2022 First Edition of the
Annual Report on Taiwan's Biobanks

Foundation of Precision Medicine

Development of Taiwan's Biobanks

Ministry of Health and Welfare

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2022 August

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Preface

Academia Sinica
Academician
Chien-Jen Chen

In 2009, TIME magazine reported that biobanks would be among the top 10 innovative scientific concepts that would change the world. Biobanks recruit people from two categories. One category consists of people from the community for the periodic collection of biodata. After tracking them for several years, when a sufficient number of participants have fallen ill, differences in the genetics, biomarkers, and dietary habits of healthy people and sick people can be compared, and possible pathogenic factors can be identified. This is a generational tracking study. Already in 1970, Dr. R. Palmer Beasley recruited a cohort from the Government Employees' Clinic Center (GECC) in Taipei. In 1991, he recruited the REVEAL-HBV cohort. The research participants were recruited from the GECC or from seven townships, respectively. Questionnaire surveys were conducted to collect demographic information, dietary habits, and personal and family medical histories. In addition, biological specimens such as blood, urine, nails, and mucosal cells were collected and frozen for future use. The second category consists of patients with specific diseases and their normal counterparts without these diseases. Differences in their genetics, biomarkers, and dietary habits are compared. This is a case-control study design. Studies like these have identified many risk prediction factors for patients with hepatitis B to develop liver cancer, such as testing positive for the hepatitis B e antigen and the amount of virus within serum. These discoveries have been included in the clinical treatment guides for hepatitis B.

Biobanks recruit people in conformity with the ethical and legal regulations of each country to collect demographic data and biological specimens to establish biospecimens and health information of high quality, diversity, and frequency. Researchers can apply for studying them for human disease prevention, diagnosis, and treatments, leading to a new era of precision health. In response to the arrival of the genomics generation, in the early 2000s, Taiwan invited scholars, experts, and clinical physicians to reach a consensus on founding a representative biobank to track the biological specimen markers and disease conditions in the long run to explore disease prevention strategies, in order to promote health and well-being of the people of Taiwan.

In 2011, I served as vice president of Academia Sinica and participated in the founding of the Taiwan Biobank, the first biobank in Taiwan. With the full support from the government, academic research units, and medical institutes, as of this year (2022), Taiwan has established 35 biobanks, each with its own specialties and characteristics. Overall, domestic biobanks collect specimens ranging from the blood, body fluids, lesions and normal tissues of healthy individuals and patients with specific diseases to their DNA and RNA.

Biobanks are the basis for precision medicine, and they play the critical role of collecting, treating, and storing biospecimens. To promote the development of medical research and the biomedical industry, biobanks must simultaneously apply information calculation and artificial intelligence for connecting data and turning specimen data into information and data that can be used in academic research, clinical applications, and medical product development.

To establish a consensus among industry, government, academia, and research to fully exercise the capacity of Taiwan's biobanks, the Human Biobank Management Act was passed in the last decade to establish rigorous information security regulations, benefit feedback methods for commercial use, and a complete set of measures for the protection of research ethics. This Act serves as the legal basis for the management of biobanks. In 2019, when I was vice president of Taiwan, the government founded the National Biobank Consortium of Taiwan to promote the sharing of the biological specimens, personal data, and health information preserved in individual biobanks, thereby exercising the maximum benefit of the biological specimens. The platform also integrates domestic biobanks and improves their quality, allowing Taiwan to steadily develop in the field of precision medicine and earn a global reputation this field.

This annual report introduces the history of biobanks in Taiwan. Through the collaboration of the Executive Yuan, Ministry of Health and Welfare, Academia Sinica, National Health Research Institutes, Joint Commission of Taiwan, and major medical institutions, we are gradually promoting the development of biobanks and establishing a new milestone in the development of biobanks and precision medicine in Taiwan.

Overall, biobanks provide critical contributions to the etiology exploration, risk prediction, and diagnosis and treatment of diseases. Ensuring their sustainable management is a huge challenge. In the future, the Health Big Data Platform should be employed to conduct cross-technology integration to increase the level of biomedicine technology and to promote the digital health industry in Taiwan, facilitating the growth of Taiwan's precision medicine and benefiting the health and well-being of everyone.

Academician of Academia Sinica

陳建仁

Preface

State of the Executive Yuan and National Science and Technology Council

Minister
Tsung-Tsong Wu

In late 2018, as the Minister of the National Science and Technology Council, I invited the heads of Academia Sinica, the Ministry of Health and Welfare, and the National Health Research Institutes to discuss how to integrate and use databases in Taiwan to generate the greatest benefit. Subsequently, I visited the presidents of several medical centers to communicate and promote the importance of the collaboration among the biobanks of various hospitals. Thanks to the support of many hospitals, the National Biobank Consortium of Taiwan was established in late October 2019. Representatives from all 31 biobanks in Taiwan were present at the official launch. Many presidents or vice presidents of hospitals came to show their support despite their busy schedules. The ex–vice president Chen Chien-Jen was also present to witness this milestone. Under the joint effort of the Ministry of Health and Welfare, the National Health Research Institutes, Academia Sinica, and various biobanks, we have currently connected 32 biobanks, including 19 medical centers in Taiwan and the Taiwan Biobank from Academia Sinica. This connection was a huge breakthrough in the last several decades in that it allows individual biobanks to be connected into a large BioData network with extensive contents.

BioData is a precious resource of Taiwan, and it is the foundation for industries to have innovative developments. In 2020, as COVID-19 assailed the world, we employed the biobank mechanism to establish the Taiwan COVID-19 Biobank to assist domestic companies to develop relevant test reagents or preventive medicine products to protect Taiwanese people's health and safety.

Looking ahead to 2030, we expect a future with precision health covering health care, prevention, diagnosis, treatment, and care. We hope that the BioBank Consortium can continue to promote the step-by-step integration of resources as the foundation for the future. Within the competition of the next-generation biomedical industry, the Consortium will serve as the rich soil for creating an innovative ecology, allowing industries to spread roots, blossom, and grow seeds, showing the world Taiwan's rich resources and technological capacity.

National Science and Technology Council

吳政忠

Preface

Ministry of Health and Wlfare

Minister
Jui-Yuan Hsueh

Precision medicine and emerging medicine have become a critical trend worldwide. Thus, establishing biobanks and maintaining their quality is a critical asset for the development of digital medicine and the integration of artificial intelligence. In recent years, the Ministry of Health and Welfare has been proactively establishing measures related to biobanks and linking world-class clinical medicine technology, hoping to lead relevant industries to set their sights on the world and allowing Taiwan's biotechnology industry to shine on the international stage.

The Ministry of Health and Welfare has established a national-level biobank and accumulated data on disease prevention and diagnosis and medical care. Through the integration of medical information and biobanks, we have reinforced data connections and value-added analyses. By integrating smart medical technology, the biobank can greatly boost the standard of medical research and overall precision medicine in Taiwan. However, Taiwan is facing challenges such as population aging, emerging infectious diseases, and the rapid development of biomedical technology. In response to the challenges faced by existing biobanks, we must focus on the needs of the medical health care end and promote the collaboration of upstream, midstream, and downstream medical services and cross-domain industries. For example, artificial intelligence can be applied to assist in the interpretation of medical big data to increase the efficiency of medical personnel and the accuracy of their diagnosis. In addition, big data analysis can be integrated with emerging medicine technology to develop treatment methods with new biomarkers and medicine, thereby establishing an innovative service model of health care and industry development.

