and governance in Bhutan									
		(1) [Customer] Identification of customer segments and customer needs, customer long lists									
		(2) [Value] Formulation of value proposition hypotheses that meets the needs									
		(3) [Channel /Relation] Consideration of how to deliver value to customers and rule-making									
		(4) [Revenue] Revenue flow from customers or other payers									
		(5) [Resources] Necessary facilities, equipment, supplies, personnel, and funds									
		(6) [Activities] Operations and specific activities related to the development and promotion of biobank									
		(7) [Partners] Potential collaboration with donors, international organizations, local companies, etc.									
		(8) [Costs] Costs associated with the above resources, activities, and partner collaboration									
7	Analysis	Preparation of cash flow statements by scenarios, NPV calculation, development of Go/No Go criteria									
8	Proposal	Development of a basic policy for the biobank operation of the GoB									
9	Proposal	Development of a work plan and process/roadmap of a biobank for the GoB									
10	Proposal	Consideration of draft cooperation program by JICA									
(2) Exploring concrete ideas for collaboration with relevant Japanese organizations through an invitation program for Bhutanese officials											
11	Invitation program	Preparaton prior to the invitation program									
12	Invitation program	Organizing a seminar for related organizations in Japan						▲			
13	Invitation program	Individual interviews, site visits, and follow-up with relevant Japanese organizations						▲ ▲			
(3) Consideration and reporting											
14	Consideration	Consideration of the possibility of industrial promotion through biobank development									
15	Reporting	Creation of a work plan, a work progress report, a report on invitation program and a final report		▲					▲	▲	▲

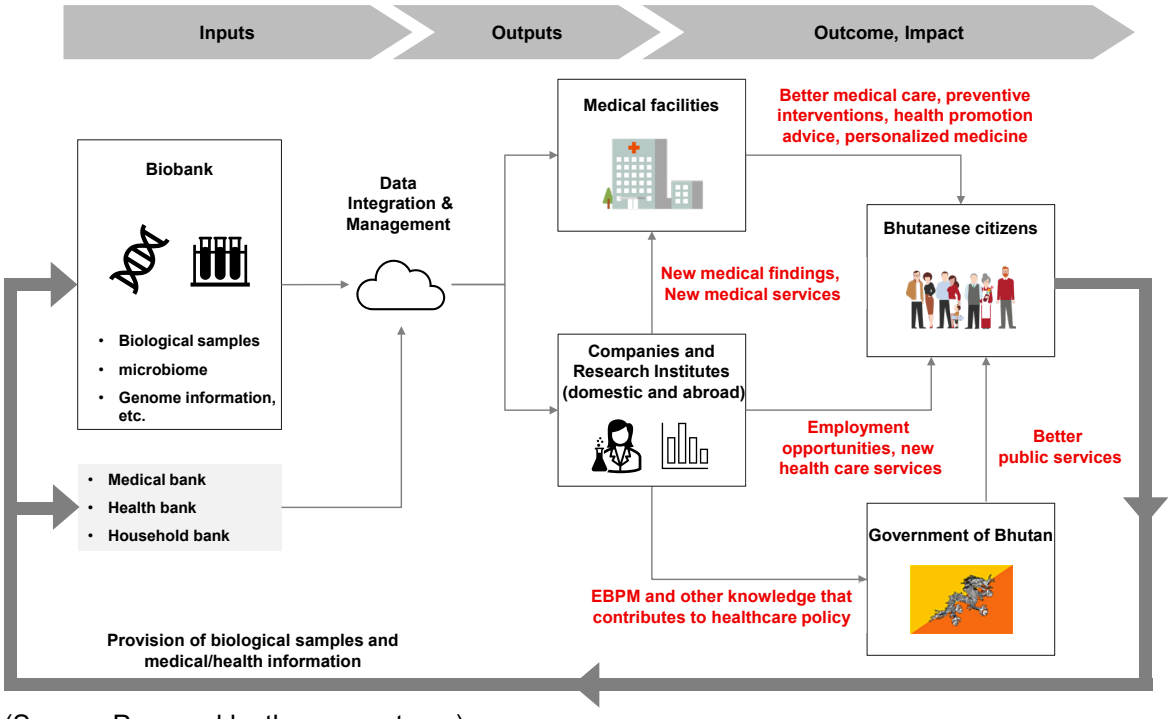
Legends: On-site work Work in Japan ▲ Event / report

Chapter 2. Value Proposition and Medium to Long-Term Strategy of a Biobank in Bhutan [Recommendation]

2-1. Purpose of establishing a biobank

As already mentioned in "1-1. Background of the survey," the utilization of biological samples and related data collected by a biobank is generally expected to promote medical and pharmaceutical research by clarifying pathological conditions, promote personalized medicine based on genome information, develop preventive medicine by identifying disease risk factors, and promote the development of new drugs and technologies. In Bhutan, the integrated use of biological samples and data from the biobank, together with data accumulated in the medical bank, the health bank, and the household bank, is expected to ultimately "improve the health and well-being of the people of Bhutan" and "promote industry, including the creation of attractive job opportunities." These two points are the purposes of the biobank that Bhutan is aiming for, and we propose a strategy and business plan to achieve them in this report. The figure below illustrates the value creation process of how inputs such as biological samples and genomic information collected and analyzed by the biobank can create outcomes that lead to the realization of these purposes.

Figure 2-1 Value creation process of a biobank in Bhutan



(Source: Prepared by the survey team)

Providing advice on optimal treatment, prevention, and health promotion to providers of biospecimens at medical institutions, based on the individual's medical and health information, and genomic information is regarded as primary use of information, and can return values to the Bhutanese people, the beneficiaries, in a relatively short period of time, directly contributing to improvement of their health and wellbeing. However, in a country with limited medical resources, the availability of drugs and other resources for treatment often becomes an issue, therefore there are high expectations for value return in the areas of prevention and health promotion. On the other hand, utilizing knowledge gained from the complex analysis of accumulated data on a large number of participants as a group for the design of new medical services, for research and development of healthcare services, and for government policy making, which are secondary use of information,

requires medium to long term time until the value is finally created. However, the research and development, policy research, and other activities undertaken in this process will contribute to the creation of intellectual industries in Bhutan. It will also lead to the creation of attractive job opportunities, such as an increase in the number of researchers at domestic research institutions using these data and the emergence of domestic private companies for the development of new medical and healthcare services.

We describe the pathways to achieving the two purposes of "industrial promotion" and "improving the health and well-being of the people" below.

2-2. Pathways for realizing industrial promotion - value proposition and business areas that leverage Bhutan's strengths

There are already a large number of biobanks around the world, mainly in developed countries, which are used to provide high-quality medical services to the people of those countries and for research and development in various life science fields[6], including the pharmaceutical industry. In order for Bhutan to establish a new biobank as a latecomer and to promote the use of information by foreign private companies and research institutions (i.e. to become a biobank to be selected), it is necessary to make a distinctive value proposition that is not found in biobanks in other countries, and to communicate it to the world. Based on the results of the interviews, field surveys, and benchmarking surveys conducted in this survey, the hypotheses in the table below are considered promising value propositions, especially for the purpose of industrial promotion.

Figure 2-2 Value proposition hypothesis for industrial promotion, leveraging Bhutan's strengths and opportunities

Value proposition for industrial promotion	Bhutan's strengths and opportunities
(1) Accumulate information for microbiome research Integrate data from microbiome[7] samples such as gut microbiota and metagenomic analysis[8] with relevant indicator on lifestyle, residential environment and well-being, and make it available for use.	Experience in the storage and utilization of animal and plant specimens for biodiversity conservation at the National Biodiversity Centre (NBC)
	Soil and land resource management and research for agriculture, food systems, and ecosystem conservation at the National Soil Services Centre (NSSC)

[6] A research area for elucidating the complex and sophisticated mechanisms of biological phenomena and applying the results to the development of medicine and drug discovery, as well as to the resolution of food and environmental problems.

[7] The totality of microorganisms (bacteria, fungi, viruses, etc.) that live symbiotically in the human body. Microbial communities exist in every place where the human body contacts with the external environment, including the digestive and skin, oral cavity, nasal cavity, respiratory tract, and reproductive organs, and each place has its characteristic microbial communities. Recent studies have gradually revealed that the human microbiome is closely related to health and disease.

[8] A technique that directly analyzes the genetic material of all microorganisms present in a particular sample (soil, water, stool, etc.), especially bacteria. It enables the study of the microbial community as a whole without the need to isolate and cultivate individual bacteria.

	Potential data integration with the health bank (especially health records related to diet), the household bank (especially information related to living environment), and Gross National Happiness (GNH) Survey (information related to happiness)
(2) Enable tracking and stratified analysis of specific populations Collect and store data regularly over the life course to enable the recording and tracking of changes in individuals over time. It also enables the extraction, tracking, and stratified analysis of specific population segments in line with research needs	Widespread use of national IDs (including digital IDs) throughout Bhutan
	Bhutan App, an app developed by GoB for citizen service delivery, becomes popular.
(3) Build a large-scale cohort with genealogical information Establish a large population-based biobank by collecting specimens and data as a cohort with genealogical information[9] from pregnant women and their families	Bhutan has a high percentage of institutional deliveries (94.5%, 2019)[10], and there are regular touch points with expectant mothers.
	Public trust in His Majesty the King and the GoB can make it possible to collect biological samples and related information on a large scale in a short period of time in.

(Source: Prepared by the survey team)

With regard to the value proposition hypothesis (1), the microbiome research area has been the focus of much attention recently, and various studies are being actively conducted, such as the relationship between the intestinal microbiota and immunity. The market size is expected to expand, as it has been suggested to be related to numerous disease areas and health promotion[11]. The gut is also called the "second brain," and the brain and gut closely influence each other (brain-gut interaction). If it becomes possible to collect stool samples in a population-based biobank targeting healthy people and to integrate them with household information collected in the GNH Survey and the household bank, the correlation between the intestinal environment and mental status, happiness, well-being, stress will become clear, and it could lead to the development of new healthcare services. The microbiome has the potential to be utilized not only in the medical and healthcare fields, but also in research and development in various sectors, such as food, beauty, agriculture, and environmental and ecosystem conservation, and is a promising area where Bhutan can take advantage of its strengths, achievements, and potential for integration with other banks.

Regarding the value proposition hypothesis (2), the ability to track changes in individuals over time, i.e., to compare the healthy time (baseline) with the time being affected by some disease, will increase the value of the research subject. In addition, the ability to select specific segments of the population for continued tracking, to conduct additional observational studies, or to perform stratified analyses, depending on the needs of companies or research institutions, would be highly attractive to researchers. Furthermore, as a biobank from a developing country, tracking various

[9] If biological samples can be collected from three generations of grandparents, parents, and children, it will be possible to efficiently search for the causes of diseases caused by a complexity of genetic and environmental factors, thereby contributing to personalized medicine and preventive medicine. A similar three-generation cohort study is being conducted in the Tohoku Medical Megabank Project in Japan, but there are few examples worldwide.

[10] Source: WHO, The Global Health Observatory

[11] Market Size and Market Share Analysis of Human Microbiome - Growth Trends and Forecasts (2024-2029). https://www.mordorintelligence.com/ja/industry-reports/human-microbiome-market

indicators as a population along the process of economic development is a value proposition that cannot be realized by existing biobanks in developed countries.

Regarding the value proposition hypothesis (3), it is assumed that prenatal and postnatal checkups and hospitalization period for delivery are promising opportunities as reliable touch points for collecting biospecimens and related information. Not only information can be efficiently collected and accumulated, but if biological samples can be collected simultaneously from the expectant mothers as well as their families and children, it will be possible to form a valuable population-based biobank as a cohort with genealogical information.

2-3. Pathways for improving the health and wellbeing of the people

As already mentioned in "2-1. Purpose of establishing a biobank," if the results of clinical laboratory tests and disease risk information suggested by genome analysis can be returned to the providers of biological samples[12], and if medical professionals can provide advice on lifestyle improvement and health checkups according to individual health conditions and disease risks, it is expected that the biobank will be able to provide efficient health services in Bhutan, where regular health checkups are not as widespread as in Japan, and to change behaviors of the population toward disease prevention and health promotion. If continuous acquisition of PHR through apps becomes common in the health bank initiative, it could be even more effective.

In addition, related to the construction of a cohort with genealogical information proposed in "2-2. Pathways for realizing industrial promotion," if newborn mass screening (assuming those without genetic testing) to detect diseases such as congenital metabolic abnormality in newborns can be conducted by taking advantage of the opportunity to collect biological samples, Early detection and early treatment of such diseases can save children's lives and prevent the onset of such diseases, thereby preventing physical and mental disabilities of the children. Since newborn mass screening is not currently conducted in Bhutan, the introduction of this new system is expected to have a significant effect. However, there are many items that need to be considered in advance, such as the need to identify target disease and establish a system to deal with the disease by medical intervention, including definitive diagnosis and provision of therapeutic foods which are available in Bhutan. Since this issue was not fully discussed and examined in this survey, the proposal from this survey does not design a biobank with the implementation of newborn mass screening.

Other outcomes of the utilization of biobank data by companies and research institutions include the development of new drugs, the possibility of new medical interventions, the availability of new healthcare services, and so on, although it needs more longer-term perspective. It is also envisioned that the information collected by the Digital Health Platform, including the biobank, will be used for the evidence-based policy making (EBPM) in healthcare policy, leading to better healthcare-related public services.

2-4. Medium- and long-term strategy and roadmap

Initially, the GoB envisioned a biobank that would collect biological samples from the "entire population" of Bhutan. However, the "WMA Declaration of Helsinki"[13], which sets ethical principles for medical research involving human participants, and the "WMA Declaration of Taipei

[12] The communication of advice by a physician to a biospecimen provider, based on the results of clinical laboratory tests and disease risk information suggested by the results of genomic analysis, is described as "return". The biospecimen itself is not returned.

[13] WMA Declaration of Helsinki - Ethical Principles for Medical Research Involving Human Participants https://www.wma.net/policies- post/wma-declaration-of-helsinki/

on Ethical Considerations regarding Health Databases and Biobanks"[14] declare the main principle of obtaining specific and free informed consent from participants who have the capacity to consent. Therefore, the government should not force the collection of biological samples from all citizens or create a social environment in which people are disadvantaged by not cooperating in the collection of specimens. It is unethical that a biobank advocates the collection of specimens "from the entire population" in their policies.

While based on this premise, it is also desirable to aim for the inclusion of as many people as possible in Bhutan, since the value of information held by a population-based biobank generally tends to increase with the number of people participated. On the other hand, in order to promote the utilization of biological specimens and genome information by private companies and research institutions and to realize industrial promotion, specimen collection, processing, and storage under very high quality[15] management and appropriate management of data are required, as well as the scale of the biobank. This will require significant resources, so that the number of participants and population coverage should be carefully considered as feasible goals. Increasing the size of the biobank will mean an increase in costs, and a concern of a reduction in per capita resources, leading to lower quality biospecimens and data. In addition, if the biobank is expected to link with three other databanks to create a larger collection of information that can be analyzed by AI, a uniformed high-quality data set may be preferred over the overall size of the biobank.

Based on the purposes and value proposition of establishing a biobank and the multiple considerations above, we propose a medium- to long-term roadmap based on the following assumptions (the major premises)

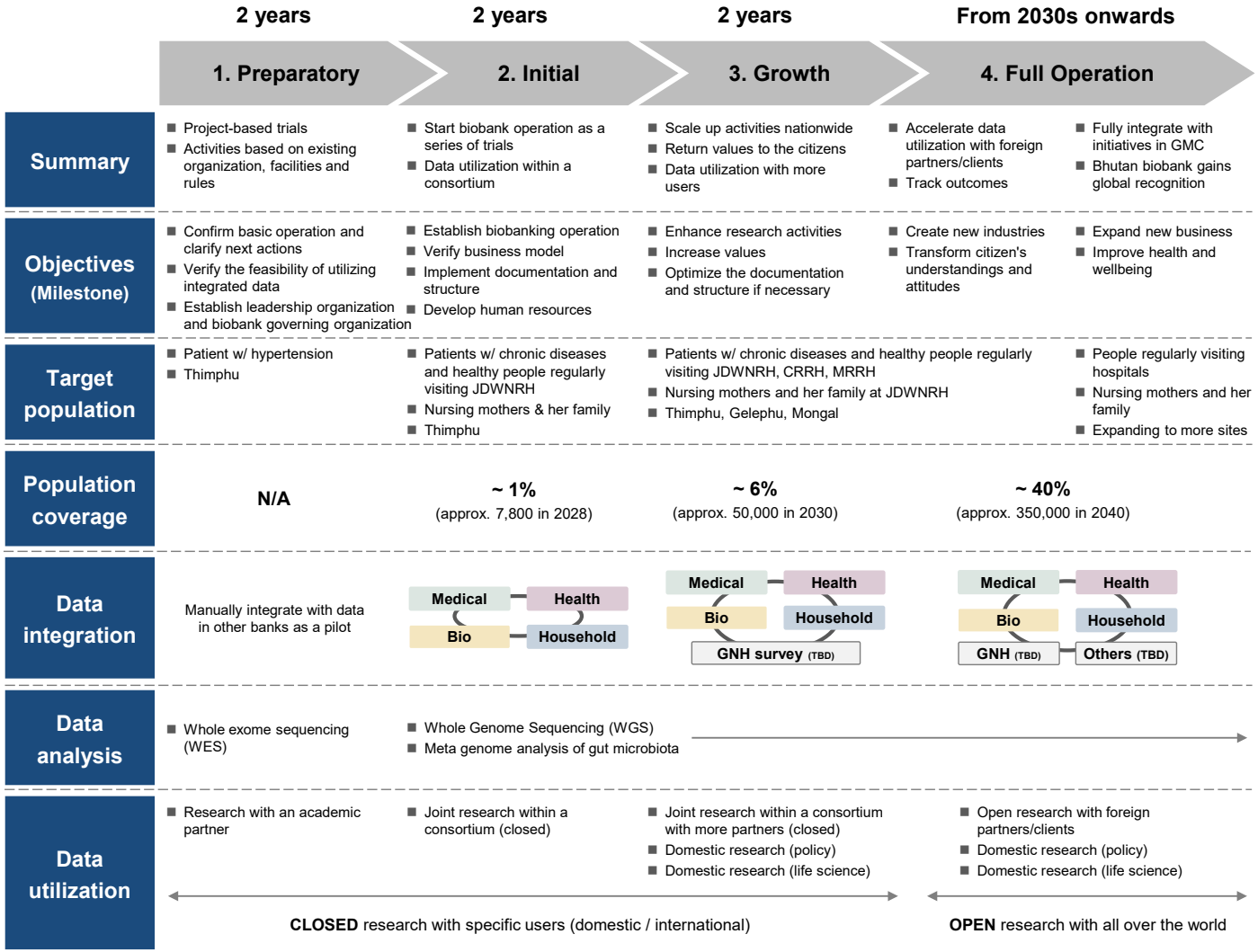
- Pursue the realization of the two objectives of "improving the health and well-being of the Bhutanese people" and "promoting industry, including the creation of attractive job opportunities.
- Consider business plans that can create value for the three value proposition hypotheses (1) promotion of microbiome research), (2) possibility of tracking and stratified analysis of specific populations), and (3) cohort with large-scale genealogical information proposed in "2-2. Pathways for realizing industry promotion".
- Separate the consideration of whether or not to introduce newborn mass screening from the consideration of biobank (implementation of newborn mass screening is not assumed in this proposal).
- Consider a process and resource (facilities, equipment, human resources) plan that aims to establish a population-based biobank of several hundred thousand people, but prioritize the establishment of a high quality control system over the expansion of the scale of the biobank.

The table below outlines the medium- to long-term roadmap currently envisioned based on these assumptions.

[14] WMA Declaration of Taipei on Ethical Considerations regarding Health Databases and Biobanks https://www.wma.net/policies-post/wma-declaration -of-taipei-on-ethical-considerations-regarding-health-databases-and-biobanks/

[15] In order to create information with high values to use, it is important to make efforts to minimize "quality differences" coming from differences in procedures and protocols, as well as to pursue "high quality" in the process of handling biological specimens and information.

Figure 2-3 Medium- and long-term roadmap for the Bhutan Biobank



(Source: Prepared by the survey team)

The proposed medium- to long-term roadmap is to cover about 40%[16] of the total population (about 350,000 people) 15 years after the start of the biobank activities. Although this number of people is not as large as the UK Biobank in the UK, which is currently considered the largest in the world, it is larger than the one planned by Precision Health Research, Singapore (PRECISE) in Singapore and the Tohoku Medical Megabank Project in Japan. It is considered to be internationally competitive. In this roadmap, activities will be gradually expanded in four phases: Preparatory phase (2 years), Initial phase (2 years), Growth phase (2 years), and Full Operation phase (2030s and beyond). At the timing of phase transition, whether the objectives (i.e., milestones) set forth in each phase have been achieved is evaluated, as well as the budget and detailed plan for the next phase are finalized. Achievement of milestones and finalization of budgets and detailed plans are the conditions for phase transitions. In the Initial and Growth phases, a "consortium" will be formed with private companies, research institutions, universities, and other organizations that show interest in utilizing biobank specimens and genome information, and data utilization will be promoted within the consortium. The consortium will also utilize the requests, needs, and feedback from the consortium member institutions in its business plan, while upgrading its management system and structure. The consortium is expected to include organizations in and outside of Bhutan.

The operation of the biobank and the creation of value through data utilization need to be addressed over the medium to long term. It is necessary to flexibly update the roadmap and plans for each phase based on market trends (i.e. data utilization needs), technological trends, and the maturity of management system of the biobank in Bhutan. As for the growth strategy after the 15th year of its establishment, it is difficult to evaluate the plan and its appropriateness at this point, and we expect that the GoB will take the lead in planning the strategy through concrete activities in the future.

The table below summarizes possible points of consideration and their respective advantages and disadvantages when reviewing the roadmap and business plan after the Initial phase. None of the options, however, override the assumptions (major premise) of the medium- to long-term roadmap already described on page 11.

Figure 2-4 Points to be considered to review the roadmap and plan

Points to be considered	Advantages	Disadvantages
(1) Only collect information that companies and research institutions want on a needs basis	・ Minimizes specimen storage, thus possible to significantly reduce investment costs	・ Since only certain segments of the population will be selected to provide samples, realization of the objective of improving the health and well-being of the citizen will be limited (population coverage will also decrease) ・ There is a risk of lack of public understanding ・ In addition to the costs and resources associated with specimen and data quality control, a high level of management is required to understand user needs, coordination and communication, and rapid specimen collection and converting it to available data

[16] Percentage of people who have had at least one biological sample collected and managed with associated information linked to the national ID. It is assumed that some people will have had multiple samples taken by 15 years after the start of the biobank, but this is not be counted as duplication.

(2) Minimize specimen storage of biological samples and accumulate only data-format information	・ Significant reduction in investment costs for specimen storage ・ If costs could be reduced, it would be possible to aim for more population coverage	・ Failure to meet users' needs in biospecimen[17], halving the outcomes for industry promotion ・ Server costs for data storage may increase
(3) No whole genome sequencing and minimize the storage of biological samples, while enhancing information related microbiome	・ Easier to promote as a value proposition unique to Bhutan ・ If costs could be reduced, it would be possible to aim for more population coverage.	・ Failure to meet users' needs in biospecimen, halving the outcomes for industry promotion ・ Personalized medicine based on genomic information will be difficult to achieve

(Source: Prepared by the survey team)

Regarding the point (1) above, it would be challenging due to the risk of not being understood by the public and the fact that it would incur operational costs (i.e. requiring advanced management). Regarding the points (2) and (3), it may be possible to minimize the disadvantages and maximize the advantages, depending on the precise analysis of user needs and the definition of information to be converted into data. The points (2) and (3) are reflected in a detailed roadmap in the Annex (undisclosed) with an estimation of necessary resources and costs.

2-5. Future vision

As already mentioned in "2-2. Pathways for realizing industrial promotion" and "2-3. Pathways for improving the health and well-being of the people," the main purposes of the biobank in Bhutan are both to promote industry and improve people's health and well-being. Currently, Bhutan has announced the concept of Gelephu Mindfullness City (GMC), an economic hub and a special administrative zone to be established in Gelephu in southern Bhutan, with a master plan based on Bhutanese values such as nature, culture, and GNH. The GMC is positioned as "a land of bridges, connecting nature and people, past and future, and local and global."[18] The GMC has various ambitious plans, including urban development, infrastructure development, and the creation of new industries. The idea of the GMC is highly compatible with the vision of the biobank and the Digital Health Platform[19] and has the potential to become a biobank that attracts global attention in the future by operating within the GMC concept and developing in a way different from biobanks in other countries[20].

[17] Some interviewees stated that genomic information/data alone is not sufficient for utilization in research, and that biological samples are indispensable.

[18] Reference: GMC website (https://gmc.bt/), His Majesty the King's speech in December 2023 (https://gmc.bt/wp-content/uploads/2024/09/Speech_HM_Final.pdf), related articles https://architecturephoto.net/197844/)

[19] For example, research areas such as microbiome and metagenome analysis are areas at the nexus of the nature and human. The approaches to promote behavioral change for the future based on the medical, health, and genomic information accumulated to date and to promote utilization of biological samples and information accumulated in Bhutan with foreign partners to solve domestic problems and develop advanced products and services can be regarded as the values of GMC.

[20] Because of the expected affinity with GMC, the proposal recommends to establish a biobank in Gelephu in addition to RCDC in the Full Operation phase of the mid- to long-term strategy and roadmap (note: its strategic significance, appropriateness, and feasibility should be examined through actual activities in the Initial and Growth phases).

Chapter 3. Business Model of the Biobank in Bhutan [Recommendation]

3-1. Governance and leadership

3-1-1. Expected roles of existing organizations

In order to realize the two objectives of "industrial promotion" and "improvement of the health and well-being of the people" through the operation of a biobank and the utilization of data, a wide range of organizational functions must be implemented in a viable manner, including visionary strategic planning and commitment from a medium- to long-term perspective, budget management and coordination, investment implementation, human resource development, quality control of biological samples and data, explanation to the citizens, and client communication. The main organizations that are expected to be involved in biobank operations and data utilization in Bhutan, and their expected roles are summarized in the table below.

Figure 3-1 Main organizations involved in biobank operations and data utilization with their expected roles

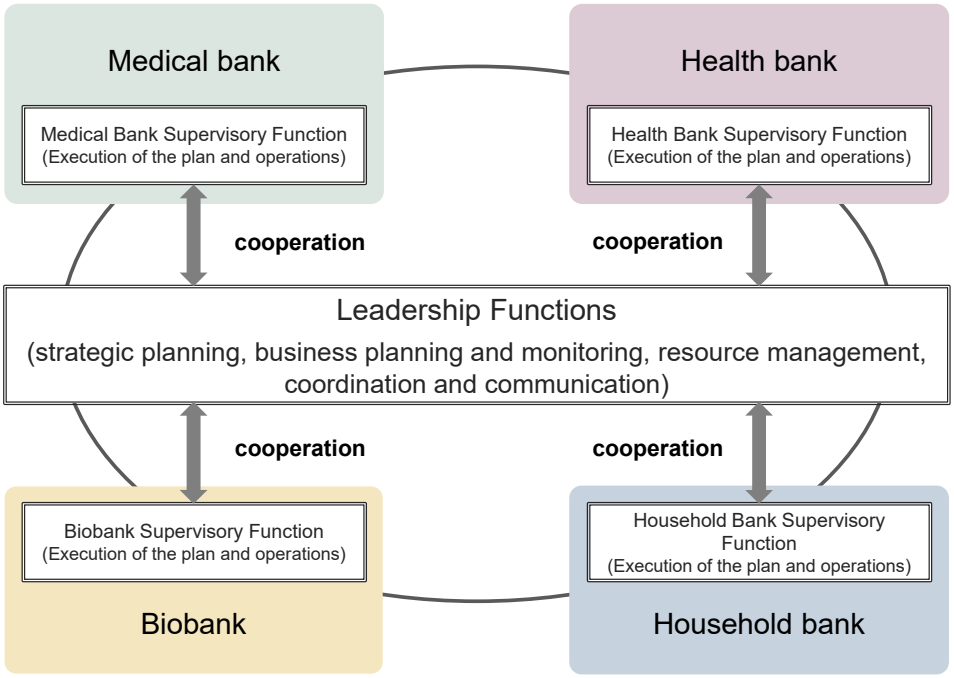
Organization	Expected roles
GovTech Agency	・ Supervision of information coordination and integration of the four banks (up to implementation of leadership functions) ・ Consideration of data governance including genomic information
Ministry of Health (MoH)	・ Jurisdiction over the biobank (up to implementation of leadership functions) ・ Develop health-related laws, regulations, and guidance
Ministry of Industry, Commerce & Employment (MoICE)	・ Development of policies and regulations related to foreign investment and loans and attracting foreign companies
Ministry of Finance	・ Securing budget for biobank operations
National Statistics Bureau (NSB)	・ Jurisdiction over various statistical data and EBPM promotion
Jigme Dorji Wangchuk National Referral Hospital (JDWNRH)	・ Collection and processing of biological samples and transport to the biobank ・ Return of results from clinical laboratory tests and various analyses ・ Technical guidance and technology transfer to other medical institutions
Royal Centre for Disease Control (RCDC)	・ Biobank operations (specimen storage, analysis)
Khesar Gyalpo University of Medical Sciences of Bhutan (KGUMSB)	・ Promote research in the life science field using biobank samples and information ・ Training of medical personnel and researchers
National Biodiversity Centre (NBC)	・ Sharing experiences and lessons learned from the operation of a biobank for animals and plants
National Soil Services Centre (NSSC)	・ Cooperation with research related to soil resources
Druk Holding and Investments Limited (DHI)	・ Promotion of the development of life science industry from the private sector's perspective

(Source: Prepared by the survey team)

3-1-2. Leadership function over all databanks and supervision of each bank

In the life science field, including genomic medicine, markets and technologies are expected to change constantly. Therefore, the biobank must have expertise in understanding mid- to long-term global trends (i.e. scientific progress and market changes) and the leadership and implementation skills to direct operations while reflecting these trends in the biobank's strategies and plans. Under the current organizational structure of the GoB, it is assumed that RCDC, JDWNRH, and KGUMSB will play a central role in biobank operations and in promoting research using the data. It is essential to implement a function to lead the execution of the plan and the operation as the main body of biobank management ("Biobank supervisory function"). On the other hand, once data utilization actually starts in the four banks of the Digital Health Platform, it is expected that requests for various conditions, applications for data utilization, and questions will arrive from inside and outside the country, and these are not necessarily limited to the biobank. A function will be needed to lead the strategic planning, business planning and monitoring, resource management, and coordination and communication of the entire Digital Health Platform ("leadership function"), while responding to requests and questions from customers and the public in a one-stop manner. This leadership function is expected to cover necessary business expenses for the operation of each bank.

Figure3-2 Proposed overall Digital Health Platform and supervisory functions of each databank



(Source: Prepared by the survey team)

Our idea is to establish a supervisory function in each bank as an "executing organization" responsible for the execution of plans and operations of each bank under the leadership function. Since the supervisory function of each bank will be responsible for actually handling data in and out of the bank, it would be appropriate for the owner of the stored information to have the supervisory function. In other words, for the biobank, we propose that the RCDC, an organization where a biobank is established, should be strengthened to implement a supervisory function. The cases of other databanks are outside the scope of this survey, but it would be appropriate for the MoH to have the functions for the medical bank and the health bank. For the household bank, it would be desirable to have a system centered on the NSB, which can also collaborate with related ministries such as the MoH and the GovTech Agency.

The table below shows the requirements for the "leadership function" and the "supervisory function of each bank."

Figure 3-3 Requirements and roles of the leadership function

Function	Requirements and roles
Strategic planning	Understanding of long-term market trends in the life science area
	Formulation of medium- to long-term strategies and business plans based on the global trends
	Development of laws, regulations, and guidelines necessary for the implementation of digital health platform projects (see "3-2. Codes, regulations, and guidelines" for details)
Business planning and monitoring	Development and determination of short- and mid-term business plans and KPIs
	Provision of execution instructions for implementing plans for the supervisory functions of each databank
	Monitoring and evaluation of operations of each databank
Resource management	[People] Planning human resource development and allocating the right people to the right places
	[Material] Procurement planning and implementation of facilities, equipment, and materials.
	[Capital] Financial planning and budget management **(covering the business expenses necessary for the operation of each bank)**
	[Capital] Negotiations with funding sources (considering various fundraising, not just government funding)
	[Information] Analysis and management of data collected and stored on the Digital Health Platform (deployment of bioinformaticians and medical information engineers)
	[Information] Formulation of guidelines and operational procedures for providing information to customers and external partners.
	[Information] Data server management (with the Government Data Center)
Coordination and communication	Coordination and negotiation with relevant ministries and stakeholders
	Acting as a one-stop contact point with external parties such as customers and partners
	Risk communication response to requests and questions from the public
	Building relationships with potential customers and partners in Bhutan and abroad (sales and marketing)
	Dissemination of information to increase the international presence of Bhutan Biobank (PR)

(Source: Prepared by the survey team)

Figure 3-4 Requirements and roles of the “supervisory functions of each bank”

Function	Requirements and roles
Strategic planning	understanding global trends in the areas of each databank
	Expertise in identifying technological trends in the areas of each databank
Business implementation	Implementation of specific activities based on the business plan
	Development of the standard operating procedures (SOPs)
	Operational-level PDCA at the sites of each databank (autonomy within the budgetary limits)
	Suggestions from the operational side for the business plan for the next fiscal year
Resource management	[People] Human resource development (execution based on the business plan)
	[Material] Maintenance and management of facilities, equipment and materials
	[Capital] Execution based on the budget plan
	[Information] Management of data collected and stored by each bank
Coordination and communication	Participation and relationship building with international academic societies and other international collaboration frameworks in the areas of each bank
	Ability to coordinate and negotiate with stakeholders at operational level

(Source: Prepared by the survey team)

The table below lists possible organizational options and their respective advantages and points to note with regard to what type of organization should have the “leadership function” of overseeing the entire Digital Health Platform in Bhutan. Considering that the purpose is not only to “improve the health and well-being of the people” but also to “promote industry, including the creation of attractive job opportunities,” it is possible to establish a new organization as an independent government entity, or to form a new organization as a state-owned enterprise (SOE) under Druk Holding and Investment Limited (DHI) in addition to being under the umbrella of existing ministries such as the MoH or the GovTech Agency. It is also possible to build a structure that enables flat cooperation with each stakeholder. In some cases, the profit and public sectors could be separated and set up as separate leadership functions. Further discussions within the GoB should be continued on the detailed organizational structure and governance, and it is expected that they express a commitment to establish the leadership function.

Figure 3-5 Organizational options for the leadership function

Organizational structure	Advantages and points to note
(1) Independent organization (SOE) under DHI	・ The organizational structure as a state-owned enterprise is optimal in terms of market development (marketing), financing (attracting foreign investment), industrial promotion, business planning and monitoring, etc. ・ On the other hand, this platform does not necessarily pursue only economic value/profit (it has a strong public service aspect), so it is essential to consider the functions under its jurisdiction. ・ Formulation of laws, regulations, guidelines, and human resource development plans require cooperation with the ministries and agencies in charge of each
(2) Independent government organization	・ Utilizing the governance structure of existing government organizations, while bringing in expertise from various ministries and agencies for cross-ministry operation ・ There is a risk of not being able to take agile planning and actions (i.e., stick to the government thinking) in industrial promotion, which requires private-sector thinking
(3) An organization under the umbrella of MoH or GovTech Agency (including existing RCDC)	・ Smooth transition from the structure of the current digital health technical cooperation project ・ If the RCDC under the MoH can be addressed by strengthening its functions, there is no need to fundamentally reform the organizational structure within the GoB ・ As a leader of diverse stakeholders, it must be able to think outside the box from a medium- to long-term perspective, but there is a risk of falling into thinking within the scope of the belonging organization or taking a short-term view.