In response to the digital transformation trend of the global medical industry, industries such as digital health and smart medicine will become the norms of future care. However, no good study can be completed by individual research teams alone. All research requires cross-technology integration. On the basis of Taiwan's favorable foundations, individual biobanks and the National Biobank Consortium of Taiwan play critical roles as mediums or catalysts in promoting the explosive growth of the research capacity of Taiwan. They can also lead to more innovative research and development, products, and industries, leading Taiwan towards the development of precision health industries and the early prevention of diseases, thus promoting the well-being of everyone. This report provides the reader with a comprehensive overview of the features of Taiwan's biobanks. Looking towards the future, I believe that Taiwan will one day become the biotech island of Asia.

Minister of Health and Welfare

薛瑞元

Preface

Ministry of Health and Wlfare
Former Minister
Shih-Chung Chen

In 1982, Taiwan listed biobanks as a critical point in technological development. Later, in 2005, biobanks were included as one of the key development points of the Biomedical Technology Island Plan promoted by the Executive Yuan, planning the development blueprint for Taiwan's biobanks.

In the past, through the pioneering research of Academia Sinica, recruitment standards were researched and established, an ethical governance committee was founded, and suitable models for the operation of databases were established. These results contributed substantially to the subsequent biomedical research and the health of people in Taiwan. However, the development of the biomedical industry is changing rapidly. To ensure that the promotion of policies is sound and forward-looking, Taiwan has been promulgating regulations since 2010, such as the Human Biobank Management Act, the Administrative Regulations on the Establishment of Human Biobanks, the Benefit Sharing Regulations of Human Biobanks, the Human Biobank Information Security Specification, and the Human Biobank Examination Fee Charging Standard, to lay the foundations for the establishment of biobanks by various institutions and to ensure the basic quality of biobanks. As of today, 35 biobanks have been approved, serving as the research capacity for relevant studies in Taiwan. In addition, to ensure the operational quality and sustainable development of biobanks, the government regularly carries out biobank inspections, and it promotes projects such as the Enhancing the Utility of and Adding Values to Biobanks in Taiwan and The Biobanking Training Program: Increasing Knowledge and Advancing Proficiency for Biobankers.

From precision medicine to precision health, biobanks play a critical role. To greet the coming of the precision era, Taiwan founded the National Biobank Consortium of Taiwan in 2019 to strengthen the connection of individual biobanks in Taiwan and to promote the quality of biological specimens and the usage benefits. The Consortium has invigorated Taiwan's biomedical industry while demonstrating comprehensive performance in leading Taiwan further into the world, providing new momentum for Taiwan's biomedicine field and economic growth.

Precision medicine, regenerative medicine, and smart medicine are the key development points of advanced countries worldwide. To fasten the upgrade of Taiwan's industry, we will focus on the integration of biobank data and information in the future to achieve cross-domain database connections, thereby expanding and increasing resource effectiveness.

I hope that through this annual report, industry, academia, medicine, and the general public can have a comprehensive understanding of the history and future outlook of Taiwan's biobanks. I hope that each domain will continue to make progress, together writing a new chapter for biobanks.

Former Minister of Health and Welfare

Preface

Taipei Medical University
General Consultant
Hong-Nerng Ho

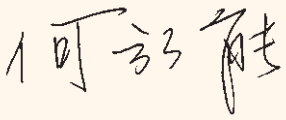
An indispensable foundation for biomedicine research is the collection, preservation, and application of biodata. In the past, individual researchers often collected tissues or cells themselves for academic research, and individual hospitals usually had their own tissue banks for researchers within their organization to use. However, as the awareness of ethics, regulations, autonomy, personal information, and population genetics grew, people have increasingly come to emphasize biobanks and become more concerned about the rigorous management of such banks. At that time, Taiwan was preparing to establish Taiwan's first biobank, the Taiwan Biobank, attracting the attention from society and legislative organizations. In 2010, the Human Biobank Management Act was passed by the Legislative Yuan, and in 2011, the Administrative Regulations on the Establishment of Human Biobanks were established. Thus, the foundation for institutions in Taiwan to establish biological gene databases was laid, and institutions everywhere established their own databases.

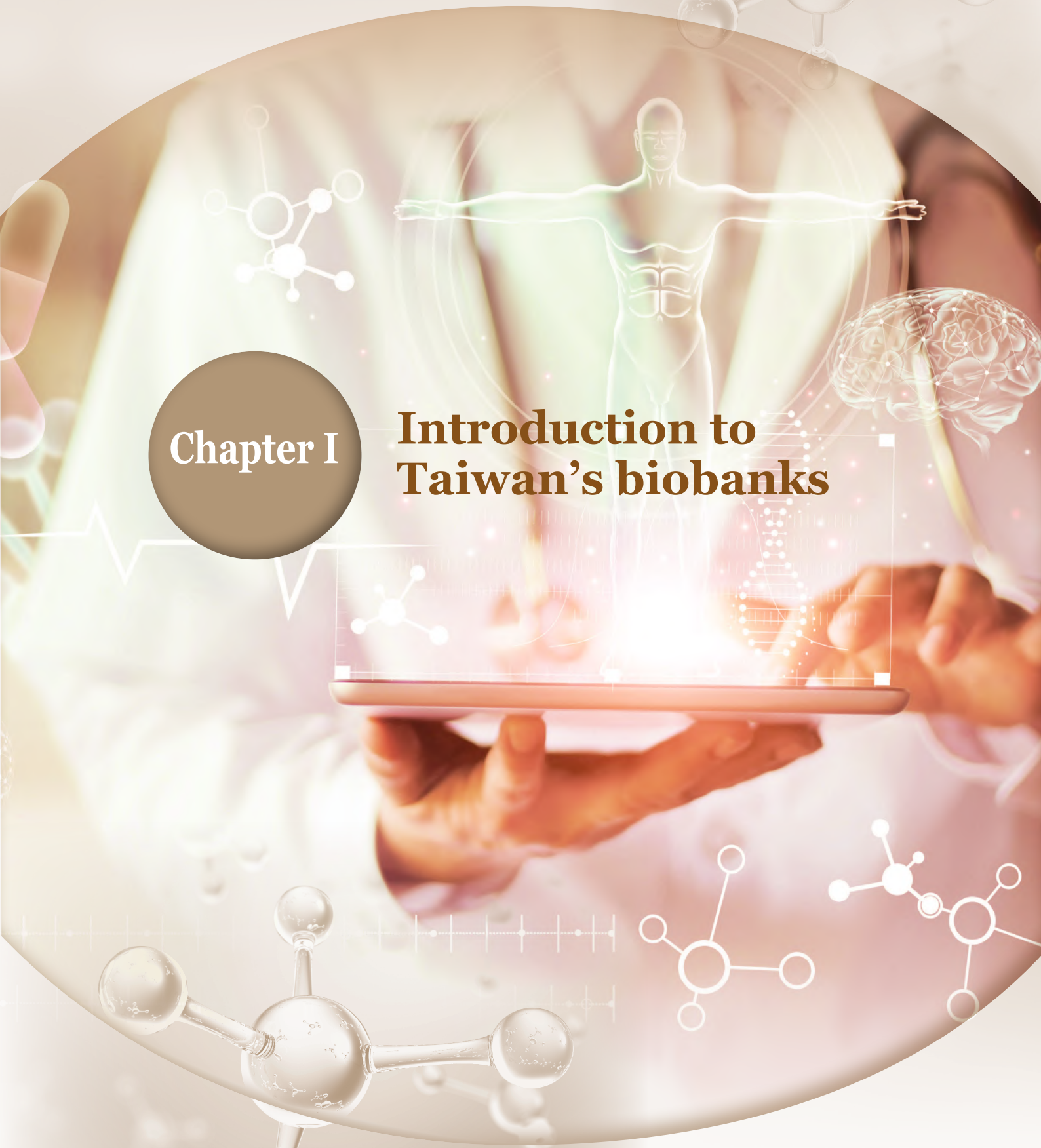
Taiwan is a leader in biotechnology and information technology. Together with its comprehensive health data and outstanding medical system and with the assistance of a variety of non-biological data, Taiwan meets every essential criterium for developing biobanks. Taiwan's unique geographical location and historical factors have resulted in a population of 23 million people consisting of Indigenous people, immigrants from the Ming and Qing dynasties, and immigrants from various provinces in China that came to Taiwan with the government of the Republic of China. In recent years, the population has expanded to include new immigrants from Southeast Asia. Thus, Taiwan can be seen as a condensed version of East Asia. Such a rich and diverse biobank has its uniqueness and usefulness.