(Source: Prepared by the survey team)

As a reference for biobank management, it may be useful to review the leadership and governance structure of public biobanks in Japan and the background of the establishment of such biobanks. Public biobanks in Japan are often operated by universities or national research institutes. Large-scale biobanks storing more than several tens of thousands of specimens are generally established after a government-led committee deliberates the plan and determines its direction, and the plan is updated approximately every five years. The operating body formulates the plan with goals to be achieved and expected outcomes over a span of 5 and 10 years or more, which are then deliberated by the committee. The committee is appointed and operated by the ministry or agency in charge of the large biobank in question[21]. During the five-year period, interim reports and mid-evaluations, as well as final reports and post-evaluations, are made, although post- evaluations are often made in the fourth year if the biobank is assumed to continue. The budget is generally stable for the five-year period of the plan, but at the end of the five-year period, a fundamental review may be conducted in consideration of consistency with government policies and other factors.

[21] For example, Biobank Japan and Tohoku Medical Megabank Organization are under the jurisdiction of Ministry of Education, Culture, Sports, Science and Technology (MEXT), while the National Center Biobank Network Project is under the jurisdiction of Ministry of Health, Labour and Welfare (MHLW).

The operating body is often the organization to which the researchers who were central to the planning process at the time of its establishment belong, but it may be partially reorganized during the course of the project. At the time of plan update, the operating body may be determined through an open call. For example, Biobank Japan was jointly operated by the Institute of Medical Science of the University of Tokyo and RIKEN at the time of its establishment, but was later changed to solely operated by the Institute of Medical Science of the University of Tokyo. The biobank is located within the Institute of Medical Science, but several researchers from departments of the University of Tokyo other than the Institute are involved in its operation. As another example, Tohoku University proposed the Tohoku Medical Megabank Project to the government as a reconstruction project after the Great East Japan Earthquake, and when the government approved and budgeted the project, the Tohoku Medical Megabank Organization was established as a department dedicated to the project. Iwate Medical University, which participated in the plan, also established the Iwate Tohoku Medical Megabank Organization as a dedicated department. Currently, the two universities cooperate in the management of the project, and the Japan Agency for Medical Research and Development (AMED) is responsible for managing the progress of the project.

Originally, the establishment of biobanks was influenced by major global medical and research trends: the Human Genome Project, which began in 1990 and was completed with the release of a draft version in 2001 and a completed version in 2003, had a great deal to do with the establishment of biobanks in the early 2000s. The international project decoded the entire genome of one person, and many countries, anticipating a shift in focus to the differences in each person's genome, began to establish biobanks based on genome research. Iceland was a pioneering example in 1998, and Sweden, Estonia and other countries followed, and Biobank Japan was also established at around the same time of 2003. In the U.K., after the completion of the human genome sequencing, a research report was issued by a government agency, and the establishment of a large-scale biobank was deemed necessary, which led to the establishment of the UK Biobank.

Because of these differences in the process and timing of biobank establishment, as well as the relationships between industry, government, and academia in each country, it is considered necessary for Bhutan to establish a system that is unique to Bhutan, while referring to the management systems of biobanks in other countries.

3-1-3. Transition from the Preparatory phase

From the preparatory phase under the medium- and long-term roadmap, high-level policy making and business planning, including investment and human resource development will be required. In the Preparatory phase, the governance structure of the current digital health technical cooperation project will be utilized, and the Sub-Committee for the biobank will play a central role in preparing for the Initial phase and beyond. It is assumed that the leadership function proposed in 3-1-2 will be established as a permanent organization before the Initial phase starts, and the establishment of this organization will be a prerequisite for the start of the cooperation project described later. Other items that require consideration and commitment prior to the start of biobank operations are listed in the table below. The items proposed in this report should be considered by the GoB as a starting point.

Figure 3-6 Items that need to be determined, agreed upon, and committed to by Bhutan before the start of the biobank operations

Item	Relevant sections of this report	Details
Governance and leadership	3-1. Governance and leadership	· Implement a leadership function and a biobank supervisory function (establishment as a permanent organization) · Clarify the roles and scope of the leadership and biobank supervisory functions (authority of budget, personnel, business implementation, etc.)
Vision/Strategy	2-4. Medium- and long-term strategy and roadmap	· Scrutinize, agree, and decide the goals of the biobank and the path to achieve them · Refine the value proposition hypothesis (including consideration of whether or not newborn mass screening should be performed) · Develop roadmap for the next 10-15 years, with specific milestones for each phase (including Growth and Full Operation phases)
Regulation	3-2. Codes, regulations, and guidelines	· Establish laws, regulations, and guidelines necessary to begin the Initial phase (compliance with ethical principles, research use of human genetic resources, access to genetic resources and the fair and equitable sharing of benefits arising from their utilization, international standards compliance and self-checking systems, framework for international collaboration, medical data governance)

Operation	3-4. Operations	・ Establish procedures for implementation of activities during the Initial phase (definition of participants, methods for recruit, how to obtain an informed consent, how to collect samples, transport, process, and store, methods for analysis, how to return the results, etc.) ・ Identify issues and specific actions for quality control of biological samples ・ Scrutinize, agree, and decide implementation system of clinical laboratory testing (including whether or not to operate in-house or outsource it) ・ Scrutinize, agree, and decide whether or not to conduct whole genome analysis and the implementation system (including whether or not to operate in-house or outsource it) ・ Scrutinize, agree, and decide the data analysis system for the entire Digital Health Platform
Human resource	3-5. Resources (human resources)	・ Scrutinize, agree, and decide staffing and human resource development plan ・ Coordinate with related ministries and specialized agencies
Investment and maintenance	3-6. Resources (facilities, equipment, materials, etc.) 3-7. Costs	・ Scrutinize, agree, and decide cost and investment plan for facilities and equipment (based on the equipment to be installed, also consider the necessity of facility renovations and transportation infrastructure) ・ Establish a data storage, management, and analysis system for the entire Digital Health Platform, including plans for expansion of supercomputers and data center ・ Commit expenditures for maintenance costs for facility and equipment ・ Develop financing plan (initiate negotiations with the funding sources)

(Source: Prepared by the survey team)

3-2. Codes, regulations, and guidelines

3-2-1. Ethical principles

The World Medical Association (WMA), a federation of non-governmental organizations representing physicians worldwide, adopted the "WMA Declaration of Taipei on Ethical Considerations regarding Health Databases and Biobanks" [22] (hereinafter referred to as the "Declaration of Taipei") in 2016 to provide guidance on ethical principles and practices related to biobanking activities. The Declaration of Taipei was made as a supplement to the "Ethical Principles for Medical Research Involving Human Participants"[23] (hereinafter referred to as the "Declaration of Helsinki"), which was adopted in 1964. In the October 2024 revision of the Declaration of Helsinki, the existing Article 32, regarding obtaining the informed consent of the individual, was made more detailed, including an explanation of anticipated secondary uses, and compliance with the Declaration of Taipei was added.

Bhutan will need to develop laws and guidelines for biobank operations and data utilization, all of which need to be considered in a manner that complies with the above ethical principles.

3-2-2. Research use of human genetic resources

The first international document on the ethical aspects of human genetic research was the "Universal Declaration on the Human Genome and Human Rights," adopted by the United Nations Educational, Scientific and Cultural Organization (UNESCO) in 1997. In addition to respect for human rights in the handling of genetic information, such as the prohibition of discrimination based on genetic characteristics (Article 6) and confidentiality of genetic information (Article 7), the Declaration also stipulates in Article 19 four matters to be encouraged in the framework of international cooperation with developing countries.[24]

- Assessment of the risks and benefits pertaining to research on the human genome to be carried out and abuse to be prevented
- The capacity of developing countries to carry out research on human biology and genetics, taking into consideration their specific problems, to be developed and strengthened
- Developing countries to benefit from the achievements of scientific and technological research so that their use in favor of economic and social progress can be to the benefit of all
- The free exchange of scientific knowledge and information in the areas of biology, genetics and medicine to be promoted

[22] The WMA Declaration of Taipei on Ethical Considerations regarding Health Databases and Biobanks. https://www.wma.net/policies-post/wma-declaration-of-taipei-on-ethical-considerations-regarding-health-databases-and-biobanks/

[23] WMA Declaration of Helsinki – Ethical Principles for Medical Research Involving Human Participants. https://www.wma.net/policies-post/wma-declaration-of-helsinki/

[24] Universal Declaration on the Human Genome and Human Rights. https://www.unesco.org/en/legal-affairs/universal-declaration-human-genome-and-human-rights

Furthermore, UNESCO adopted the International Declaration on Human Genetic Data in 2003, which defines the special status of human genetic information (Article 4) as below[25]. The Declaration indicates various principles to be observed in the collection, processing, use, storage, promotion, and implementation of human genetic information.

- They can be predictive of genetic predispositions concerning individuals
- They may have a significant impact on the family, including offspring, extending over generations, and in some instances on the whole group to which the person concerned belongs
- They may contain information the significance of which is not necessarily known at the time of the collection of the biological samples
- They may have cultural significance for persons or groups.

From such context, specific guidelines for the research use of human genetic information have been developed internationally or on a country-by-country basis, including the adoption of the "OECD Guidelines on Human Biobanks and Genetic Research Databases"[26] in 2010 by the Organization for Economic Cooperation and Development (OECD). In addition, the COVID-19 pandemic in 2020 raised international awareness of the importance of genomic research in global health. The WHO Science Council, established in April 2021, identified the use of genome technologies as a topic to be addressed in the future at its first meeting, and in July 2022, it compiled a report entitled "Accelerating access to genomics for global health: promotion, implementation, collaboration, and ethical, legal, and social issues"[27]. The report outlines 15 recommendations for WHO and Member States to accelerate the establishment of genomic technologies and keep continue their beneficial use. Furthermore, in November 2024, the principles for human genome data collection, access, use, and sharing for policy makers, researchers, and health professionals involved with human genome data, WHO released "Guidance for human genome data collection, access, use and sharing."[28]

To date, Bhutan has no policies, laws, or regulations governing the acquisition and research use of human genetic resources. Prompt consideration and development of these policies and regulations is required to promote the establishment of a biobank and their utilization, especially from outside of Bhutan.

[25] International Declaration on Human Genetic Data. https://www.unesco.org/en/legal-affairs/international-declaration-human-genetic-data

[26] OECD Guidelines on Human Biobanks and Genetics Research Databases. https://bbmri.at/wp-content/uploads/2023/08/44054609.pdf

[27] WHO, "Accelerating access to genomics for global health: promotion, implementation, collaboration, and ethical, legal, and social issues." https://www.who.int/publications/i/item/9789240052857

[28] WHO, "Guidance for human genome data collection, access, use and sharing." https://www.who.int/publications/i/item/9789240102149

3-2-3. Access to genetic resources and the fair and equitable sharing of benefits arising from their utilization[29] (ABS)

The Convention on Biological Diversity, adopted in 1992, defines three objectives in Article 1: "the conservation of biological diversity," "the sustainable use of its components," and "the fair and equitable sharing of the benefits arising out of the utilization of genetic resources."[30] Regarding the "the fair and equitable sharing of the benefits arising out of the utilization of genetic resources," Article 15 stipulates the following two points[31].

- Recognizing the sovereign rights of States over their natural resources, the authority to determine access to genetic resources rests with the national governments and is subject to national legislation
- Access to genetic resources shall be subject to prior informed consent (PIC) by the government of the providing country and mutually agreed terms (MAT) with the provider

"Genetic resources" as defined by the Convention on Biological Diversity refers to plants, animals, microorganisms, and others, and does not cover human genetic resources, but does cover microorganisms that exist in the human body, such as intestinal bacteria[32]. "The Nagoya Protocol on Access to Genetic Resources and the Fair and Equitable Sharing of Benefits Arising from their Utilization to the Convention on Biological Diversity" (hereinafter referred to as the "Nagoya Protocol") was adopted at the 10th meeting of the Conference of the Parties (COP10) to the Convention on Biological Diversity held in Nagoya in 2010 as an international instrument establishing procedures to ensure the steady implementation of the above. This requires each country, either as a provider country or as a user country, to establish rules to ensure that genetic resources are provided and acquired appropriately in accordance with Article 15. Bhutan ratified the Nagoya Protocol in 2014, and to date has established the following four rules.

[29] It is generally referred to as Access and Benefit-Sharing (ABS), from "the access to genetic resources" and "the fair and equitable sharing of the benefits arising from their utilization."
[30] The Convention on Biological Diversity. https://www.cbd.int/convention/text
[31] ABS: Opportunities for the acquisition of genetic resources and the fair and equitable sharing of benefits arising from their use (in Japanese). http://abs.env.go.jp/index.html
[32] ABS Academic Task Force Team of the National Institute of Genetics, "Frequently Asked Questions and Answers: what is a genetic resource?" (in Japanese). https://idenshigen.jp/nagoya/faq059/

Figure 3-7 ABS-related policies, guidelines and regulations in Bhutan

Name of document	Category	Overview
ABS Toolkit for management of genetic resources and associated traditional knowledge in Bhutan	Explanatory information	· Provides necessary information on the legal, administrative and policy framework for the implementation of ABS in the country · Also serve as a communication, education and publication awareness material on ABS
The ABS Policy of Bhutan 2015	Policy Strategy Action plan	· Defines the basic policies to realize that access to and utilization of Bhutan's genetic resources and associated traditional knowledge should affirm the cultural and spiritual values of the Bhutanese people, and contribute to the well-being of the planet and the current and future generations · **It does not apply to access of human genetic resources**
The Biodiversity Act of Bhutan 2022	Law	· Promote the wise use of natural resources as a development asset to contribute to the sustainable social and economic development of the country and the benefit of humankind · Promote the conservation and sustainable use of biological resources and covers the research and commercial utilization of Bhutanese genetic resources, their derivatives, and traditional knowledge · Provide the protection of plant varieties and the rights of breeders to encourage the development of new varieties. Further, the Act will protect the rights of farmers in respect of their contributions made in conserving, improving and making available the plant and animal genetic resources
Biodiversity Rules and Regulations 2023	Rules	· Regulations to support implementation of the Biodiversity Act of Bhutan 2022 · The use of genetic resources and related traditional knowledge, divided into scoping phase and actualization phases, requires access proposal, PIC, and Access and Benefit Sharing Agreement · Also defineses for the resource sustainability assessment, management of invasive alien species, establishment and management of Bhutan ABS fund, and monitoring and enforcement of regulatory compliance.

(Source: Prepared by the survey team based on the Bhutan country profile on the ABS Clearing-House website (https://absch.cbd.int/en/countries/BT) and various documents.

3-2-4. International Standards for Biobanks

The International Organization for Standardization (ISO) has published the international standard document "ISO 20387:2018 Biotechnology - Biobanking - General requirements for biobanking" for the collection and storage of biological samples in 2018. This document specifies general requirements for the competence, impartiality and consistent operation of biobanks including quality control requirements to ensure biological material and data collections of appropriate quality.[33] In Japan, the Japanese Industrial Standard JIS Q 20387 (General requirements for biobanking) was established in 2023 based on this document, and the first four institutions, ToMMo, National Center for Geriatrics and Gerontology, National Center of Neurology and Psychiatry, and the Faculty of Medicine of Kyoto University were accredited in April 2024[34].

ISO accreditation is expected to enhance the credibility of biobanks by assuring the competence of biobank activities and the quality of biological samples and related data, and to promote utilization and external collaboration. On the other hand, obtaining accreditation requires many procedures and time, including pre-application preparation, submission of application documents, visiting review, document review, on-site review, and corrective actions, as well as periodic reviews to continue accreditation[35]. In addition to the expenses required for each of these reviews, it can also be a significant burden for a biobank, especially in terms of properly documenting a system for maintaining quality and carefully operating, recording, and verifying the quality in accordance with that system.

In this context, the "Research on the establishment and implementation of international standards for the quality and accuracy of tests related to biobanks and genomic medicine, and the establishment of a collaboration system between biobanks" (Principal Investigator: Toru Masui), a project of a "Program for Promoting Platform of Genomics based Drug Discovery" of the Japan Agency for Medical Research and Development (AMED), has developed the "Biobank Self-Assessment Sheet." This was developed to provide a framework for small to medium scale biobank activities that handle human specimens and information, while retaining some of the concepts of ISO 20387:2018. This self-assessment sheet, with less than 10% overlap with the ISO texts, is intended to "provide a map or benchmark that illustrates an overall picture of biobanks and biobanking activities for those in charge of the operation of biobanks, as well as the administrative staff and employees involved, so that biobanks can know their own activities and ensure their smooth operation."[36] In Japan, this self-assessment sheet is used as a quality assurance mechanism with a certain degree of objectivity or as a first step toward higher quality biospecimen management, and ISBER, discussed below, has also created the Biobank Assessment Tool as a relatively simple quality assurance tool.

Based on the above, it is considered useful for the biobank in Bhutan in the Initial and Growth phases to conduct such self-assessment tools for quality assurance, fostering understanding among those involved in the operation, and improving the operation. Although obtaining ISO 20387 accreditation is not a prerequisite for the operation of the biobank and the utilization of information, aiming for the accreditation could be considered in the long term in order to increase the credibility of the biobank from external organizations such as private companies and research institutions.

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[33] ISO, "ISO 20387:2018 Biotechnology - Biobanking - General requirements for biobanking." https ://www.iso.org/standard/67888.html

[34] ToMMo, "ToMMo received the new ISO accreditation for biobanks JIS Q 20387:2023 (ISO 20387:2018) firstly in Japan" (in Japanese). https://www.megabank.tohoku.ac.jp/news/57758

[35] Japan Accreditation Board, "Accreditation of Biobank: ISO 20387" (in Japanese). https://www.jab.or.jp/cms/files/items/services/File/biobank.pdf

[36] AMED Program for Promoting Platform of Genomics based Drug Discovery "Research on the establishment and implementation of international standards for the quality and accuracy of tests related to biobanks and genomic medicine, and the establishment of a collaboration system between biobanks (Principal Investigator: Toru Masui)," "Biobank Self-Assessment Sheet Ver. 4.00" (in Japanese). https://www.amed.go.jp /content/000069066.pdf

3-2-5. International collaboration opportunities

International Society for Biological and Environmental Repositories (ISBER) is the only global forum that addresses scientific, technical, legal, and ethical issues for biobanks and biorepositories. It provides a forum for experts from around the world to collaborate on issues in repository operations and promotes the sharing of knowledge and technology[37]. Specifically, its activities include the following:

Figure 3-8 ISBER's initiatives

Category	Name of activity	Overview
Education and Training	Biobanking 101	・ Access to videos of workshops held by ISBER in 2023 and 2024 (approx. 4 hours, fee required) ・ "Quality of Biobanking Activities" and "Introduction of Biobank Assessment Tool" in 2023, and "Essentials of Biobanking Course" and "Information Management in Biobanking Activities" in 2024
	Essentials of Biobanking Course	・ An online course on key elements of planning, establishing, maintaining, and utilizing a biobank (approximately 7-11 hours, fee required)
	ISBER Mentoring Program	・ An educational service that supports the professional development of biobanks; ISBER Mentoring Program matches mentors with mentees ・ Experienced mentors in the field of biobanking will be available to answer mentees' questions
	Webinar	・ Webinars on discussions and information in the biobanking field
Evaluation	Qualification in Repository Science (QBRS)	・ A collaborative credentialing program between ISBER and the American Society for Clinical Pathology (ASCP) for professional personnel in the field of biobanking. Upon meeting specific educational and experience requirements for the qualification, candidates will be eligible to complete an online examination ・ Subsidies are available for candidates from developing countries
	Biobank Assessment Tool	・ A tool developed to assist repositories in evaluating how well they follow ISBER's Best Practices and, on a higher level, also the ISO 20387 Standards. ・ It is a questionnaire that consists of nearly 300 questions, each question has "risk-balanced assessment score" attached to it. The questions cover general quality management for biobanking

[37] ISBER https://www.isber.org/

	Biorepository Proficiency Testing Program	・ An external quality assessment tool to verify the precision and accuracy of biospecimen testing methods, and the efficiency of processing methods ・ The 2024 program includes 22 testing and processing schemes
Presentation and dissemination of the latest technologies and findings	BIO Journal	・ Peer-reviewed journal on the field of biospecimen procurement, processing, preservation and banking, distribution, and use
	Annual and Regional Meetings	・ One annual meeting and one regional meeting each year
	Best Practices for Repositories	・ A global guide for managing and operating biobanks, introducing either evidence-based or consensus-based practices for collection, long-term storage, retrieval and distribution of specimens ・ Fifth edition to be published in 2024

(Source: Prepared by research team based on ISBER website)

3-2-6. Medical data governance (personal information protection, handling of medical information, etc.)

In establishing and operating a biobank, it is also important to develop basic medical data governance, including the protection of personal information of participants who provided specimens and the handling of medical information such as medical records and prescription information. In Bhutan, however, these are matters to be considered for the Digital Health Platform as a whole, including the medical bank, health bank, and household bank, and are therefore omitted from this section.

3-3. Customer segments and channels for delivering value

As summarized in “Figure2-1 Value creation process of a biobank in Bhutan” shown in “2-1. Purpose of establishing a biobank,” information accumulated in the biobank will be provided to medical institutions and private companies and research institutes (domestic and abroad) under a proper management after being integrated it with data from other banks. The main segments for which the information is expected to be provided are listed in the table below.

Figure 3-9 Potential customer segments for which the biobank is expected to provide information

Category	Customer segments (current assumptions and examples)
Medical institutions	JDWNRH (from the Initial phase)
	Regional Referral Hospitals (after Growth phase)
	District Hospital (after Full Operation phase)
Private-sector companies	Pharmaceuticals (e.g., research and development in areas such as gastrointestinal diseases, immunological diseases, and psychiatric diseases)
	Foods, supplements
	Beauty, Healthcare
	Agriculture, environment (e.g., research areas such as soil, water systems, animals and plants, microorganisms, etc.)
	Data analysis (e.g., big data analysis, AI applications)
Research institutions	KGUMSB
	National Biodiversity Centre (NBC)
	National Soil Services Centre (NSSC)
	Policy research departments in various ministries of the GoB
	Foreign academia (universities, public research institutions, etc.)

(Source: Prepared by the survey team)

The leadership function mentioned in "3-1. Leadership and governance" needs to formulate rules and procedures for information provision for each customer segment, while consulting with each of these information users. Regarding the provision of information to medical institutions, it is necessary to organize data items that contribute to improving the health and well-being of the people of Bhutan, as well as to discuss how to utilize the data for medical services and how to return the results to the participants. The MoH and its subsidiary, National Medical Services (NMS), should play a central role in this process. During the Initial and Growth phases, discussions with private companies and research institutions should be conducted mainly by the consortium member institutions, and rules should be formulated based on customer needs (information types, information access methods, etc.), laws and regulations, international trends, etc. In particular, for the provision of information to foreign companies and research institutions, rules and procedures need to be formulated from various perspectives, including the items indicated in the section "3-2. Codes, regulations, and guidelines," access methods outside Bhutan, frameworks for investment and financing, and international joint research.

After the biobank data is used by medical institutions and private companies and research institutions based on their needs and roles, the value will be returned to the people of Bhutan and the GoB. Medical institutions will return the results of general clinical laboratory testing and genome analyses, and provide advice on disease prevention and health promotion, mainly to the providers of biobank specimens. As well as the physician in charge of the participant, collaboration with clinical geneticists, genetic counselors, and other professionals, as described later, will also be

needed. These efforts will lead to personalized medicine based on individual data and will improve the quality of medical care provided in Bhutan.

If private companies and research institutions can stimulate research using specimens and data from the biobank, this will increase the need for human resources in these research areas, which in turn will provide attractive job opportunities for the society. This is a value that can be expected in a relatively short period of time, such as during the Initial and Growth phases. On the other hand, the development and implementation of new medical knowledge and new products and services based on the results of research must be undertaken from a medium- to long-term perspective, and it is necessary to closely monitor trends in research and development while simultaneously considering how to deliver value to the people and GoB (e.g., development of a certification system for products and services).

With regard to the utilization of biobank information to connect with EBPM by the GoB, this survey has not yet reached a specific consideration of organizational structure or process -- which institutions will conduct such studies, and how the findings from the studies will be reflected in policy making. It should be developed during the Initial and Growth phases, through repeated trial and error based on actual data, to formulate an effective process.

3-4. Operations

The following figure shows the process of operations of a biobank, from obtaining an informed consent to utilizing data. In order to achieve the purposes of the biobank, which are “improving the health and well-being of the people” and “promoting industry, including the creation of attractive employment opportunities”, all steps from obtaining an informed consent to data utilization are important and cannot be selected or discarded.

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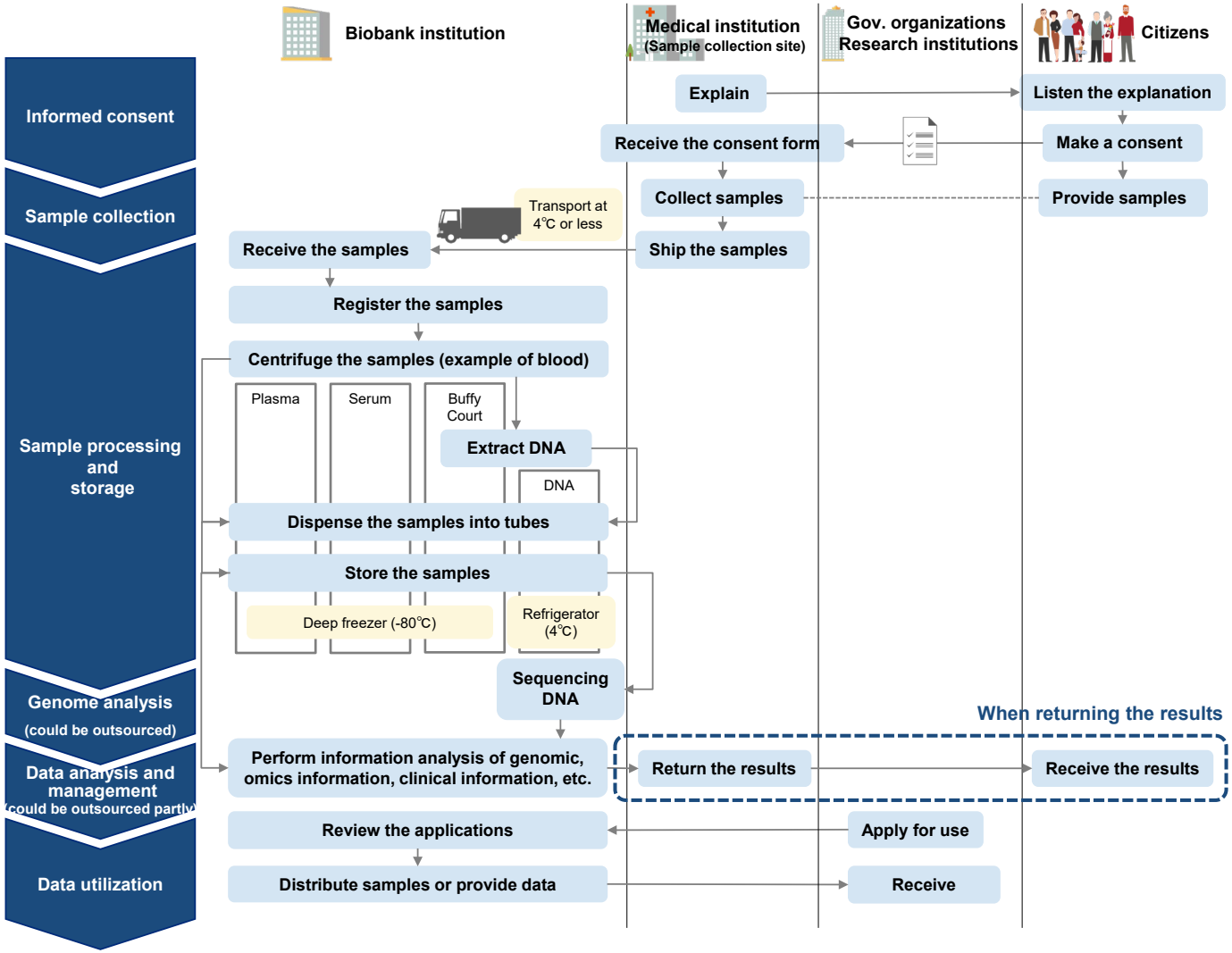
Figure 3-10 Operational flow of a biobank



(Source: Prepared by the survey team)

The key issues in the process of the flow are summarized below.

3-4-1. Recruitment of participants

In general, there are two protocols of recruiting participants: waiting style, in which applicants visit the specimen collection sites, and invitation style, in which a biobank approach specific participants. In the waiting style, participants may be biased toward certain groups, such as those with a high level of interest in health or those who live near the specimen collection site. On the other hand, the invitation style requires obtaining personal contact information and medical information that can be used as a reference in selecting participants when the requests of providing specimen are sent. In Bhutan, the invitation style could be possible because of the ongoing construction of the Digital Health Platform, as well as the Bhutan App[38], a widely used government app for participating in the National Day and other civic services. However, since this survey did not examine the specific process or conduct a feasibility assessment of the invitation style, as indicated in the medium- to long-term roadmap, it is assumed that the target population in the table below will be recruited at specific medical institutions based on the waiting style.

Figure 3-11 Target population of participants

Phase	Segmentation of target population	Sample collection sites
Preparatory phase	· Hypertension patients	· JDWNRH
Initial phase	· Patients with lifestyle-related and chronic diseases · Healthy individuals who visit the hospital on a regular basis (e.g., accompanying patients, participating in NCDs screening) · Pregnant women and their families	· JDWNRH (including the maternal and child health hospital[39])
Growth phase		· JDWNRH (including the maternal and child health hospital) · CRRH · ERRH
Full Operation phase		· JDWNRH (including the maternal and child health hospital) · CRRH · ERRH · District hospitals located near the above hospitals

(Source: Prepared by the survey team)

3-4-2. Return of the results to participants

The primary purpose of a biobank is to support medical research through accumulated specimens and data, the results of which are returned to the public as medium- to long-term advances in medicine. Returning results of clinical laboratory tests and analysis is generally not an essential part of biobank operations, but it is one important means by which the participants can realize the value of the biobank. In addition to returning the results, the biobank can also serve as a simple health checkup by providing advice on how to improve health, which is especially useful in Bhutan, where

[38] Bhutan App https://bhutanapp.bt/
[39] Gyaltsuen Jetsun Pema Wangchuck Mother and Child Hospital

health checkups are not common, and is an important activity that can contribute to improving the health and well-being of the people.

3-4-3. Quality control of biological samples

As already mentioned in "2-4. Medium- and long-term strategy and roadmap," in order to promote the utilization of biological samples and genomic information by private companies and research institutions and to realize industrial promotion, specimens must be collected, processed, and stored under the extremely high-quality control. It is no exaggeration to say that quality and the quality control system are directly related to gaining the trust of researchers.

In particular, the "time" and "temperature" from the collection of biological specimens at a medical institution to their storage in a biobank affect the quality of biological specimens and the results of analyses. The degree of influence of time and temperature on quality varies depending on the targeted research and analysis, and it is difficult to establish a general standard.[40] However, the time from specimen collection to storage in the biobank should be within half a day to one day. In order to establish procedures to meet this requirement, further study is needed to evaluate the following points.

- Capacity of processing specimen at medical institutions (number and skills of laboratory technicians, capacity of laboratory equipment, etc.)
- Capacity of processing specimen at the biobank (number and skills of laboratory technicians, capacity of laboratory equipment, etc.)
- Protocols for transporting specimens from medical institutions to the biobank (frequency of specimen collection, temperature control during transportation, vibration control measures, etc.)
- Facilities and equipment for cold chain for temporary storage at the medical institutions and transportation to the biobank

Regarding the capacity of processing specimen at medical institutions, the survey team visited the JDWNRH in Thimphu, as well as a nearby district hospital and a 10-bedded hospital, but none of these facilities seemed to have the capacity (facilities, equipment, and human resources) to process specimens for biobanking under high quality control in parallel with routine clinical laboratory operations. Since it is assumed that it would be difficult for these medical institutions to expand their facilities extensively or install additional equipment, it would be appropriate to strengthen the capacity of processing specimen at the biobank and increase the frequency of transportation to handle quality control of biospecimens during the Initial and Growth phases. In the Growth phase, the roadmap proposes that specimens will be collected at the Regional Referral Hospitals (RRHs) in Gelephu and Mongar, but this survey did not fully examine how specimens will be transported to the RCDC in Thimphu, or whether intermediate storage facilities similar to those at the RCDC will be newly established in each region, which is a point to be examined further.

Again, even if a large-scale biobank of several hundred thousand biospecimens is established, if the quality of each biospecimen is low or not homogeneous, it will be of no use at all. We emphasize once again that the quality control of biospecimens is the foundation of biobank operations.

[40] For example, when performing proteome analysis, the time from specimen collection to storage greatly affects the analysis results. On the other hand, DNA is a stable substance, so if the DNA extraction is performed at a medical institution, the time and temperature until storage do not become a much concern.

3-4-4. Possibility of automating and outsourcing each process

In the operational flow of a biobank, the number of equipment and personnel to be deployed will vary depending on "whether to automate" and "whether to outsource," which are important factors that needs to be considered.

With regard to "automation," in particular, if specimen processing and warehouse management is conducted entirely manually by laboratory technicians, quality control risks will increase (tend to make human errors such as specimen mix-ups), and automation such as automatic sample dispenser or pipetting machine and automatic warehouse system should be actively considered. During the Initial phase, it is possible to conduct the entire process fully manually to train personnel, but once it becomes necessary to handle more than 10,000 specimens, introduction of equipment to automate the various processes would be essential. The table below summarizes the advantages and disadvantages of automation of the processes versus manual management.

Figure 3-12 Advantages and disadvantages of automating specimen storage and warehousing versus manual management

	Advantages	Disadvantages
Automation	· Stable and minimal temperature fluctuations inside the storage · Minimize the temperature rise of the samples because picking can be done one by one · Efficient warehouse operations · Minimize human errors · Work logs can be recorded and tracked · Utilize the storage space at maximum · Ensured and improved safety of the operators · Redundancy can be ensured	· High initial investment and running costs · Takes time to start operations · May be less agile, such as sudden system changes · Restrictions on available storage tubes
Manual management	· Low initial investment and running costs · It does not take long time to start operations · Flexibility and agility to respond to sudden changes · Wide choice of storage tubes available	· Time-consuming registration, search, and retrieval of specimens · Uneven temperature in the storage occurs. Temperature rise of the samples in the same rack is unavoidable when picking · Risk of human errors · No work logs are kept

(Source: Prepared by the survey team based on the article by Thermo Fisher Scientific[41])

The necessity of "outsourcing" should be considered in the processes of (1) specimen processing and overall laboratory operations, (2) microbiome analysis, and (3) whole genome analysis. With regard to (1), it is necessary to confirm in detail whether it is possible to process and manage the

[41] Reference: Thermo Fisher Scientific, How to manage samples in biobanks - advantages and disadvantages of automated versus manual management, https://www.thermofisher.com/blog/learning-at-the- bench/biobank-freeze-preservation-lpd-24027/

tens of thousands of additional biobank specimens that are generated annually by solely expanding the clinical testing systems currently in place on a routine basis. As mentioned above, as far as the cases of clinical laboratories of JDWNRH and neighboring district hospitals, there are limitations in terms of facilities, equipment, and human resources in expanding the clinical laboratories in existing hospitals. In order to handle biobank specimens accurately and efficiently, it is necessary to consider one of the following measures: (a) establish a procedure and system to transport specimens to the biobank promptly after specimen collection, (b) establish a separate laboratory specializing in clinical testing attached to the hospital, or (c) attract a clinical testing company and outsource the work to them. As for (2), two options, either strengthen the functions of the NBC and RCDC, or outsource to a specialized analyzing company, are possible. In the latter case, if the samples are transported outside of Bhutan, it will be necessary to follow the ABS regulations as stipulated in the Nagoya Protocol. As for (3), it is the item that has the greatest impact on costs and human resource allocation. The table below summarizes the advantages and disadvantages of in-house and outsourced whole genome analysis. The initial cost of a sequencer for whole genome analysis ranges from 100 to several hundred million yen, the annual maintenance cost is tens of millions of yen, and the analysis cost ranges from several tens of thousands to several hundred thousand yen per sample (depending on the number of samples processed at a time and analysis equipment). If whole genome analysis is outsourced, the initial cost can be reduced, but the outsourcing cost increases as a running cost. Continued verification and discussions are needed on whether to perform in-house or outsource for each process in the biobank.