However, in recent years, relevant projects have revealed that individual biobanks had different standards, uneven quality, and lax management, and difficulties in integrating different biobanks, leading to problems such as low usage rates of specimens and data. As a result, people from different fields realized the criticalness and essentialness of integrating domestic biobanks.

On the premise of the overall development of the biomedical industry and the sustainable collaboration of industry, government, academia, and research, the Taiwanese government allowed the independent operation of the biobanks of different institutions to enhance their vertical development and uniqueness. Moreover, the government advised and guided the Ministry of Health and Welfare to establish the National Biobank Consortium of Taiwan to promote the horizontal communication and integration across institutions. It is hoped that this Consortium can exercise its comprehensive effectiveness and gather Taiwan's research capacity to provide experts and scholars with more diverse research subjects. I hope that through this report, we can further increase researchers' use of specimens and data and increase the output of relevant research results, creating the value and impact of biobanks in Taiwan.

Honorary Professor of National Taiwan University,
General Consultant of Taipei Medical University,
Chairperson of the Ethical Governance Committee of Taiwan Biobank





Chapter I
Introduction to Taiwan's biobanks

Chapter I. Introduction to Taiwan's biobanks

I. Development history

The history of Taiwan's biobanks started in 2005, when biobanks were included as one of the key development points of the Biomedical Technology Island Plan promoted by the Executive Yuan. As for the infrastructure, the National Science Council of the Executive Yuan (predecessor of the National Science and Technology Council) launched a call for proposals in 2003 for the "Feasibility Assessment of Establishing Taiwanese Disease and Gene Database" project to be implemented by Academia Sinica. Later, from 2005 to 2007, the Council promoted the "Research Project of the Establishment of Taiwan Biobank and Generation Tracking of Multiple Risk Factors and Multiple Diseases". Then, from 2005 to 2011, the Health Administration (predecessor of the Ministry of Health and Welfare) commissioned Academia Sinica to implement the "Preliminary Planning for the Establishment of Taiwan's Biological Database" and its subsequent projects. The main goal of these projects was to construct a protype and determine the scale of Taiwan's biobanks. At the same time, the projects had to solve issues at various levels, such as ethical, legal, and social issues, the treatment, storage, and management of large amounts of biospecimens and relevant data, the analysis and handling of data, and the confidentiality of personal data. Because this preliminary project involved several professional fields, it was divided into four subcategories, namely genetic medicine, ethics and laws, information platform, and industry development. Gradually, the preliminary blueprint of Taiwan's first biobank, the Taiwan Biobank, was drawn (Fig. 1-1-1).

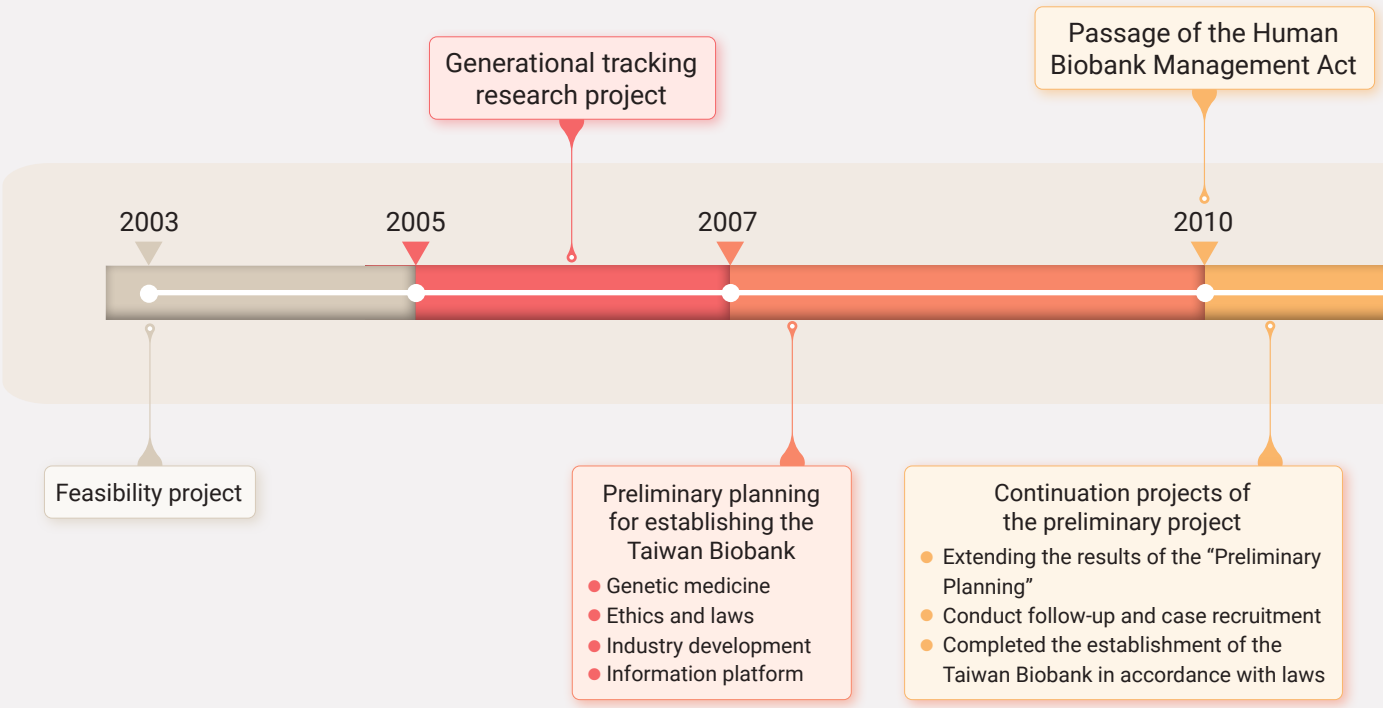
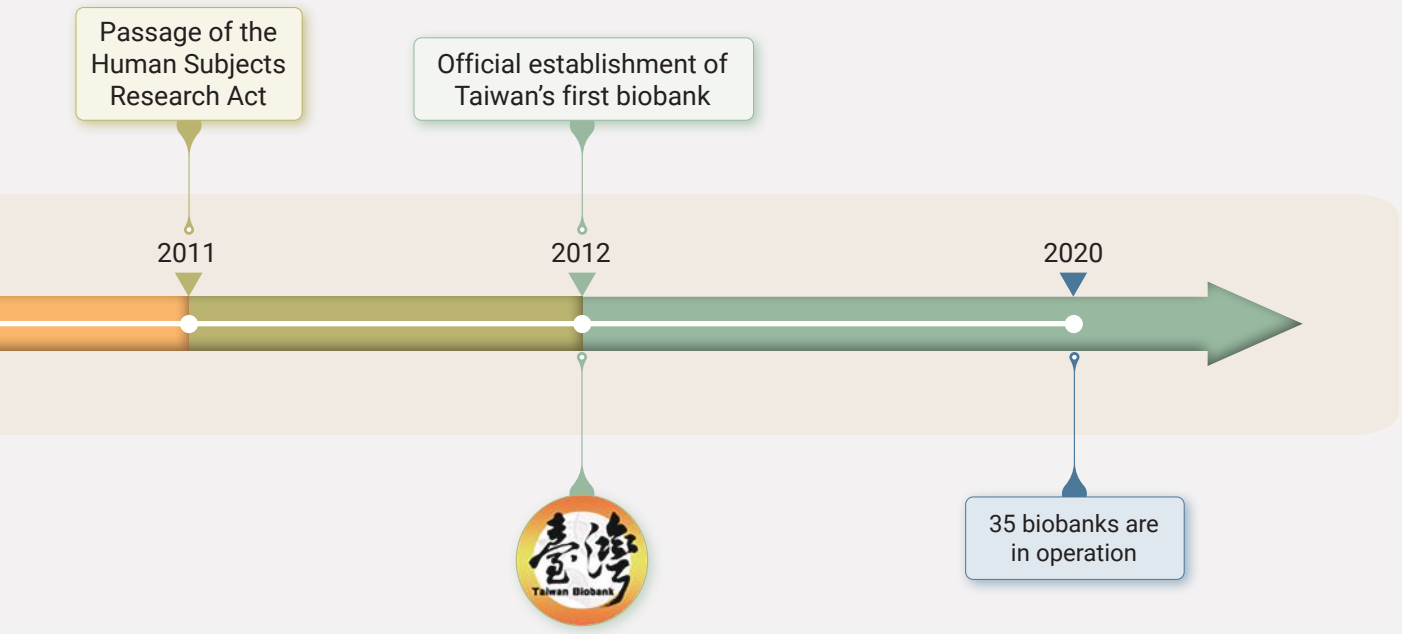