Figure 3-13 Advantages and disadvantages of in-house vs. outsourcing whole genome analysis

	Advantages	Disadvantages
In-house performance	・ Lower costs in case of analysis above a certain scale[42] ・ Thorough information management	・ Need the costs of purchasing and maintenance of the analysis equipment, and purchasing reagents ・ Data quality depends on the skill of the laboratory technicians
Outsourcing	・ Reduce the costs of purchasing analysis equipment (initial cost) and reagents (running cost) ・ Stable data quality with a specialized vendor	・ Outsourcing can be more expensive especially for large-scale analysis of large numbers of specimens than in-house performance ・ Requires additional resources for information management

(Source: Prepared by the survey team)

Considering the premise that the goal is to establish a population-based biobank of several hundred thousand participants, the conclusion of this survey is that whole genome analysis should be performed in-house as much as possible, and that the portion that cannot be analyzed by the introducing whole genome sequencer alone should be outsourced as appropriate. However, when partially outsourcing, measures are needed to avoid situations where the results from different protocols interfere with overall analysis. Based on these above points, advantages and disadvantages, and the necessary costs, appropriate modification should be made if necessary, after more detailed discussions within the GoB.

[42] If more than about 150 specimens per day (several thousand per month) can be analyzed in batches, the cost per specimen can be reduced to about 50,000 to 60,000 yen, providing a greater cost benefit than outsourcing. (Source: Suggestions from ToMMo's actual operation)

3-5. Resources (human resources)

The following table summarizes the human resources needed and their roles in each operational process of the biobank.

Figure 3-14 Personnel and their roles necessary for biobank operations (To-be)

Process	Assumed location	Personnel	Roles and details
1. Informed consent	Medical institution	Genome Medical Research Coordinator (GMRC)	In research using human genomes, communicate with sample providers and explain the research, confirm their consent, and process withdrawals of consent
2. Sample collection	Medical institution	Nurse	Collect specimens (blood, urine, stool, etc.)
		Clinical laboratory technician	Properly process and test the collected specimens
		Administrative assistant	Provide (assistance of) recording and clerical work to ensure traceability of the specimens
3. Specimen processing and storage (WET)	Biobank institution	Laboratory technician	Process the specimens for storage and analysis in the biobank and manage incoming and outgoing specimens
4. Genome analysis	Biobank institution	Laboratory technician	Perform genome analysis
5. Data analysis and management (DRY)	Biobank institution	Bioinformatician	Analyze information such as genomic, omics, and clinical information as a researcher with knowledge in both life science and information science (statistics and computer science)
		Healthcare information technologist	Develop, maintain and operate biobank information systems
6. Management and operation of the facility and system	Biobank institution	Facility manager	Maintain, manage, and utilize biobank facilities to improve the operating environment of the biobank
7. Return of the results	Medical institution	Clinical geneticist	Return genome information to the participants. In addition, provide medical care based on genome information (genetic medicine) in collaboration with specialists in various medical departments

		Genetic counselor	Provide patients and families in need of genetic medicine with appropriate information and support systems to psychologically and socially support autonomous decision-making by the parties involved
		Nutritionist	Return screening results and provide nutritional guidance and other advice (when implementing newborn mass screening).
8. Data utilization	Research institutions, government agencies	Researcher	The biobank specimens and data will be used to conduct research in Bhutan and collaborative research with researchers inside and outside Bhutan. (Mainly researchers in the fields of microbiome, biodiversity, pharmacology, agriculture, environmental studies, informatics, etc.)
		Research coordinator	Support researchers by communicating and coordinating with external researchers and research institutions

(Source: Prepared by the survey team)

The as-is status of the above human resources in Bhutan is as follows. Overall, there are not enough human resources to operate a biobank in Bhutan currently, and a plan needs to be developed to train and deploy new personnel.

Figure 3-15 Current human resources needed for biobank operations (As-is)

Process	Assumed location	Personnel	Status and issues
1. Informed consent	Medical institution	Genome Medical Research Coordinator (GMRC)	No such personnel are available. It is necessary to plan the development and assignment of such personnel.
2. Sample collection	Medical institution	Nurse	There is a serious outflow of nurses out of the country, and there is a significant shortage of personnel. It is necessary to reconsider the development plan, including the roles of the personnel and the incentive design.
		Clinical laboratory technician	The outflow of technicians out of the country and thus the issue of personnel shortages has become apparent. It is necessary to reconsider the development plan, including the roles of the personnel and the incentive design.

		Administrative assistant	There are administrative staffs in charge of outpatient reception, but no personnel to manage specimen information. The development and assignment of such personnel should be planned.
3. Specimen processing and storage (WET)	Biobank institution	Laboratory technician	There are dedicated personnel to handle infectious disease specimens from other Dzongkhags. The number of such personnel should be increased.
4. Genome analysis	biobank institution	Laboratory technician	Although there are personnel who perform genome analysis of pathogens, they do not perform genome analysis of human specimens. It is necessary to develop and assign personnel skilled in handling human genome analysis.
5. Data analysis and management (DRY)	Biobank institution	Bioinformatician	Although there are personnel who are proficient in pathogen bioinformatics, they do not handle the human genome. It is necessary to develop and assign personnel who are proficient in the analysis of human genomes.
		Healthcare information Technologist	No such personnel are available. It is necessary to plan the development and assignment of such personnel.
6. Management and operation of the facility and system	biobanking institution	Facility manager	New assignment or training for existing personnel is needed to manage the biobank facility.
7. Return of the results	medical institution	Clinical geneticist	No such personnel are available. It is necessary to plan the development and assignment of such personnel.
		Genetic counselor	No such personnel are available. It is necessary to plan the development and assignment of such personnel.
		Nutritionist	Nutritionist may accompany the patient as needed based on the physician's treatment plan, but this is not provided as a special service. If newborn mass screening is to be implemented, their development and assignment should be planned.
8. Data utilization	Research institutions, government agencies	Researcher	There are currently two candidates, but is a need to develop researchers in the fields of epidemiology, health economics, and biostatistics.
		Research coordinator	One research officer and demographer, one research assistant.

(Source: Prepared by the survey team)

As previously mentioned in "3-1. Governance and leadership," the leadership function that oversees the biobank and the Digital Health Platform as a whole will include "management personnel responsible for strategic planning and business planning," "marketing personnel responsible for market analysis in the life science industry," "personnel responsible for communication, coordination, and customer management for domestic and international data users such as companies and research institutions," "personnel responsible for public relations strategies such as dissemination of information to enhance the international presence of the biobank in Bhutan," and "personnel responsible for the sustainable operation of the biobank," in addition to the personnel listed in the table above. This issue should not be considered for the biobank alone, but needs to be implemented based on the consideration of data utilization policy and data management/governance for the entire Digital Health Platform. For example, regarding data analysis, bioinformaticians and healthcare information technologists need to be assigned at the biobank institution as mentioned above, but what kind of system should be implemented to conduct data analysis including the medical bank, the health bank, and the household bank in addition to the biobank? This question is expected to be discussed within the current digital health technical cooperation project and the GoB.

3-6. Resources (facilities, equipment, materials, etc.)

3-6-1. Facilities

The biobank is considered to be established in RCDC, which has ample space, and it would be possible to set a new section dedicated to the biobank. Although minimal improvements such as power and cooling water systems for equipment, temperature and humidity control systems, and security control systems for entry and exit, it would not be necessary to construct or reconstruct a large-scale building. However, the facility may need to be reinforced in order to bring install heavy equipment such as automatic warehouse system, and this will need to be confirmed.

Figure 3-16 Example of automatic warehouse system

(Source: Photo taken by the survey team at ToMMo)

The medical institutions that will collect specimens will be limited to JDWNRH during the Initial phase, but will include RRHs in the central and eastern regions during the Growth phase, and will include district hospitals near JDWNRH and the RRHs during the Full Operation phase. Whether or not each medical institution will be able to secure space for collection, processing, and temporary storage of biobank specimens, in other words, whether to renovate the facility, will need to be confirmed and discussed. In addition, as previously mentioned, from the perspective of temperature control and time required until storing specimens in the biobank, it will also be necessary to consider whether to have an intermediate storage facility for transporting specimens from each medical institution to the RCDC.

3-6-2. Equipment

In order to establish a biobank in Bhutan and implement the plan described in the medium- and long-term roadmap, it will be necessary to purchase and install new equipment listed in the table below. The quantity of equipment to be installed has been examined at each phase based on the roadmap, and detailed in Annex (undisclosed).

Figure 3-17 List of new equipment needed for biobank operations

Location	Equipment	Details
Medical institution	Refrigerator (4℃)	For temporary storage until transporting to the biobank institution. To avoid specimen mix-ups, specimens should be managed separately from regular clinical specimens.
	Deep freezer (-80℃)	For temporary storage of serum, plasma, stool, and urine specimens, when temporary storage time exceeds a half day due to the frequency of specimen transportation, etc.
	Centrifuge	For processing specimen in the hospital (availability of currently used equipment needs to be confirmed)
	Biohazard safety cabinet	Cabinet for biohazard prevention during processing specimen
	Labelling system	For generating labels for specimen management
Biobank institution (RCDC)	Refrigerator (4℃)	For storage of DNA samples. Deep freezer can be used
	Deep freezer (-80℃)	For storage of serum, plasma, stool, and urine samples
	Automatic warehouse system (-80℃)	Deep freezer with automatic entry and exit of specimen Assumed to be in operation from the Growth phase
	Centrifuge	For processing specimen
	Automatic sample dispenser (pipetting machine)	Automates the dispensing of large volumes of specimens

	Biohazard safety cabinet	Cabinet for biohazard control during processing specimen
	Biospecimen information management system and server	System for recording specimen information (ID, time of entry/exit, correspondent personnel, etc.), similar to Laboratory Information Management System (LIMS)
	Labeling system	For generating labels for specimen management. Coded tubes are used for final storage, but necessary to ensure traceability at the stages of processing specimen
	Temperature and humidity control system	Systems for measuring and monitoring temperature and humidity in specimen storage areas
	Uninterruptible power supply (UPS)	Equipment that provides a stable power supply for a certain period of time in the event of a power failure
	Next generation sequencer	Equipment for whole genome analysis. For genome analysis of microorganisms such as human genome and intestinal microflora
Data Center (Needs to be reviewed*)	Supercomputer	Computational infrastructure required for various omics analyses including large-scale genome analysis
	Data server	Data server for storing genome information.

*The design should be based on the data governance and architecture of the four banks, not the biobank alone.
(Source: Prepared by the survey team)

The data center for computational infrastructure and data storage required to perform various omics analyses including large-scale genome analysis[43] is expected to be located at the Government Data Center, but it is necessary to integrate, store, manage, and analyze not only genomic and microbiome information from the biobank, but also data from the medical bank, the health bank, and the household bank. This needs to be considered in the current digital health technical cooperation project.

3-6-3. Materials and supplies

Tubes for specimen storage, reagents for testing, labels for specimen management, and reagents for genome analysis are expected to be needed.

[43] A method that comprehensively examines the various molecules that make up a living body. The name of the analysis differs depending on the part of the cell: genome analysis for DNA, transcriptome analysis for mRNA transcripts, proteome analysis for mRNA translated proteins, and metabolome analysis for metabolites degraded from proteins. To perform these analyses, advanced analytical equipment, electronic computer systems and databases, an infrastructure for handling large amounts of information, are required.

3-7. Costs

Based on the medium- to long-term roadmap, the required amount of equipment indicated in "3-6. Resources (facilities, equipment, materials, etc.)" in the previous section was calculated, and the expected cost was estimated for each year. See the Annex (undisclosed) for details tentative calculation. It should be noted that at this stage these are rough estimates based on a number of assumptions. The table below summarizes those assumptions and, in particular, the factors that could have a significant impact on the estimation.

Figure 3-18 Key assumptions and impacts on cost estimation

Element	Assumption	Major impacts
Number of specimen providers	・ Initial phase: 1,000~6,500 persons/year ・ Growth phase: 20,000-30,000 persons/year ・ Full Operation phase: 30,000-70,000 persons/year	Impact on all including equipment-related costs and implementation systems
Types of specimen	・ Blood (serum, plasma, for DNA extraction), stool	
Number of tubes per specimen type[44]	・ Initial phase: 3 tubes ・ Growth phase: 4 tubes ・ Full Operation phase: 8 tubes	
Percentage of specimens transferred (vs. total number of specimens in storage)	・ Initial and Growth phase: 10% ・ Full Operation phase (1st half): 20% ・ Full Operation phase (2nd half): 30%	
Overall implementation system of laboratory testing	・ Expanding the laboratory capabilities of existing medical institutions instead of outsourcing to testing companies.	If outsourcing, initial and running costs must be carefully examined
Number of specimens that can be stored per refrigerator and deep freezer	・ 25,000~40,000 specimens (depending on the type of specimen)	Impact on installation and maintenance costs of such equipment
Number of automatic warehouse systems, unit price, and number of specimens that can be stored per unit	・ Install one unit of the system capable of storing 1 million specimens (unit price: 250 million yen[45]) in the 3rd year and one unit in the 6th year ・ Install one unit of the system capable of storing 2 million specimens (unit price: 400 million yen) the 9th year	Impact on the installation and maintenance costs of such equipment and facility renovation costs

[44] For each stored specimen, divide and store specimens by purpose and use, such as for utilization (external and R&D use), for utilization (domestic and policy research use), and for permanent storage.
[45] Estimation including construction and related infrastructure costs.

Unit cost of whole genome sequencers, number of sequencers in operation, and number of samples that can be analyzed per unit	· Unit price: 100 million yen/unit · Initial phase: 0 units (done in Japan) · Growth phase: 5 units · Full Operation phase: 7~14 units · Number of specimens/unit/year that can be analyzed: 2,000	Impact on the introduction and maintenance costs of such equipment, related material costs, and the implementation structure (human resource development policy)
Whole genome analysis system	· In-house analysis with the installed sequencers · Outsourcing what cannot be analyzed in-house	
Percentage of whole genome analysis performed (vs. number of people participated)	· Initial phase: 20% · Growth phase and Full Operation phase: 50%	
Implementation structure of Microbiome-related analysis	· All outsourced to external vendors · Unit price: 20,000 yen per specimen (assuming bulk order of 100 or more specimens)	Impact on the introduction and maintenance costs of related analysis equipment, related material costs, and implementation structure (human resource development policy)
Capacity and unit cost of supercomputer and data server for analysis	· Analysis for 1,000 persons/unit · 100 million yen per unit	Impact on initial and maintenance costs

(Source: Prepared by the survey team)

Based on the above assumptions, it is estimated that the capital investment of 240-2,000 million yen per biennium after the Initial phase, annual running costs of 70-200 million yen per year during the Initial phase, 1,400-1,600 million yen per year during the Growth phase, and more than 1,800 million yen per year during the Full Operation phase. In the final year of the roadmap, approximately 4,300 million yen/year will be required. Since the estimation based on the assumptions of the medium- and long-term roadmap requires a huge budget, it will be necessary to examine the costs very closely, focusing on factors that have a large impact on the estimation, and to consider cost reduction measures while revising the above assumptions. In particular, the factor related to the implementation structure for whole genome analysis (in-house or outsourced) has a significant impact of several hundred million yen, and the factor related to the installation of supercomputers and data servers has a great impact of several hundred million yen to several billion yen. The need to consider whether to introduce each equipment and system, the management structure and policies, and the system design should continue to be examined through activities within the consortium during the Initial and Growth phases, while keeping in mind that these are variable factors that significantly affect the initial and running costs of the biobank as a whole.

3-8. Revenue

How and what kind of income can be obtained from the samples and information accumulated in a biobank requires careful consideration from various aspects. First, biobanks in each country operated by public institutions basically do not receive income directly from processing, storage, and analysis of samples and information, but rather from user fees and commissions for individual use. On the other hand, stable income cannot be expected from a method in which individual fees are charged at each use. Therefore, representative biobanks in many countries have formed consortium that collect membership fees on an annual basis, and have explored and partially implemented a method of charging for the framework of acquiring new specimens and information itself. In the biobank in Bhutan, it is necessary to consider securing income through a consortium style while charging a certain amount of fees for individual use. In the operation of the biobank at ToMMo, a consortium is being formed while charging a limited amount for individual use.

Figure 3-19 Example of fees for transferring samples and information of ToMMo (Reference)

In case of receiving 100 samples (DNA, serum), clinical and genomic information in the main application (custom dataset) after information search in the prior application

User registration

Free

Prior application

(Unit: Yen)

Item	For custom data sets
Basic charge	30,000
Fees for information search and consultation (4h)	40,000
Total (including tax)	**70,000**

Main application

Item	DNA (For 100 participants)	serum (For 100 participants)	Genomic Information* (For 100 participants)
Basic charge	40,000		
Information extraction fee	60,000		
Information preparation fee	10,000		30,000
Transfer fee	200,000	300,000	-
Total (including tax)	**310,000**	**410,000**	**130,000**

*: For genome information, a case of "Whole Genome Analysis Information 15K
(Note) In addition to the above, other expenses are required such as shipping costs and return postage for the specialized box.

(Source: Prepared by the survey team based on publicly available information from ToMMo)

The survey did not reach a certain conclusion regarding the charging system and individual pricing for a biobank in Bhutan. It is necessary to continue to be considered with the GoB and partners (see next section) through specific activities in the future, as well as by examining the needs for the use of samples and information.[46]

In the early stages of the biobank, Initial and Growth phases, the goal should not be to generate revenue (pursue economic value), but rather to accumulate academic achievements by presenting the results of research in journals and academic meetings based on the information of thousands to tens of thousands of people, and to aim for the recognition of efforts by the biobank in Bhutan in the global academic community.