Fig. 1-1-1 Promotion history of the Taiwan Biobank Project

Looking back at the history of the establishment of biobanks in Taiwan, it all began with the establishment of relevant regulations in 2010 that laid the foundation for the establishment of biobanks by various institutions. Since then, individual organizations have started to establish their own biobanks. However, each biobank was independent, and they faced problems in collecting specimens and applying data. Moreover, the connectedness of medical information was low.

In 2017, the Taiwanese government started to conduct periodic biobank inspections. It also promoted the Enhancing the Utility of and Adding Values to Biobanks in Taiwan and the The Biobanking Training Program: Increasing Knowledge and Advancing Proficiency for Biobankers to continue improving the operational quality of biobanks in preparation for the coming of the precision era. To gradually reinforce the connection between biobanks in Taiwan and to increase the quality of biological specimens and usage efficiency, the National Biobank Consortium of Taiwan (NBCT) was founded in 2019 to construct a domestic biobank network to invigorate the domestic biomedical industry. The National Center for High-performance Computing of the National Applied Research Laboratories provided national-level high-performance internet services and cloud computing facilities to assist the government in constructing Taiwan's health big data system and mutually beneficial platforms for the analysis and sharing of data. Next pape presents a chronology of important events for Taiwan's biobanks.



Chronology of important events for Taiwan's biobanks

Year	Important event
1982	Yun-Suan Sun, president of the Executive Yuan, announced at the Second National Science and Technology Conference that biotechnology has been listed as one of the eight main technologies for development in Taiwan.
1995	The promotion plans of the biotechnology industry were reinforced as critical guiding principles for promoting the development of the biotechnology industry.
2002	The Executive Yuan approved the "Planning and Implementation of the Challenge 2008 National Development Plan (2002–2007)", in which the biotechnology industry was listed as one of the Two Trillion and Twin Star Industries.
2003	The National Science Council of the Executive Yuan commissioned Academia Sinica to implement the "Feasibility Assessment of Establishing Taiwanese Disease and Gene Database" project.
2005	The Executive Yuan launched the Biomedical Technology Island Plan, which included establishing Taiwan's biobanks as a critical development objective (April 2005).
2005–2011	The "Preliminary Planning for the Establishment of Taiwan's Biological Database" and its subsequent projects (December 2005–December 2011).
2009	The Taiwan Diamond Action Plan for Biotech Takeoff (2009–2012) accelerated the development of the biotechnology industry.
2010	• A presidential decree enacted and announced the Human Biobank Management Act (February 2010). • The Health Administration announced the Human Biobank Information Security Specifications (July 2010). • The Health Administration established and announced the Benefit Sharing Regulations of Human Biobanks (September 2010).
2011	• The Health Administration established and announced the Administrative Regulations on the Establishment of Human Biobanks (January 2011). • The Health Administration established and announced the Human Biobank Examination Fee Charging Standard (February 2011). • The Health Administration announced the Application Instructions on the Establishment of Biobanks (February 2011).
2012	The Health Administration approved of the establishment of Taiwan's first biobank (Taiwan Biobank of Academia Sinica) (October 2012).
2013	Taiwan Diamond Action Plan for Biotech Takeoff (2012–2015). Medical management services were included in the scope of promotion, and talent training in the biotechnology industry was enhanced.
2016	Taiwan Bioeconomy Industry Development Program. Value was added to the health industry through the introduction of biotechnology.

2017
The Ministry of Health and Welfare commissioned the Joint Commission of Taiwan to establish biobank inspection regulations.

2017
Conducted a consensus meeting of inspections surveyor for the first cycle of onsite inspection of biobanks.

Year	Important event
2017	• The Ministry of Health and Welfare commissioned the Joint Commission of Taiwan to establish biobank inspection regulations (February 2017). • The Ministry of Health and Welfare announced the Criteria for Review of International Transmission of Human Biobank Data or Export of Biospecimen Derivatives (September 2017). • Conducted the first cycle of onsite inspections of biobanks (November 2017). • The Biomedical Industry Innovative Promotion Program set out to make Taiwan a major industrial center for biomedical research and development in Asia Pacific.
2018	The office of the Board of Science and Technology, Executive Yuan, invited units such as Academia Sinica and the Ministry of Health and Welfare to hold a chiefs' meeting to draft a biobank integration platform (March–December 2018).
2018–2019	The Ministry of Health and Welfare invited representatives from individual biobanks to hold a coordination meeting regarding the NBCT (April 2018–November 2019).
2019	• The Ministry of Health and Welfare commissioned the National Health Research Institutes (NHRI) to establish the NBCT (May 2019). • The office of the Board of Science and Technology, Executive Yuan, invited the Ministry of Finance and Academia Sinica for discussion to comprehensively reduce the charging standards for using digital data from the Taiwan Biobank (August 2019). • The office of the Board of Science and Technology, Executive Yuan, guided the Ministry of Health and Welfare to host the Launch Meeting of Taiwan's Precision Medicine and the Establishment of the Biobank Integration Platform Alliance (October 2019). • Offered biobank personnel professional knowledge and ability training courses (December 2019). • Established the attribution of rights and responsibilities and review order of the Institutional Review Board (IRB) and Ethical Governance Committee (EGC).
2020	• Constructed the Taiwan COVID-19 Biobank in response to COVID-19 (August 2020). • Conducted the second cycle of onsite inspections of biobanks (October 2020). • Conducted educational training for the biobank inspection surveyor (November 2020).
2021	• Amended and promulgated the Human Biobank Management Act (January 2021). • Amended and promulgated the Administrative Regulations on the Establishment of Human Biobank (October 2021). • The Biomedical Industry Innovative Promotion Program 2.0 and the six core-strategy industry promotion project for Taiwan's precision health were employed to construct a gene and health care big data database to develop a precision prevention, diagnosis, and treatment care system.

2019
The Office of the Board of Science and Technology, Executive Yuan, guided the Ministry of Welfare to host the Launch Meeting of Taiwan's Precision Medicine and the Establishment of the Biobank Integration Platform Alliance.