3-9. Partner

Through the interviews with Japanese companies and research institutions and the invitation program in Japan, this survey confirmed that there are institutions that support the biobank project in Bhutan and can be expected to collaborate with it in the future. In particular, during the Initial and Growth phases, a consortium should be formed with such institutions to design an operational system that meets the needs of the institutions, and to try to optimize the implementation structure and infrastructure during the Full Operation phase by quickly implementing the cycle from specimen collection to utilization (preferably aiming to establish a track record by publishing research results). In addition, this survey would like to emphasize again the importance of strong leadership as described in "3-1. Governance and leadership" for effective collaboration with partner institutions to develop a truly valuable biobank.

In the areas of personalized medicine, preventive medicine, and utilization of healthcare data, collaboration with UN agencies and international organizations working in Bhutan is also expected. While continuously sharing the progress of the biobank project with related organizations, it is necessary to continuously consider joint implementation of mutually related projects and human resource development.

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[46] Therefore, the cash flow statement and net present value (NPV), which were expected at the beginning of the study, are not to be addressed, as it does not have any significance in calculating them at this time.

Chapter 4. Proposed Cooperation Program by JICA [Recommendation]

4-1. Overall picture

Based on the resources (human resources, facilities, equipment, materials, etc.) and cost analysis described in Chapter 3, it is considered necessary to implement financial and technical cooperation in a well-coordinated manner in order to achieve sustainable operation of a biobank in Bhutan and to generate the expected impacts. In each phase of the roadmap proposed in Chapter 2, goals should be defined in terms of infrastructure and capability, and cooperation projects should be designed accordingly.

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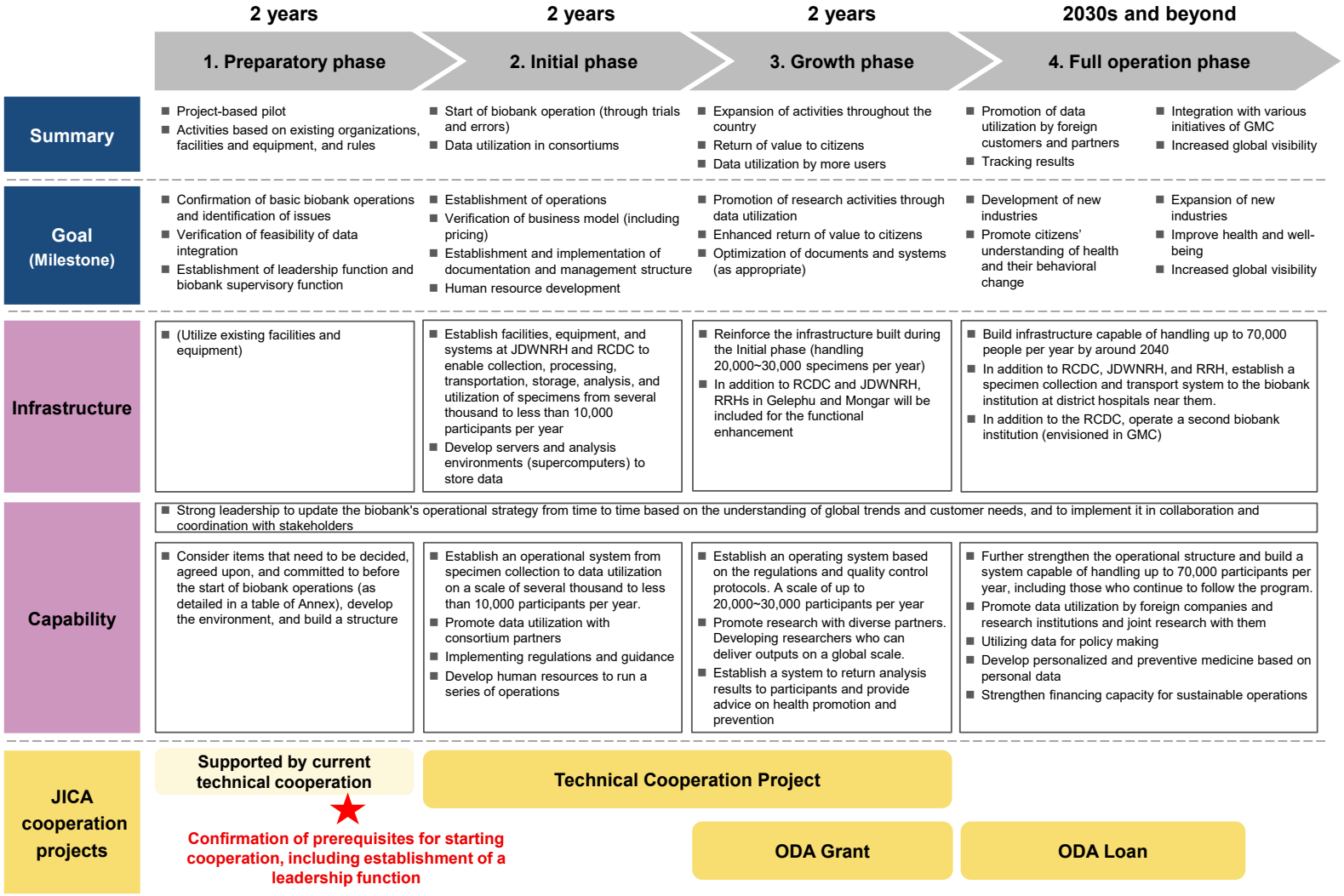
Figure 4-1 Targets for strengthening infrastructure and capabilities in each phase of the medium- to long-term roadmap and JICA cooperation projects



(Source: Prepared by the survey team)

4-2. Conditions to start cooperation by JICA and matters to be addressed by the Government of Bhutan

In order to maximize the effects of JICA cooperation projects, the GoB needs to discuss in detail, agree, and express a commitment regarding a concrete plan for the design and operation of the biobank, before the start of the cooperation projects. Specifically, the cooperation projects should be initiated on the condition that the GoB formulate a plan for the items listed in the table below. In particular, the organization of the leadership function and the biobank supervisory function as a permanent organization is a prerequisite for the effective operation and achieving the purposes of the biobank and the Digital Health Platform as a whole.

Figure 4-2 Items that need to be determined, agreed upon, and committed to by Bhutan before the start of the biobank operations (reiterated)

Item	Relevant sections of this report	Details
Governance and leadership	3-1. Governance and leadership	· Implement a leadership function and a biobank supervisory function (establishment as a permanent organization) · Clarify the roles and scope of the leadership and biobank supervisory functions (authority of budget, personnel, business implementation, etc.)
Vision/Strategy	2-4. Medium- and long-term strategy and roadmap	· Scrutinize, agree, and decide the goals of the biobank and the path to achieve them · Refine the value proposition hypothesis (including consideration of whether or not newborn mass screening should be performed) · Develop roadmap for the next 10-15 years, with specific milestones for each phase (including Growth and Full Operation phases)
Regulation	3-2. Codes, regulations, and guidelines	· Establish laws, regulations, and guidelines necessary to begin the Initial phase (compliance with ethical principles, research use of human genetic resources, access to genetic resources and the fair and equitable sharing of benefits arising from their utilization, international standards compliance and self-checking systems, framework for international collaboration, medical data governance)

Operation	3-4. Operations	・ Establish procedures for implementation of activities during the Initial phase (definition of participants, methods for recruit, how to obtain an informed consent, how to collect samples, transport, process, and store, methods for analysis, how to return the results, etc.) ・ Identify issues and specific actions for quality control of biological samples ・ Scrutinize, agree, and decide implementation system of clinical laboratory testing (including whether or not to operate in-house or outsource it) ・ Scrutinize, agree, and decide whether or not to conduct whole genome analysis and the implementation system (including whether or not to operate in-house or outsource it) ・ Scrutinize, agree, and decide the data analysis system for the entire Digital Health Platform
Human resource	3-5. Resources (human resources)	・ Scrutinize, agree, and decide staffing and human resource development plan ・ Coordinate with related ministries and specialized agencies
Investment and maintenance	3-6. Resources (facilities, equipment, materials, etc.) 3-7. Costs	・ Scrutinize, agree, and decide cost and investment plan for facilities and equipment (based on the equipment to be installed, also consider the necessity of facility renovations and transportation infrastructure) ・ Establish a data storage, management, and analysis system for the entire Digital Health Platform, including plans for expansion of supercomputers and data center ・ Commit expenditures for maintenance costs for facility and equipment ・ Develop financing plan (initiate negotiations with the funding sources)

(Source: Prepared by the survey team)

4-3. Technical cooperation project

It is proposed to implement technical cooperation projects during the four years of the Initial and Growth phases for the purpose of fostering human resources necessary for biobank operations and establishing an operational structure, as summarized in section "3-5. Resources (human resources)." The human resources to be developed are broadly classified into those of medical institutions, those of biobank institution, and those of research institutions (researchers). The human resource development will be based on on-the-job training (OJT) under the guidance of experts, and will be carried out through the PDCA cycle in the actual biobank operations to acquire and establish the required competencies. The following table outlines the expected overview of the technical cooperation project.

Figure 4-3 Outline of the technical cooperation project (draft)

Item	Assumed contents
Project title	Project for sustainable biobank operation and promotion of data utilization
Project site	Thimphu (mainly JDWNRH, RCDC, and KGUMSB, but also in cooperation with NBC and other related organizations)
Period of cooperation	4 years (from the start of the Initial phase to the completion of the Growth phase)
Name of counterpart organization	Ministry of Health, GovTech Agency
Overall goal	Data collected and analyzed by the biobank will be used to foster new industries and promote the health and well-being of the people of Bhutan.
Project purpose	A series of processes for collection, processing, storage, data analysis (including whole genome analysis), and data utilization of biological samples will be implemented.
Output	● Medical institution (JDWNRH): (1) A quality control system will be established based on laws, regulations, guidelines, and ethical considerations for the collection and processing of biological samples. (2) Healthcare professionals can provide optimal information and advice on health promotion and disease prevention to each sample provider based on the analyzed data. ● Biobank institution (RCDC): (3) Establish a quality control system for specimens and data in accordance with international standards. (4) A system that is accessible to domestic and international users of specimens and data will be proposed and tested. ● Research institution (KGUMSB): (5) A consortium is formed with domestic and international companies and research institutions to conduct research using specimens and analyzed data collected in the biobank, and the results are submitted to an academic journal as a paper.

Activities	(1) Establishment of inspection and quality control systems for biospecimens at medical institutions ・ Activity 1-1: Develop Genome Medical Research Coordinators ・ Activity 1-2: Increase the number and capacity of nurses and clinical laboratory technicians ・ Activity 1-3: Develop written procedures for handling biobank specimens (2) Return of results and provision of advice to specimen providers at medical institutions ・ Activity 2-1: Develop clinical geneticists ・ Activity 2-2: Develop genetic counselors ・ Activity 2-3: Develop procedures for returning the results of clinical laboratory tests and analysis and providing advice (3) Establishment of a quality control system for specimens and data in biobank institution ・ Activity 3-1: Increase the number and strengthen the capacity of laboratory technicians ・ Activity 3-2: Develop and assign bioinformaticians and healthcare information technologists ・ Activity 3-3: Assign a facility manager ・ Activity 3-4: Develop a biobank self-assessment sheet and operating procedures ・ Activity 3-5: Perform whole genome analysis (4) Study of specimen and data access mechanisms in the biobank institution ・ Activity 4-1: Develop a framework and cost structure for transferring specimens and data use ・ Activity 4-2: Establish rules for transporting specimens abroad and accessing data from abroad (including ABS rules for genetic resources) (5) Conduct research using specimens and analyzed data collected in the biobank ・ Activity 5-1: Form a consortium with Japanese companies and research institutions ・ Activity 5-2: Consortium members and Bhutanese researchers conduct joint research ・ Activity 5-3: Submit research results as a paper to an academic journal

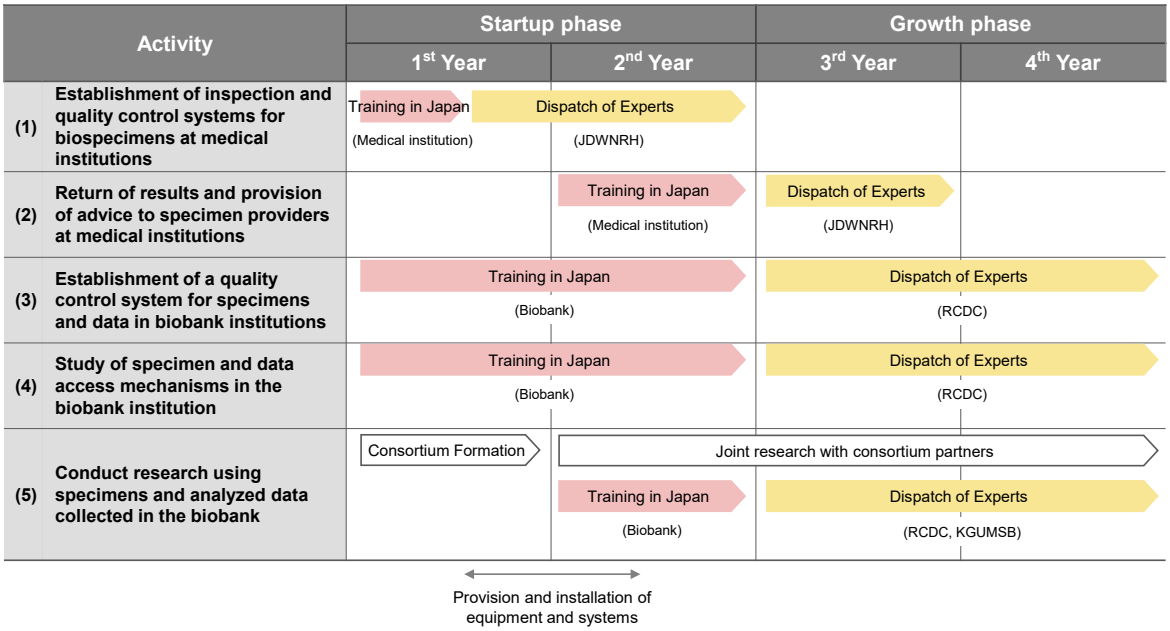
Inputs (Japan)	● Training in Japan[47]: On-the-job training at a Japanese biobank and on-the-job training at Japanese medical institutions (partner institutions of the biobank) ● Dispatch of experts: Experts familiar with strategic planning and operation of population-based biobank, experts in establishing clinical laboratory testing systems in medical institutions, clinical geneticists and genetic counselors, researchers in the life science field ● Provision of equipment and systems (refrigerators, centrifuges, biohazard safety cabinets, labeling system, etc. required for specimen collection and processing at JDWNRH) ● Formation of a consortium by private companies and research institutions, and provision of joint research opportunities within the consortium
Inputs (Bhutan)	● Formation and staffing of a counterpart (leadership and biobank supervisory functions) ● Equipment required for processing specimen and storage at RCDC during the Initial phase ● Materials required for processing specimen, testing, and analysis (e.g., reagents) ● Personnel costs for human resources involved in biobank operations

(Source: Prepared by the survey team)

Since it is assumed that the technical cooperation project will be implemented prior to the ODA grant project described later, the facilities, equipment, system database, and other infrastructure in Bhutan will not be sufficiently developed at the beginning of this project. Therefore, the first and second years of the project will focus on on-the-job training at a Japanese biobank and medical institutions. In addition, it would be good if analysis using actual specimens from Bhutanese citizens could be conducted during the training in Japan. If a data set of 1,000 to several thousand people can be established in Japan at this stage, it will be possible to immediately establish an analysis system and database in Bhutan by transferring the data set to Bhutan during the second half of the cooperation period. The refrigerator, centrifuge, biohazard safety cabinet, and labeling system, which will be used for specimen collection and initial processing, will be considered for provision within the technical cooperation project at JDWNRH if necessary (about 6 million yen). The equipment required by RCDC during the Initial phase will be approximately 38 million yen, which will be prepared either by utilizing existing equipment at RCDC or procured by the GoB (however, provision of such equipment will be considered if necessary). The following table shows the specific activities that are currently envisioned for each fiscal year.

[47] With regard to output (3) and (5), it is highly likely that it would be beneficial to incorporate long-term training aimed at obtaining degrees (masters and doctorates) in fields such as bioinformatics, biostatistics, and microbiology, or to plan such training separately, into this technical cooperation project, with the aim of improving capabilities in areas such as genome analysis, omics analysis, and intestinal flora analysis in Bhutan.

Figure 4-4 Summary of activities in the technical cooperation project by year (draft)



(Source: Prepared by the survey team)

In addition to training in Japan and dispatching experts to Bhutan, the project will form a consortium in collaboration with Japanese private companies and research institutions, in which the design and operation of the biobank will be considered based on data utilization needs and joint research with actual data. This is a unique and important component of the project.

The detailed design survey for the technical cooperation project needs to be further investigate and review mainly from the following perspectives:

- Reassessment of the roadmap feasibility (the items and costs of facilities and equipment will also be evaluated in parallel in the preparatory survey for the ODA grant and reflected in the planning of technical cooperation projects as necessary)
- Scrutiny of purpose, output, activities, and inputs
- Scrutiny of activities by year
- Calculation of the size of the technical cooperation project
- Confirmation of the status of human resources to be developed and discussion of training plans
- Assignment of invitees for training in Japan
- Whether specimens collected in Bhutan can be analyzed at a Japanese biobank (legal compliance and procedures for exporting specimens)
- Confirmation of the acceptance structure in Japan and prior consultation
- Regulatory compliance and procedures for transferring database established in Japan to Bhutan
- Prior consultations with potential consortium participants (private companies and research institutions)
- Consideration of the consortium framework
- Responses to other development agencies and international organizations

4-4. ODA Grant

The survey also proposes a two-year ODA grant project for the development of biobank facilities, equipment, and human resources for their maintenance and management, with the aim of providing facilities and equipment needed in the growth phase. The project will develop the infrastructure necessary for running a series of biobanking processes, from specimen collection and processing at medical institutions to processing specimen and storage at the biobank institution, whole genome analysis, and data management. A draft outline of the ODA grant based on the medium- to long-term roadmap is shown in the table below.