2020
Conducted educational training for the biobank inspection surveyor.

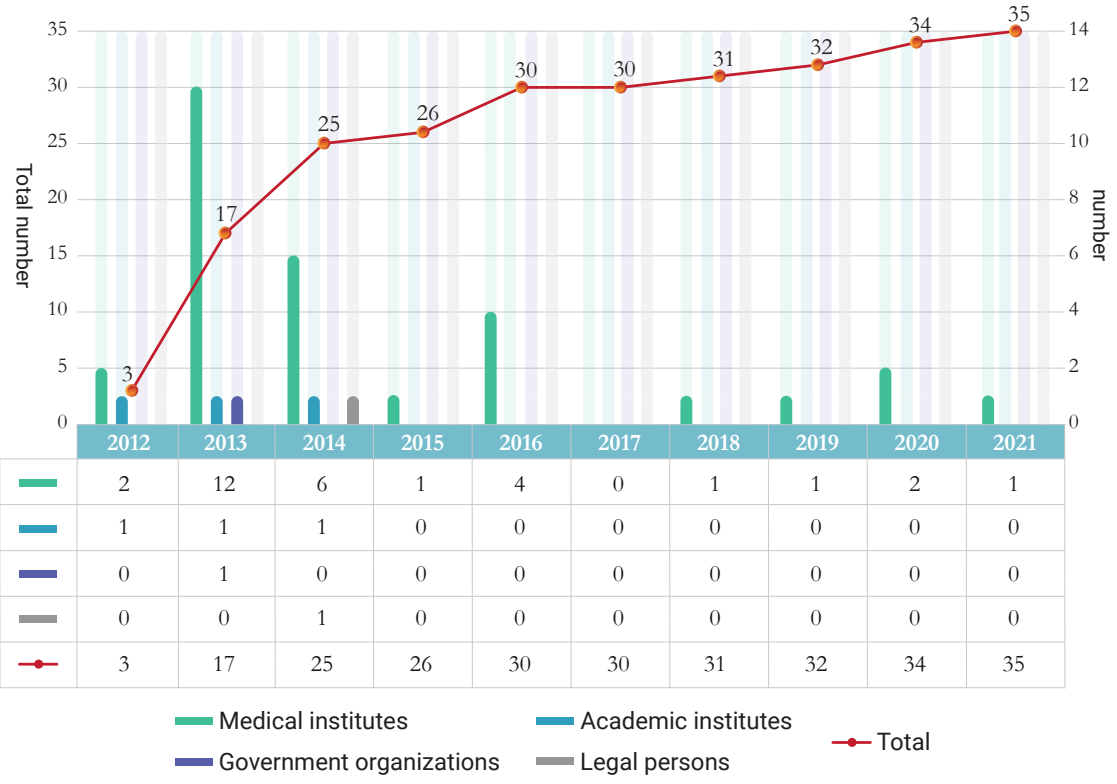
Taiwan's biobanks are organized by the Office of the Board of Science and Technology, Executive Yuan, for cross-institutional and cross-organizational promotion and integration. The organizations include the Ministry of Health and Welfare, Joint Commission of Taiwan (JCT), the NBCT operated by the NHRI, and individual biobanks. Each unit has its specialties, and together they have the comprehensive effect of bringing Taiwan to the world and creating new momentum for Taiwan's biomedicine field and economic growth. The roles played by each unit are listed in Table 1-1-1.

Table 1-1-1 Roles played by each relevant unit

Name of unit	Key tasks
Office of the Board of Science and Technology, Executive Yuan (predecessor of the Technology Office of the Executive Yuan)*	Organizing and planning Taiwan's technology development policies, resources distribution, major project review and management, and planning and hosting major technology strategy meetings.
Ministry of Health and Welfare	✓ Establishing and amending various regulations and forms related to biobanks. ✓ Approving the applications of the establishment, extension to period of validity, alteration, transfer, and cessation of operations of biobanks. ✓ Announcing the list of approved biobanks and their effective durations.
Joint Commission of Taiwan	✓ Assisting the Ministry of Health and Welfare in inspecting biobanks. ✓ Assisting the Ministry of Health and Welfare in conducting educational training courses related to biobanks.
National Biobank Consortium of Taiwan	✓ Organizing the cooperation and signing of contracts among biobanks, establishing standardized procedures for specimens, and organizing the specimens and medical information held by individual biobanks. ✓ Establishing a single window to receive applications from industry, academia, research, and medicine and to assist applicants to conduct cross-biobank matching and obtain data.
National Center for High-performance Computing	✓ Establishing an inter-ministerial platform for the sharing and analysis of health big data. ✓ Using a high-performance computing environment to conduct next-generation gene sequencing and database analysis.
Individual biobank	✓ Collecting and preserving specimens and data. ✓ Receiving applications and regularly announcing research results.

* Primary responsible organization: National Science and Technology Council

A feature of the establishment of Taiwan's human biobanks is the diversity of the organizations that have applied to establish biobanks, the diverse sources of specimens and data, and the diverse operational styles. As of June 2022, Taiwan has approved of the establishment of 35 biobanks. Further analysis revealed that in terms of the types of the organizations that established biobanks, 30 (85.8%) were medical institutes, 3 (8.6%) were academic institutes, 1 (2.8%) was a legal person, and 1 (2.8%) was a government institute. Figs. 1-1-2 and 1-1-3 show their establishment history, attributes, and distribution.



	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021
Medical institutes	2	12	6	1	4	0	1	1	2	1
Academic institutes	1	1	1	0	0	0	0	0	0	0
Government organizations	0	1	0	0	0	0	0	0	0	0
Legal persons	0	0	1	0	0	0	0	0	0	0
Total	3	17	25	26	30	30	31	32	34	35

Fig. 1-1-2 Number of biobanks in Taiwan and their attributes

Miaoli County
- National Health Research Institute Biobank

Taichung City
- China Medical University Hospital Biobank
- Chung Shan Medical University Hospital Biobank
- Taichung Veterans General Hospital Biobank
- Taichung Tzu Chi Hospital Biobank
- Tungs' Taichung MetroHarbor Hospital Biobank

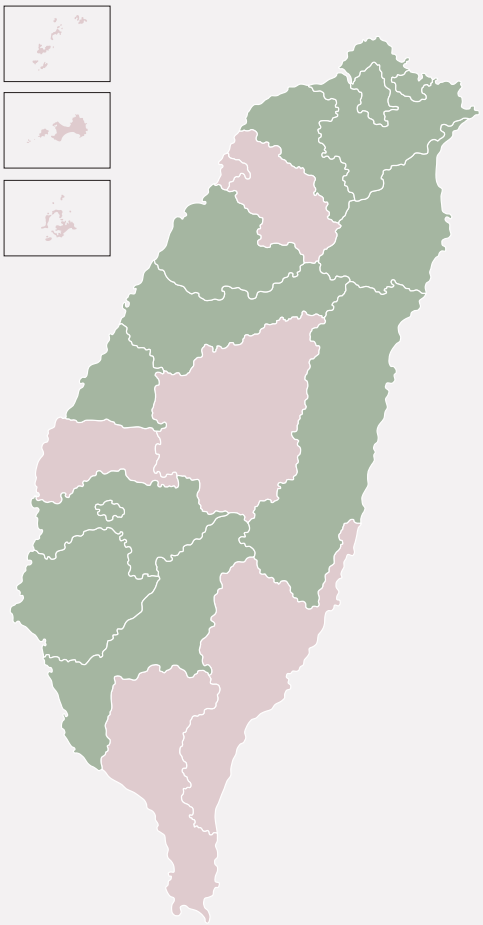
Changhua County
- Changhua Christian Hospital Biobank

Chiayi County
- Chiayi Chang Gung Memorial Hospital Biobank

Chiayi City
- Ditmanson Medical Foundation Chia-Yi Christian Hospital Biobank

Tainan City
- National Cheng Kung University Hospital Biobank
- Chi Mei Medical Center Biobank
- Tainan City Government Biobank

Kaohsiung City
- Kaohsiung Chang Gung Memorial Hospital Biobank
- Kaohsiung Veterans General Hospital Biobank
- Kaohsiung Medical University Biobank
- E-Da Hospital Biobank



Taoyuan City
- Linkou Chang Gung Memorial Hospital Biobank
- Landseed International Hospital Biobank
- Ministry of Health and Welfare Taoyuan General Hospital Biobank

New Taipei City
- Far Eastern Memorial Hospital Biobank
- Taipei Tzu Chi Hospital Biobank

Taipei City
- Tri-Service General Hospital Biobank
- Taiwan Biobank
- National Taiwan University Hospital Biobank
- Koo Foundation Sun Yat-Sen Cancer Center Biobank
- Taipei Veterans General Hospital Biobank
- Mackay Memorial Hospital Biobank
- Taipei Medical University Biobank
- Taipei City Hospital Biobank
- Cathay General Hospital Biobank
- MJ Health Data and Biobank
- Shin Kong Wu Ho-Su Memorial Hospital Biobank

Keelung City
- Keelung Chang Gung Memorial Hospital Biobank

Yilan City
- Lotung Poh-Ai Hospital Biobank

Hualien County
- Hualien Tzu Chi Hospital Biobank

Note: Biobank type
- Specific group (disease) specimens
- Population (healthy people) specimens
- Specific group (disease) and population (healthy people) specimens

Fig. 1-1-3 Distribution of Taiwan's biobanks

II. Current state of Taiwan's biobanks

(I) Development strategies of Taiwan's biobanks

To make Taiwan a biomedicine technology island, patient-centered precision medicine and the application of health big data analysis will become the critical development trends in the biomedical industry in the future. Thus, gradually extending and stabilizing Taiwan's biobank network and connecting biobank database information to domestic health big data will become the foundation of precision medicine in the future.

The development strategy of Taiwan's biobanks spanned four stages, from version 1.0 to version 4.0. The respective key implementation points of each stage are specimen collection, specimen use, digital integration, and database value-added application. The goals are to lead industry development, increase social welfare, increase data value, and refine data foundations (Fig. 1-2-1).

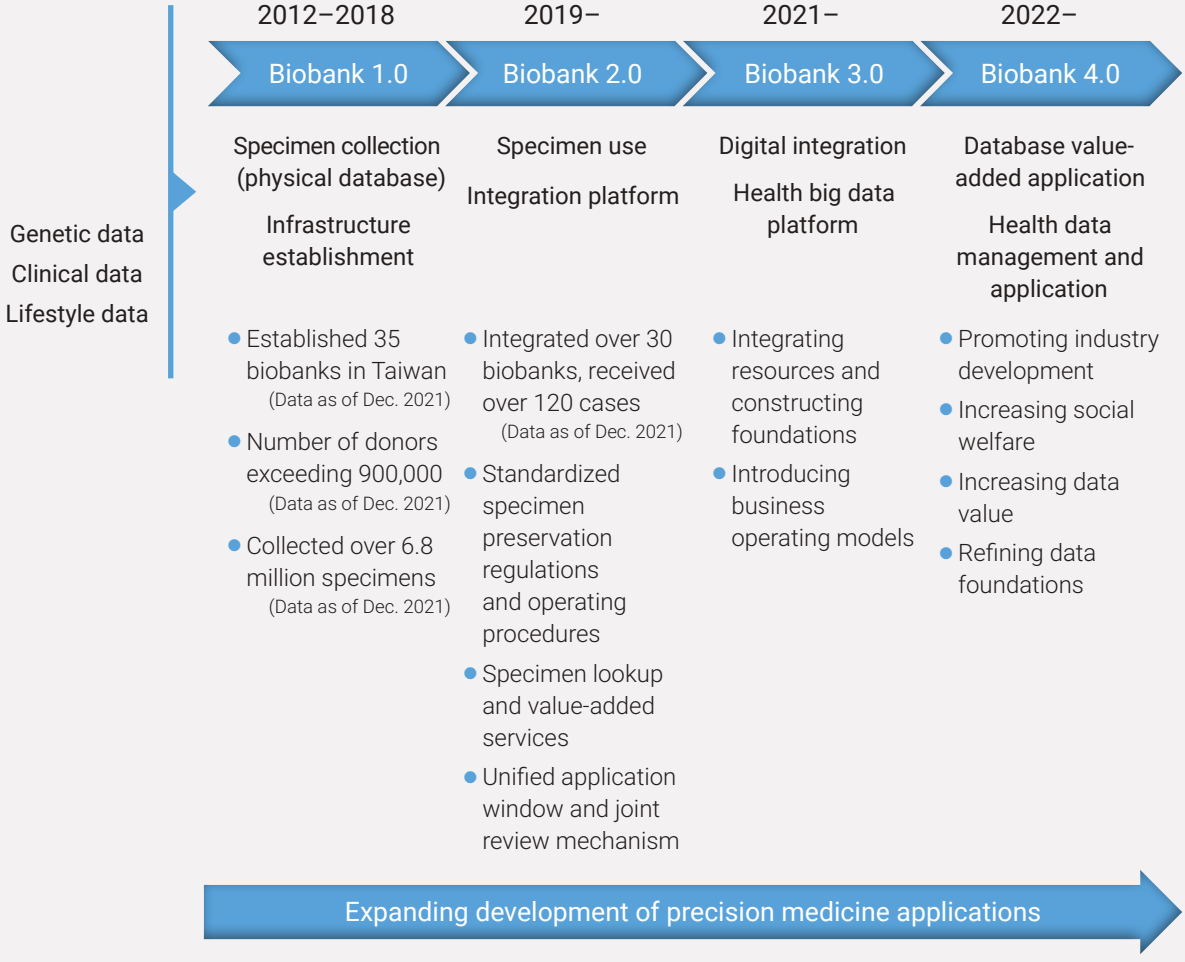


Fig. 1-2-1 Development history of Taiwan's biobank ecosystem

(II) Specimen collection and application of Taiwan's biobanks

To date, Taiwan has 35 biobanks that collect and store human specimens and health information. After data integrated analysis, they have derived various types of databases, such as specimen banks, clinical databases, genetic databases, and biomarker databases. Relevant data has been used by industry, academia, research, and medicine for research. The research and development results serve as critical references for improving the health of the public (Fig. 1-2-2 shows the specimen and data application process).