Figure 4-5 Outline of the ODA grant (draft)

Item	Assumed contents
Project title	Biobank Development Plan
Project site	・ Biobank institution: Royal Centre for Disease Control (RCDC) ・ Medical institutions: Jigme Dorji Wangchuk National Referral Hospital (JDWNRH), Central Regional Referral Hospital (CRRH), Eastern Regional Referral Hospital (ERRH) Regional Referral Hospital (ERRH) ・ Data Center: Government Data Center
Target Area	Thimphu (population approx. 120,000) and nationwide (population approx. 780,000)
Period of cooperation	FY2027 ~ FY2030 (4 years)
Name of counterpart organization	・ Biobank supervisory function (counterpart) to be established in the Preparatory phase ・ Leadership function to be established during the Preparation phase (in collaboration with the Digital Health Platform) ・ GovTech Agency (consideration of data governance) ・ Ministry of Health (development of laws, regulations, and guidance related to healthcare) ・ RCDC (biobank institution and project site) ・ JDWNRH, CRRH, ERRH (medical institutions, project sites, location of collection, processing and transportation of biological samples to the biobank, returning results of clinical laboratory testing and analysis)
Total project cost (estimate)	Approx. 2 billion yen
Project summary	By developing facilities and equipment for a biobank, which is part of the Digital Health Platform, the project aims to improve the environment in Bhutan for the accumulation of biological samples and genome information and their utilization, thereby contributing to the improvement of the health of the people and the development of medical and healthcare-related industry through the Digital Health Platform.

(Source: Prepared by the survey team)

Based on the assumptions of the medium- to long-term roadmap, the equipment and systems in the table below are assumed to be installed to deal with the number of participants and specimens in the second half of the growth phase (4th year).

Figure 4-6 Equipment to be introduced through the ODA grant and its volume (current assumptions)

Location	Equipment	Volume[48]	Details
Medical institutions (JDWNRH, CRRH, ERRH)	Refrigerator (4℃)	2 units	For temporary storage until transporting to the biobank institution. To avoid specimen mix-ups, specimens should be managed separately from regular clinical specimens
	Deep freezer (-80℃)	2 units	For temporary storage of serum, plasma, stool, and urine specimens. Assumed to install in CRRH and ERRH where temporary storage time exceeds a half day due to the frequency of specimen transportation, etc.
	Centrifuge	8 units	For processing specimen in the hospital (availability of currently used equipment needs to be confirmed)
	Biohazard safety cabinet	9 units	Cabinet for biohazard prevention during processing specimen
	Labelling system	2 units	For generating labels for specimen management
Biobank institution (RCDC)	Refrigerator (4℃)	7 units	For storage of DNA samples. Deep freezer can be used
	Deep freezer (-80℃)	1 unit	For storage of serum, plasma, stool, and urine samples
	Automatic warehouse system (-80℃)	1 unit	Deep freezer with automatic entry and exit of specimen Assumed to be in operation from the Growth phase
	Centrifuge	8 units	For processing specimen
	Automatic sample dispenser (pipetting machine)	1 unit	Automates the dispensing of large volumes of specimens
	Biohazard safety cabinet	2 units	Cabinet for biohazard control during processing specimen

[48] Excludes equipment required for the Initial phase prior to the start of ODA grant. As previously mentioned, the Initial phase assumes that equipment will be provided through the technical cooperation project or procured by the GoB.

	Biospecimen information management system and server	1 set	System for recording specimen information (ID, time of entry/exit, correspondent personnel, etc.), similar to Laboratory Information Management System (LIMS) Not eligible for grant if already installed during Initial phase
	Labeling system	1 unit	For generating labels for specimen management. Coded tubes are used for final storage, but necessary to ensure traceability at the stages of processing specimen
	Temperature and humidity control system	1 set	Systems for measuring and monitoring temperature and humidity in specimen storage areas Not eligible for grant if already installed during Initial phase
	Uninterruptible power supply (UPS)	1 unit	Equipment that provides a stable power supply for a certain period of time in the event of a power failure
	Next generation sequencer	5 units	Equipment for whole genome analysis For genome analysis of microorganisms such as human genome and intestinal microflora
Data Center	Supercomputer	1 set	Computational infrastructure required for various omics analyses including large-scale genome analysis
	Data server	1 set	Data server for storing genome information

(Source: Prepared by the survey team)

For an overview of facility renovations, see "3-6-1. Facilities." The cost of renovating these facilities and installing equipment was estimated at approximately 2 billion yen (see Annex for details (undisclosed)). At the same time, maintenance of the equipment and purchase of consumables such as tubes and reagents during the two-year cooperation period will require a total of approximately 3 billion yen, so the GoB will need to make a budget for operational expenses during the ODA grant. However, some medical equipment that is not manufactured in Japan or whose manufacturers are limited (e.g., automatic warehouse system, next-generation sequencers) will be procured from a third country. In addition, detailed design, bidding assistance, supervision of construction and procurement, and technical support for operation and maintenance of the facilities and equipment to establish a management system for the operation and maintenance of the facilities and equipment are assumed to be provided as soft components.

The ODA grant will aim to ensure that the equipment installed is properly utilized and that the basic operations of the biobank are carried out. The proposed quantitative effects are shown below.

Figure 4-7 Quantitative effects of the project (draft)

Indicator	Baseline value (Estimated value before the start of cooperation)	Target value (2 years after the end of cooperation)
Cumulative number of participants (total)	8,000	97,000
Number of specimens collected per year	74,000	1,000,000
Cumulative number of specimens stored	82,000	2,000,000
Number of whole genome analyses completed (of which, number performed in Bhutan)	1,200 (0)	16,500 (14,000)
Number of specimens for sale	9,000	500,000
Number of joint research agreements between KGUMSB or JDWNRH and foreign research institutions/companies utilizing specimens and data	10	50
Number of participants whom the results of clinical laboratory testing and genome analysis are returned (per year)	0	33,000

(Source: Prepared by the survey team)

As for qualitative effects, many of them are based on the combination with human resource development through the technical cooperation project, and it is difficult to set the effects of ODA grant alone, but the followings are considered appropriate in relation to the quantitative effects.

- Enhancement of public understanding of genome research
- Increasing public awareness of health promotion and preventive measures
- Promotion of genomic medicine
- Development of PDCA cycle for evidence-based healthcare policy making
- Networking with domestic and international research institutions

The preparatory survey for the ODA grant requires further investigation and consideration mainly from the following perspectives.

- Reassessment of the roadmap feasibility
- Whether facilities at JDWNRH and RCDC need to be reconstructed or renovated
- Close examination of equipment, volume of installations, and costs (including costs related to import/export, transportation, and installation)
- Consideration of procurement methods of the equipment (discussions with potential suppliers)
- Regarding the development of the data center, the system for handling, storing, and analyzing data from the other three banks
- Details of soft components and estimated labor costs for related personnel
- Examination and estimation of the items covered by the GoB
- Scrutiny of indicators to measure the effects of the project and confirm the methods of measurement
- Responses to other development agencies and international organizations

4-5. ODA loan

As described in "3-7. Costs," based on the medium- to long-term roadmap, the biobank will require a biennial capital investment of 240~2,000 million yen/year, annual running costs of 70~200 million yen/year for the Initial phase, 1,400~1,600 million yen/year for the Growth phase, and 1,800 million yen/year for the Full Operation phase. It is assumed that approximately 4,300 million yen/year would be required for the 14th and final year of the roadmap. For Bhutan, where the annual government budget is approximately 176.7 billion yen (FY2024-25)[49], the annual cost for the Full Operation period is a huge amount, equivalent to more than 1% (about 2% for the 14th year), and it is not easy to continuously cover this cost.

Once a detailed plan for the biobank business model has been developed and operational costs and revenues have been carefully examined, the possibility of cooperation through ODA loan could be explored for the funds needed for mid- to long-term biobank operations and data utilization. Specifically, one idea could be a results-based loan linked with the results of the biobank operation. Results indicators could include the number of participants, the number of specimens collected, the number of specimens transferred, the number of collaborative research projects conducted, and the number of results returned (if results are to be returned to participants).

Another option is a form of development policy loan for the improvement of healthcare or industrial promotion policies, with a focus on biobank project. In this case, the policy actions that would be the conditions for achievement include the introduction of health checkups combined with specimen collection, the introduction of newborn mass screening, and the dissemination of NCDs prevention in the case of healthcare policy, and the attraction of FDI and the development of domestic companies in the life science field in the case of industrial development policy. However, each of these policies consists of a large number of policy elements other than biobank, and the appropriateness of using the loan to operate the biobank must be thoroughly discussed.

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[49] Ministry of Finance of Bhutan, "National Budget Financial Year 2024-25." https://www.mof.gov.bt/wp-content/uploads/2024/06/Budget-Report-2024-25-English.pdf (converted based on OANDA rate as of December 16, 2024: 1 BTN = 1.81 JPY)

Chapter 5. Survey Results

5-1. Interviews

In order to examine potential customer segments for biobank data utilization and business scenarios for revenue generation, interviews were conducted with eight Japanese companies (in industries such as pharmaceuticals, clinical laboratory equipment, and food) (not disclosed) from June to October 2024. An outline of the interview and the companies interviewed are shown in the table below.

Figure 5-1 Outline of interviews

Interview format	Online interviews (1~1.5 hours per company)
Questions	**<Current research areas>** ・ Status of utilization of biobank samples and data (especially utilization of biobanks outside Japan) ・ Issues when using biobank samples and data **<Expectations and concerns about the Bhutan Biobank>** ・ Expectations for the Bhutan Biobank (What kind of biobank would you be willing to use samples/data?) ・ Concerns about the Bhutan Biobank (What is the bottlenecks in the utilization of the biobank?)

(Source: Prepared by the survey team)

The table below summarizes tips for the value proposition of the biobank in Bhutan and issues that need to be addressed, which were commonly pointed out during the interviews.

Figure 5-2 Summary of results from the interviews

Tips for value proposition	・ Accumulate specimens and information that contribute to research and development in areas such as microbiome and metagenomics ・ Integrate with information related to lifestyle (dietary information is particularly important in relation to the microbiome) ・ Integrate with GNH Survey data (e.g., correlation with stress and state of mind, correlation between value change and biological samples) ・ Tracking changes in various indicators along the process of economic development (changes as a group, which cannot be achieved by biobanks in developed countries) ・ Collect and accumulate data regularly over the life course (changes over time for individuals) ・ The design should allow for extraction, tracking, and stratified analysis of specific segments in line with research needs

Issues to be addressed	· Ensure quality control in accordance with international standards (specimen collection, processing, storage, and data management), especially it is difficult to control processing and storage of stool specimens · Create a mechanism to improve convenience for users (e.g., data access from abroad, taking specimens and data abroad, data analysis system) · It could be interesting as pure science, but it may not be attractive as a business (how to provide incentives for companies to conduct R&D in Bhutan, given the limited market size of the country)

(Source: Prepared by the survey team)

In particular, the research area of microbiome has been the focus of much attention recently, and is an area where various studies are actively being conducted, such as the relationship between the intestinal microbiota and immunity. The market size is expected to expand in the future, as it has been suggested to be related to numerous disease areas and health promotion.[50] In Bhutan, the NBC operates a biorepository of plants and animals for the purpose of biodiversity conservation, which has a high affinity with microbiological research. Also, information accumulated in the health bank can be used for research and development in the field of microbiology. In addition, if information on lifestyle habits (especially dietary information) accumulated in the health bank, genealogical information collected in the household bank, and GNH Survey data are integrated, its presence as a unique information source for microbiome research may be enhanced further.

On the other hand, one issue commonly pointed out by many companies is the establishment of a framework for quality control of biobank specimens and improvement of convenience. For companies and research institutions, the lack of such an environment will not only affect the success or failure of their research, but may also pose a reputational risk to their own companies, and therefore must be addressed if Bhutan is to promote the utilization of biobank specimens and data. In order to solve these issues, it is necessary not only to simply establish laws, regulations, guidelines, and procedure manuals, but also to develop human resources and systems that can properly process specimens and manage data.

[50] Market Size and Market Share Analysis of Human Microbiome - Growth Trends and Forecasts (2024-2029) (in Japanese). https://www.mordorintelligence.com/ja/industry-reports/human-microbiome-market

5-2. Field surveys

5-2-1. First field survey (June~July 2024)

The first field survey was conducted from June 28 (Fri.) to July 4 (Thu.) to confirm the status of infrastructure and human resources for biobank development. A summary of the field survey is shown in the table below.

Figure 5-3 Outline of the first field survey

Period	Friday, June 28 ~ Thursday, July 4, 2024
Objectives	・ Confirmation of the status of As-is for the establishment and operation of the biobank ・ Discussions and consideration on To-be picture of the Bhutan Biobank
Participants from the survey team	・ Yu Hasegawa, Mitsubishi UFJ Research and Consulting Co., Ltd. ・ Tomoko Kunimitsu, Mitsubishi UFJ Research and Consulting Co., Ltd. ・ Fuji Nagami, Tohoku University Tohoku Medical Megabank Organization
Survey schedule and places to visit	・ June 28 (Fri.): Preparation with local consultants, preliminary meeting with JICA Bhutan office ・ July 1 (Mon.): Discussion with Project Management Unit; discussion and facility tour with RCDC; discussion with Department of Clinical Service; discussion with DHI InnoTech ・ July 2 (Tue.): Discussion and facility tour with JDWNRH, discussion with MoICE, discussion with the president of KGUMSB ・ July 3 (Wed.): Discussion with MoFAET, facility tour of SuperFabLab, discussion and facility tour with the National Biodiversity Center, discussion with Dr. Yoriko Nishizawa of KGUMSB ・ July 4 (Thu.): Meeting with JICA Bhutan office

(Source: Prepared by the survey team)

The table below shows the results of the survey on confirming the status of As-is for the establishment and operation of biobanks.

Figure 5-4 Summary of the results of the first field survey (confirmation of As-is status)

Category	Item	Confirmed results
(1) Infrastructure	Electricity	○ RCDC has a backup power supply. Minimal impact from the frequency and times of power failure
	Transportation network	△ RCDC contracts with Bhutan Post. Need to consider whether specimens need to be transported to RCDC
	Maintenance	× Unrepaired freezers after the maintenance period (RCDC) ◎ Liquid nitrogen generator was properly maintained and continuously used for more than 10 years (NBC)
	Internet	○ No problem
	Others	△ JDWNRH has few places to store samples, and those that are 6 years old are discarded.
(2) Supply	Consumable goods	○ No problems in the procurement of general items. Special materials and equipment are procured by public procurement or negotiated contracts (RCDC)
	Large equipment	○ Sufficient space at RCDC to introduce additional equipment, but JDWNRH to be considered
	Donor assistance	— Most of the large equipment is donor-supplied
(3) Human Resources	Explanation and acquisition of consent	△ There seems to be no problem currently, but unknown for the informed consent in case of biobank research
	Sample collection	× Chronic human resource shortage at JDWNRH. Additional sample collection may be a burden
	Sample Processing	○ Appropriate specimen processing in JDWNRH and RCDC labs, but training and additional staff are needed for biobank operations
	Ethical review	○ Ethics Committee available
	Operational human resources	× Chronic human resource shortage, need to train bioinformaticians and other specialized personnel

(4) Target Population	Language	— English only is not sufficient and Dzongkha required. In addition, sometimes only oral explanation provided
	Consent record	△ No one says “No” for national research purposes (DCS Director)
	Physical examination	△ Some educated people have the concept and go to health checkups regularly, but the majority do not
	Others	— General disease understanding, idea of legal representative, trust in medical care, understanding of family tree information to be confirmed if needed
(5) Laws and regulations	Personal information	— Regulatory framework is being developed in the current digital health technical cooperation project. Genome information is required to be followed
	Obtaining of informed consent	— Same as above
	Economic benefits of research using human specimens	— Same as above
	Blood collection	— To be confirmed if needed
(6) Information	Linkage with disease Information	○ To be properly managed under ePIS
	ID	◎ Fingerprint authentication is expected to become the mainstream in the future due to the spread of 11-digit national IDs and Digital IDs
	Others	? Need to consider securing a supercomputer and data center to conduct whole genome analysis
(7) Diseases	Accuracy of medical practice and statistics	△ Currently complying ICD-10 and plans to comply ICD-11 in the near future, but training is required.
	Others	— NCDs patients in urban areas tend to have blood pressure monitor. Not common in rural areas
(8) Sanitation	Sanitary environment	— To be confirmed if necessary.

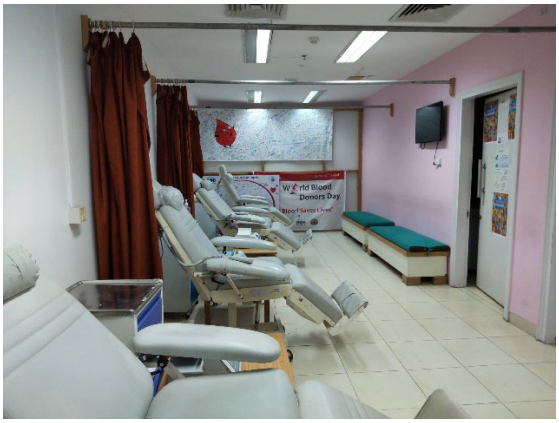
(9) Industry	Domestic healthcare industry	× There is no domestic biomedical-related industry, and it is essential to strengthen research capacity (e.g., by establishing research labs) starting from KGUMSB
(10) Medical institutions	Sample collection and storage	— Blood collection can be done at 10-bedded hospitals or higher medical institutions (DCS Director) — Provide home nursing care for cancer patients (JDWNRH Nursing Director) → Possibility of blood collection at Outreach Clinic

(Source: Prepared by the survey team)

Since the RCDC seemed to have sufficient physical space, if the biobank is to be established at the RCDC, it would be possible to set up the infrastructure by installing materials and equipment in the next phase of the cooperation project. On the other hand, JDWNRH has been repeatedly expanded and remodeled and does not have sufficient space, suggesting that securing space may be an issue if biobank specimens are to be collected, processed, and temporarily stored at the facility.