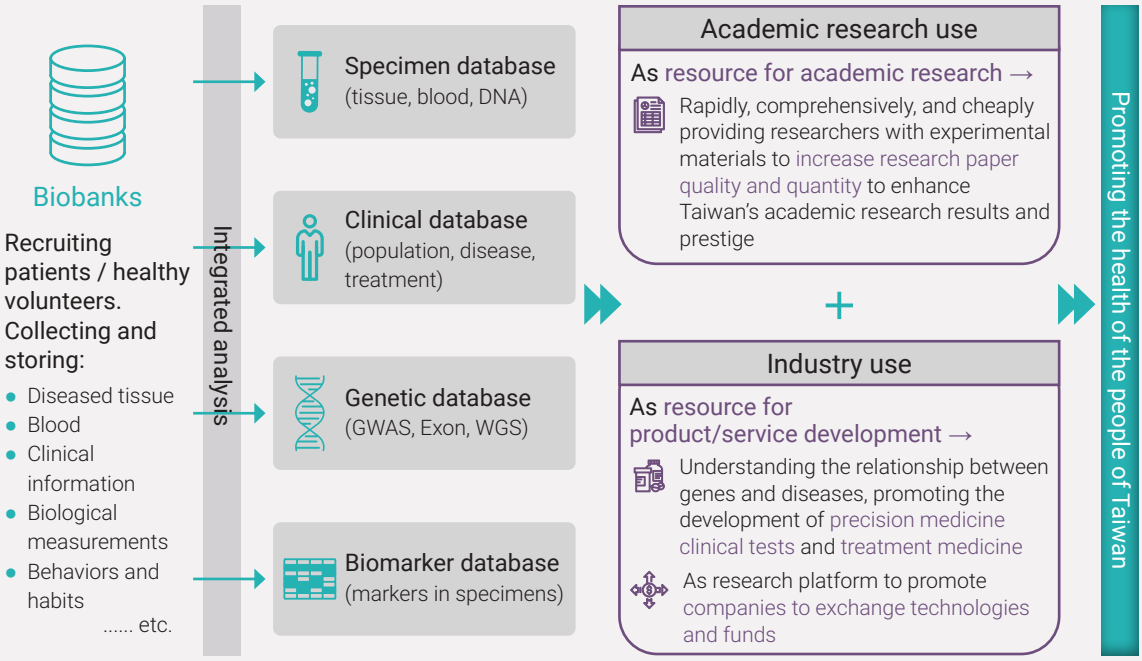


Fig. 1-2-2 Specimen and data application process of Taiwan's biobanks

The biological specimens collected by the 35 biobanks in Taiwan can be divided on the basis of their sources into population specimens (healthy people), specific disease specimens, and population and specific disease specimens. In Taiwan, most biobanks (24; 68.6%) collect specimens of specific diseases (Fig. 1-2-3).

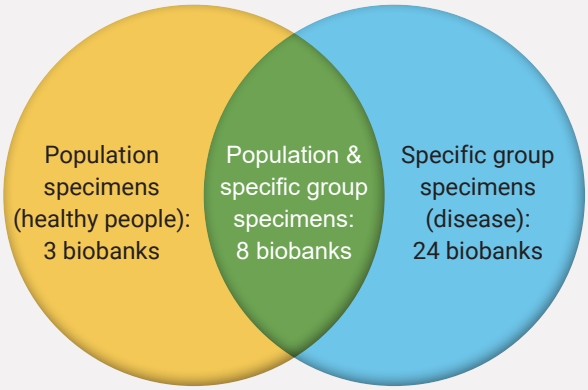


Fig. 1-2-3 Sources of biological specimens from Taiwan's biobanks

A further classification of the biological specimen types of biobanks in Taiwan is as follows (Table 1-2-1):

Table 1-2-1 Biological specimen types of biobanks in Taiwan

Specimen type	Included items
Blood specimen	Blood, serum, plasma, leukocyte
Tissue specimen	Frozen tissue blocks, paraffin blocks, paraffin sections
Body fluid specimen	Urine, pleural fluid, ascitic fluid, bone marrow fluid, cerebrospinal fluid
DNA/RNA specimen	Blood DNA, frozen tissue DNA, frozen tissue RNA

The number of specimens collected and the number of participants in the biobanks have been analyzed. As of the end of 2021, a total of 913,454 people participated in data collection, of which 299,962 were medical institution participants (33%), and 613,492 were non-medical institution participants (67%) (Fig. 1-2-4).

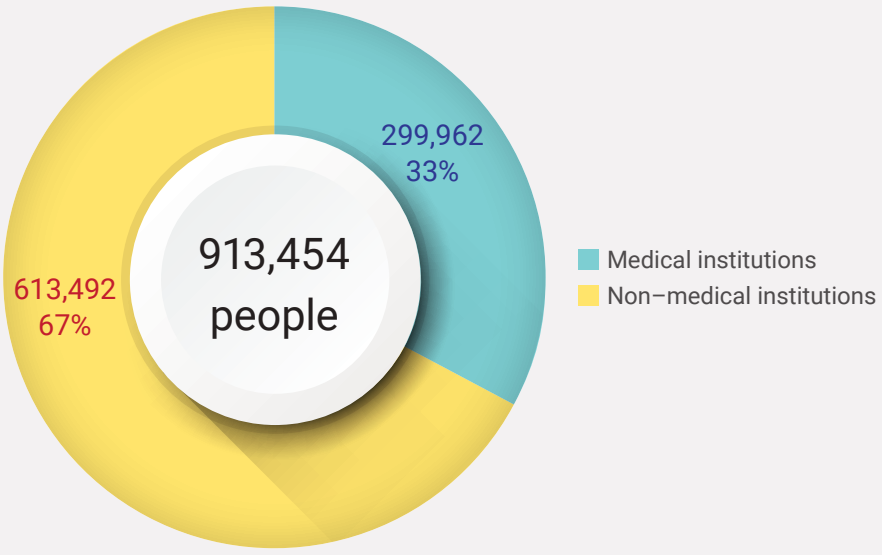


Fig. 1-2-4 Total number of participants in biobank biospecimen collection

Regarding biospecimen collection, as of the end of 2021, the total number of biospecimens collected was 6,844,648, among which blood specimens formed the majority (4,603,513; 67%). As for the numbers of specimens collected by the different types of institutions, medical institutions collected 868,988 biospecimens and non–medical institutions collected 5,975,660 biospecimens (Figs. 1-2-5 to 1-2-7).

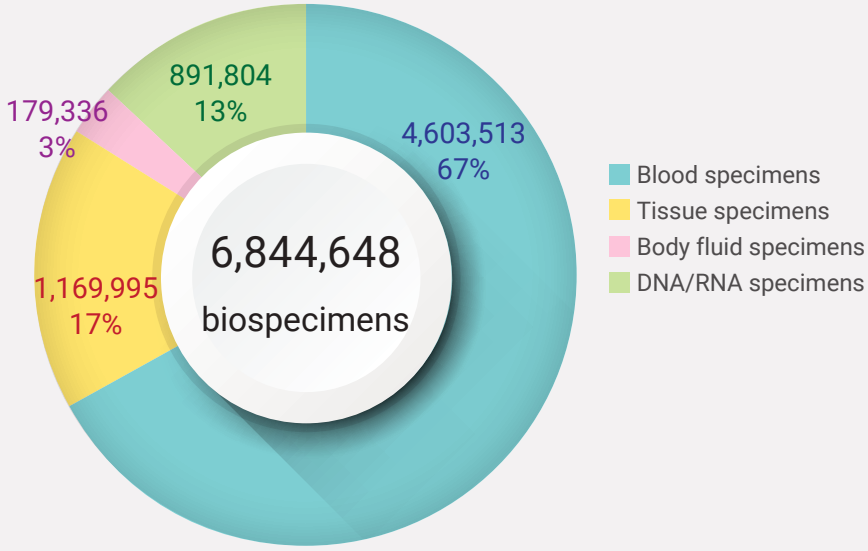


Fig. 1-2-5 Total amount of biospecimens collected by Taiwan's biobanks

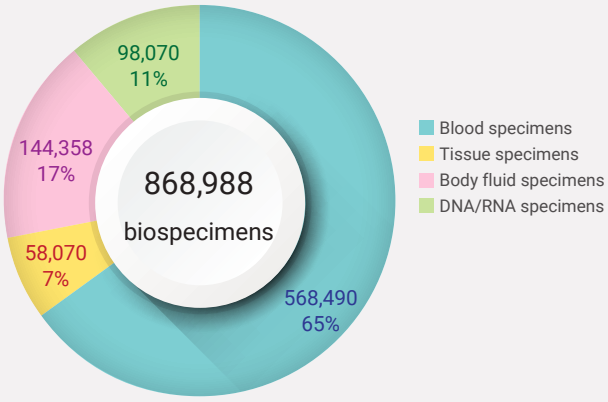


Fig. 1-2-6 Total amount of biospecimens collected by Taiwan's biobanks: collected by medical institutions