Figure 5-5 Photos at JDWNRH

JDWNRH building



Blood donation room (blood collection for clinical laboratory testing is conducted at a separate location)

A room in the laboratory unit

(Source: Photos taken by the survey team)

The biggest challenge is to secure and train human resources, as the JDWNRH faces a shortage of personnel necessary for operations associated with regular medical services, and there seems to be a very limited availability for handling additional operations such as collection and processing of specimens for biobanking, obtaining an informed consent, and recording. The RCDC also appears to be understaffed. Another issue is to establish an appropriate maintenance system for equipment and materials.

On the other hand, a “biorepository for plants and animals” (storage and utilization of plant and animal specimens at the NBC) had been operating in Bhutan for more than 15 years. It is confirmed that the institution had properly maintained its equipment and materials, and that it had a track record of joint research with foreign companies, in addition to research activities that contribute to its original purpose of conserving biodiversity in Bhutan. A collaborative system should be established to apply its experience and expertise to biobanking of human specimens.

Figure 5-6 Photos of the NBC

	
NBC building	Storage of animal and plant specimen (liquid nitrogen)
	
Liquid nitrogen generator	Storage animal and plant specimen (deep freezer)

(Source: Photos taken by the survey team)

In order to promote industry from a biobank, it is necessary to strengthen capacity in Bhutan to conduct research utilizing the biobank. As a first step to attract investment from foreign companies and create opportunities for joint research, it is considered important to disseminate research papers on a research utilizing the biobank by Bhutanese researchers and demonstrate their achievements. One idea would be to establish a research lab within KGUMSB and a curriculum to train specialized researchers. KGUMSB itself was aware of this as a challenge.

The table below shows the results of discussions with Bhutanese stakeholders regarding the To-be picture of the Bhutan Biobank, i.e., the value proposition and operations that are unique to Bhutan.

Figure 5-7 Summary of the results of the first field survey
(results of discussions and confirmed items related to To-be picture)

Basic policy for establishing and operating a biobank	・ It is difficult to operate a biobank in an economically autonomous manner as seen in other countries, and it is appropriate to maintain the motivation of those involved and gradually expand the scope of the biobank while realizing successful experiences. ・ The focus might be placed not on abroad but on domestic for the time being
Possibility of mid- to long-term industrial promotion	・ Leverage existing efforts in biodiversity conservation while creating values by integrating with other databank (in the microbiome area, utilize for research and product development in food, healthcare, beauty, nutrition and supplements, etc.) ・ Visualization of cost savings from prevention of NCDs is also important for the domestic healthcare policy and economy.
Ideas raised in the opinion exchanges (Both validity and feasibility not verified)	<Value proposition> ・ Taking the high percentage of institutional deliveries as an opportunity to conduct a three-generation cohort study[51] by collecting specimens at the time of prenatal and postnatal checkups ・ In addition to the cohort studies, newborn mass screening could save infants (about 20 diseases: limited to those with interventions, such as phenylketonuria) → publicly visible benefits of the biobank at an early stage ・ In Bhutan, the percentage of low birth weight infants varies widely by Dzongkhag (from the 4% to over 12%) and the reasons for this are not clear.[52] Conduct research on low birth weight using biobank data, as well as research on fetal nutrition and its impact on NCDs, which has received international attention ・ Connecting it to research from wider-perspective NCDs in the mid- to long-term <Operations> ・ In the initial phase of the biobank, target population would be those with a habit of health checkups and those taking prenatal and postnatal checkups (both of which have touch points that regularly visit medical institutions themselves to conduct blood collection and clinical laboratory testing) to reduce additional burden at the medical institutions ・ Specimen storage and analysis could be conducted by a Japanese research institute for the first few years of operation to minimize the cost burden in Bhutan

(Source: Prepared by the survey team)

[51] Birth cohort study of pregnant women, fetuses, their families (fathers, siblings), and relatives (grandparents)
[52] 2021 Vital Statistics Report Bhutan, https://www.nsb.gov.bt/wp-content/uploads/dlm_uploads/2022/04/VSR-2021-WEB.pdf

5-2-2. Second field survey (November 2024)

The second field survey was conducted from November 11 (Mon.) to November 16 (Sat.) to discuss the details of biobank development and to exchange information with other development agencies. A summary of the field survey is shown in the table below.

Figure 5-8 Outline of the second field survey

Period	Monday, November 11 ~ Saturday, November 16, 2024
Objectives	・ Detailed discussion for biobank development (basic policy for biobank operation, roadmap, cooperation program by JICA, etc.) ・ Exchange information with other development agencies
Participants from the survey team	・ Yu Hasegawa, Mitsubishi UFJ Research and Consulting Co., Ltd. ・ Tomoko Kunimitsu, Mitsubishi UFJ Research and Consulting Co., Ltd. ・ Fuji Nagami, Tohoku University Tohoku Medical Megabank Organization
Survey schedule and places to visit	・ November 11 (Mon.): Discussions with a local consultant ・ November 12 (Tue.): Preliminary meeting with JICA Bhutan office; discussion with Project Management Unit; discussion with the Ministry of Health ・ November 13 (Wed.): Facility tour of Gidakom Hopital; facility tour of Dechencholing Hospital; discussion with WHO ・ November 14 (Thu.): Discussion with the Cabinet Secretariat; Discussion with UNDP; Discussion with the World Bank (online); interview with a JOCV clinical laboratory technician ・ November 15 (Fri.): Discussion with participants of the invitation program in Japan; discussion with National Medical Service; discussion with DHI; discussions with ADB; meeting with JICA Bhutan office

(Source: Prepared by the survey team)

The second field survey visited Gidakom Hospital, a district hospital, and Dechencholing Hospital, a 10-bedded hospital, to confirm the possibility of collecting specimens at mid- and small-scale hospitals. The results of the visits to both hospitals are shown in the table below. Since the survey team visited one district hospital and one 10-bedded hospital only, it is difficult to assume the nationwide situation. However, it seems to be possible to collect specimens for biobanking at hospitals equivalent to Gidakom Hospital. Instead of collecting new specimens for the biobank, the remaining specimens after clinical laboratory testing could be stored in the biobank with obtaining additional informed consent for research use. Or healthy residents who would not normally visit a hospital could come to the hospital to have their specimens collected. The specimen collection process should be designed in consideration with the additional workload on hospital staff.

Figure 5-9 Summary of the hospital visits

	Gidakom Hospital (district hospital)	Dechencholing Hospital (10-bedded hospital)
Number of patients	· Outpatient: more than 100 per day (half of them are NCDs) · Hospitalization: 10 patients (separately, 6 patients hospitalized due to multidrug-resistant tuberculosis)	· Outpatients: 20 per day (excluding maternal and child health patients) · There are four beds, but no inpatients are admitted for consultation and follow-up
Number of healthcare workers	· Physicians: 2 (outpatient, inpatient and emergency)	· Medical officer, Clinical officer[53] , Dentist, Pharmacist, Nurse (including nursing assistants), 22 in total
Introduction of ePIS	· Introduced in May 2024	· Introduced around the end of January 2024
Sample collection and transportation	· Specimens are collected daily · Samples to be collected: blood (CBC, serum, plasma), urine · If testing is difficult in the hospital, transport to JDWNRH on Tuesdays and Thursdays in the hospital's multi-purpose vehicle (as needed for emergencies)	· Specimens collected daily from 8:30 to 9:00 a.m. · Samples to be collected: blood (CBC, serum, plasma), urine · Ambulance collects specimen and transports to JDWNRH at approximately 9:00 a.m. · Some patients directly go to JDWNRH for clinical laboratory testing
Sample storage	· Discarded 3 days after completion of testing	· All transported to JDWNRH, no storage at the hospital
Traceability of the samples	· Once the laboratory receives the test order in ePIS, a barcode is generated and attached to each tube · If transported to JDWNRH, barcode is currently being created again due to system issues	· No barcode, only a sticker on tube with CID and age

(Source: Prepared by the survey team)

[53] At Dechencholing Hospital, a patient will be assigned to either the Pharmacy Unit (receiving medicine), Medical Officer, or Clinical Officer based on a brief medical interview at the reception desk. If the Clinical Officer considers that he or she is unable to handle the case, the patient will be examined by the Medical Officer.

Figure 5-10 Photos of Gidakom Hospital

Gidakom Hospital building

Entrance to the laboratory unit (where blood samples are collected)

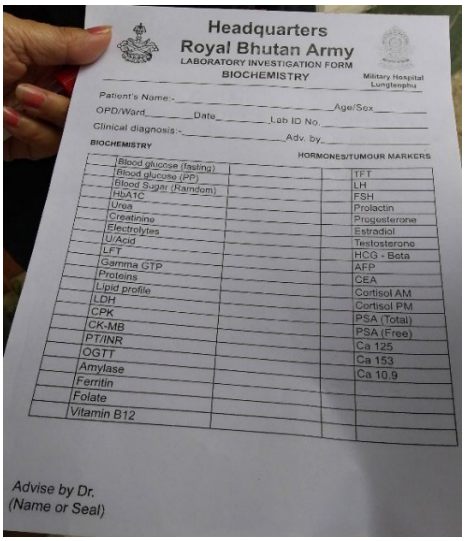
Inside the laboratory unit (analysis, temporary storage of specimens)

(Source: Photos taken by the survey team)

Figure 5-11 Photos of Dechencholing Hospital

Dechencholing Hospital (Reception)

Inside the laboratory unit



Test request form to be sent with specimen

(Source: Photos taken by the survey team)

The table below shows the results of discussions with Bhutanese officials regarding the basic policy for biobank operation in Bhutan, the roadmap, and JICA's cooperation program.

Figure 5-12 Summary of the results of the second field survey

Governance structure	・ The biobank has two major objectives: attracting foreign investment and improving the health of the people, both of which are equally important. ・ Leadership is needed to direct the strategy for the operation and utilization of the biobank in line with long-term market changes and research trends. it is difficult to cover the function for RCDC, JDWNRH, and KGUMSB solely, which are currently expected to play a central role in biobank operations, and a necessary governance structure should be considered. ・ Once data utilization actually starts at the four banks, it is expected that various questions and requests will be received both domestically and internationally. The function to respond to them and then guide to contract procedures and data provision will be necessary not only for the biobank but for the four databanks as a whole.

Resources and costs	・ In scrutinizing the required resources and costs, (1) whether to outsource whole genome analysis and (2) the number of specimens to be stored (number of participants and volume to be collected from each participant) are important. ・ Some of the personnel necessary to operate the biobank, such as physicians, nurses, and clinical laboratory technicians, would not only be involved in the biobank operation, but could be included in the MoH's human resource development plan.
Operation	・ Specimen collection should start from operations centered on JDWNRH, at least initially. Beyond that, the extent to which it is expanded to include district hospitals and 10-bedded hospitals should be carefully determined from the perspective of specimen management and traceability. ・ There are two methods of recruiting participants: waiting style, in which participants visit the sample collection site, and invitation style, in which the biobank approaches the possible participants; the latter could be considered in Bhutan. ・ When hospitals, including JDWNRH, perform additional specimen collection tasks for the biobank, there will be not only a burden of taking additional time from healthcare professionals and hospital staff, but also challenges in training and operational establishment regarding the new tasks. ・ In Bhutan, a nationwide NCDs screening began on November 14[54]. One possible idea is to take advantage of such campaign to collect many samples at once.
JICA cooperation program	・ Depending on Bhutan's legal system regarding the transfer of genetic information and specimens, and the regulations of the biobank, it may be possible to store Bhutanese specimens in a separated space of a Japanese biobank, and invite personnel from Bhutan to share knowledge and transfer technology while conducting operations and research together. ・ Once the biobank system in Bhutan is in place, specimens could be returned to Bhutan or continue to be stored in Japan as a backup. ・ The continuous costs for the specialized human resources and equipment necessary to operate the biobank must be reflected in the national financial plan. The GoB will decide whether to request a further cooperation for the project after discussions with the Ministry of Finance when the approximate costs becomes clear, as well as whether to outsource the analysis and the number of specimens to be stored.
Possibility of cooperation with other development agencies	・ WHO, World Bank, and ADB are also working on capacity building of healthcare workers, and should consider demarcation or joint implementation of similar human resource development. ・ Regarding data linkage between ePIS and the biobank (or four databanks), continuous discussions are needed to specify the processes for external users to utilize the information, such as anonymization of patients' personal information contained in ePIS.

(Source: Prepared by the survey team)

[54] Ministry of Health, "Information for Bhutanese general public : Nationwide Non-Communicable Disease Screening", https ://www.moh.gov.bt/information-for-bhutanese-general-public-nationwide-non-communicable-disease-screening/

5-3. Desktop survey

A benchmarking study of population-based biobanks in other countries was conducted to examine the design and planning of a biobank in Bhutan. See Annex for details (undisclosed).

In addition, the results of reviewing legal and regulatory systems and ethical principles that need to be developed for biobank operations are described in Chapter 3, "3-2. Codes, regulations, and guidelines."

Regarding the system and environment for the development of medical and healthcare products and services in Bhutan, there are no information on active R&D activities in the medical and healthcare fields in Bhutan. In the future, it will be necessary to investigate the system and environment for R&D activities (including joint research with Bhutanese universities, medical institutions, and companies) conducted by foreign companies in Bhutan through consortium-style pilot activities during the Initial and Growth phases of the biobank.

5-4. Invitation program in Japan

5-4-1. Preparation of invitation (coordination with Bhutanese and Japanese stakeholders)

An invitation program to Japan was conducted with the aim of exploring specific collaboration ideas with related organizations in Japan and building relationships with potential clients and partners. As a result of preliminary coordination with the GoB, the following nine Bhutanese invitees participated. The period of invitation programwas two weeks from August 26 (Mon.) to September 7 (Sat.).

Figure 5-13 Participants of the invitation program in Japan

	Name	Organization	Title
1	Tashi Choden	GovTech Agency	Sr. ICT Officer
2	Tshering Nidup	Ministry of Health	Sr. Attorney
3	Tsesum Dawa	Ministry of Industry, Commerce and Employment	Chief Industries Officer
4	Pema Chophel	Royal Centre for Disease Control	Dy. Chief Laboratory Officer
5	Rixin Jamtsho	Khesar Gyalpo University of Medical Sciences of Bhutan	Director
6	Birendra Pradhan	Jigme Dorji Wangchuk National Referral Hospital	Pathologist and Head of Dept.
7	Tshering Dema	Jigme Dorji Wangchuk National Referral Hospital	Dy. Nursing Superintendent
8	Tshering Dorji	National Biodiversity Center	Sr. Biodiversity Officer
9	Pema Rinchhen Wangchug	Druk Holding & Investments Limited	Associate Director

(Source: Prepared by the survey team)

5-4-2. Holding a seminar for Japanese related organizations

A public seminar was held on September 2 (Mon.) during the invitation program in Japan, with the aim of informing Japanese stakeholders about the biobank project in Bhutan and building relationships with them. The outline of the seminar and its program are shown in the table below. The number of participants was 26 at the venue and 109 online (there were some duplicated participation both at the venue and online).

Figure 5-14 Outline of the public seminar

Title of the seminar	The Future of Life Science and the Well-Being of the People from a Developing Country ~Digital Health Platform Initiative and Biobank~
Description	What kind of values can a biobank from a developing country bring to the world? Japanese and Bhutanese industry, government and academic representatives discussed the path to the development of the life sciences field that Bhutan, a country known for its unique rich natural environment and ecosystem, is aiming for, and how the world should be involved in this initiative.
Purpose	・ Introduce the concept of the Digital Health Platform in Bhutan (especially the biobank project) and promote awareness of the concept to private companies (from large corporations to start-ups) and research institutions in Japan ・ Identify companies and research institutions that have interests in working with Bhutan and create opportunities for future collaboration ・ Introduce the status of healthcare, economy, finance, and society of Bhutan, and explore the possibilities of contribution by Japanese companies or research institutions
Date and time	Date: Monday, September 2 2024 Time: 14:00~17:00 (2-hours seminar and 1-hour networking)
Venue	GLOBAL LIFESCIENCE HUB (Mitsukoshi-mae Station and Shin-Nihonbashi Station) Hybrid style (on-site and online)
Language	Japanese, English (simultaneous interpretation available)
Target audience	・ Private companies, research institutions and academia in the life science field (researchers and research designers involved in genomic medicine, drug discovery, microbiome research, etc.) ・ Private companies, research institutions and academia involved in medical and health big data analysis and its utilization ・ International cooperation personnel involved in development cooperation in Bhutan (including those not in the healthcare sector)

(Source: Prepared by the survey team)

Figure 5-15 Photos of the public seminar

	
Presentation by GovTech Agency	Panel discussion

(Source: Photos taken by the survey team)

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5-4-3. Individual meetings, site visits, and follow-up with relevant institions in Japan

Individual meetings and site visits were conducted in Japan as described below. The specific details of each meeting are omitted from this report, as they contain confidential information.

Figure 5-16 Schedule of the invitation program and meetings and site visits in Japan

August 26 (Mon.)	・ Arrival in Japan ・ Orientation
August 27 (Tue.)	・ Kanagawa Prefectural Government
August 28 (Wed.)	・ Tohoku University Tohoku Medical Megabank Organization
August 29 (Thu.)	・ Toyosato Community Center, Tome City ・ Tome City Hall
August 30 (Fri.)	・ Tsuruoka Science Park ・ Institute for Advanced Biosciences, Keio University ・ Yamagata University ・ Shiseido Company, Limited ・ MOLCURE Inc. ・ Tohoku University Tohoku Medical Megabank Organization (wrap-up of the first week)
August 31 (Sat.)	・ Travel day
September 1 (Sun.)	・ Day off
September 2 (Mon.)	・ Public seminar
September 3 (Tue.)	・ Foundation for Biomedical Research and Innovation at Kobe (with attendance by representatives of Kobe City) ・ Bioresource Center, International Clinical Cancer Research Center (ICCRC), Kobe University Hospital
September 4 (Wed.)	・ Sysmex Corporation
September 5 (Thu.)	・ Chitose Laboratory Corp. ・ Japan Agency for Medical Research and Development (AMED)
September 6 (Fri.)	・ Metagen Therapeutics, Inc. (online meeting) ・ OMRON HEALTHCARE Co., Ltd. (online meeting) ・ Summary session at JICA Headquarters
September 7 (Sat.)	・ Departure from Japan

(Source: Prepared by the survey team)