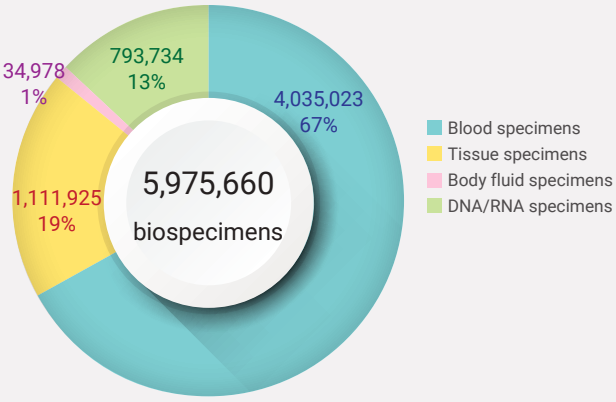


Fig. 1-2-7 Total amount of biospecimens collected by Taiwan's biobanks: collected by non–medical

Regarding the use of biological specimens, a total of 352,528 biospecimens were used, the majority being DNA/RNA specimens (187,627; 53%). As for the usage of specimens by the different types of institutions, medical institutions used 62,737 specimens, most of them tissue specimens (30,866; 49%), while non–medical institutions used 289,791 biospecimens, most of them DNA/RNA specimens (182,458; 63%) (Figs. 1-2-8 to 1-2-10).

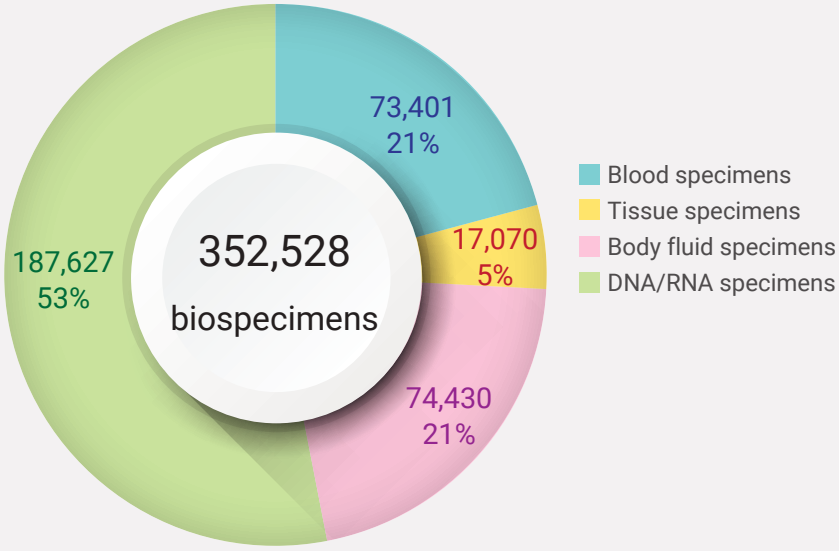


Fig. 1-2-8 Total usage of biospecimens from Taiwan's biobanks

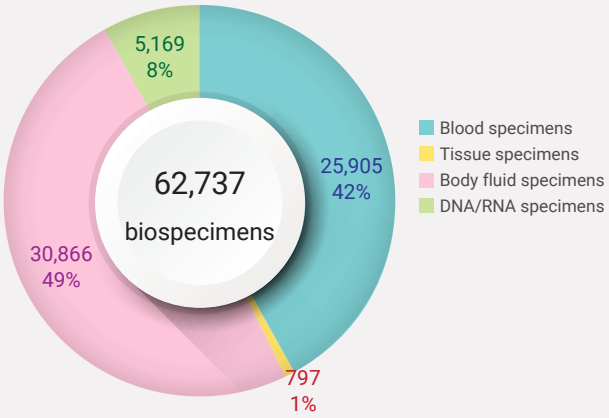


Fig. 1-2-9 Biospecimens from Taiwan's biospecimens: usage of medical institutions

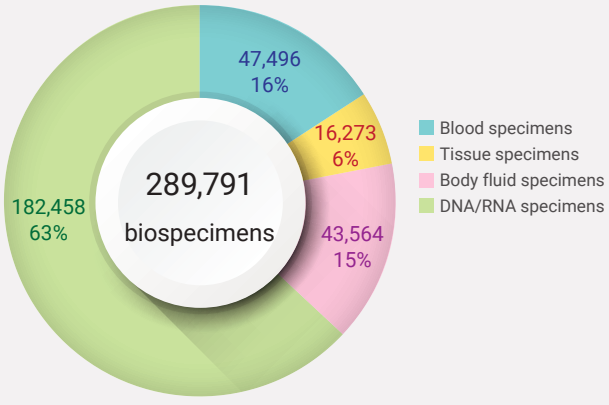


Fig. 1-2-10 Biospecimens from Taiwan's biospecimens: usage of non–medical institutions

As for the number of applications for research, as of the end of 2021, a total of 1,517 applications for research have been received; 747 (49%) from medical institutions and 770 (51%) from non–medical institutions (Fig. 1-2-11). Regarding research results, a total of 744 studies have been produced, 265 (36%) by medical institutions and 479 (64%) by non–medical institutions (Fig. 1-2-12).

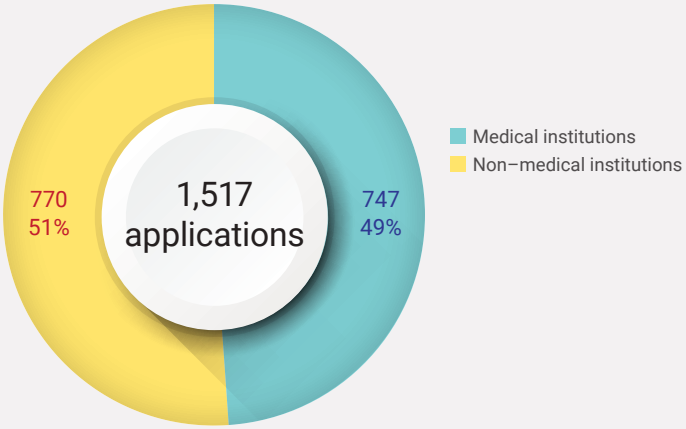


Fig. 1-2-11 The number of applications for research by Taiwan's biobanks

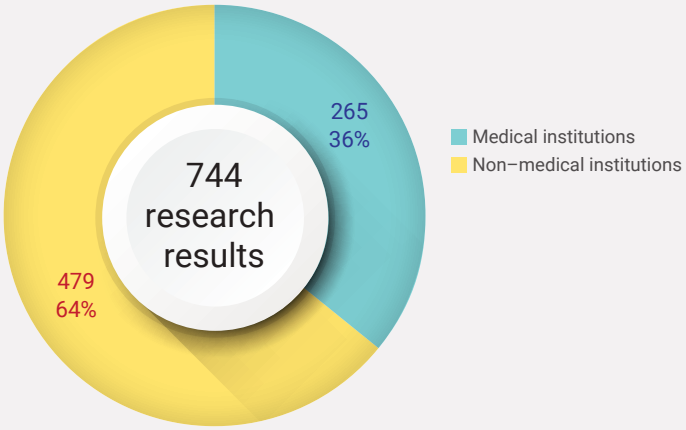


Fig. 1-2-12 Regarding research results by Taiwan's biobanks

Analysis has revealed that Taiwan's biobanks are still at the beginning stage of collecting and using specimens, applying for the use of specimens for research, and producing research results. The biobanks have diversified establishment purposes, attributes, and specimen types. Thus, through the joint effort of the government, biobanks, industry, academia, research, and medicine, Taiwan will continue to accumulate capacity to realize the strong potential of the biomedicine field and shine on the international stage.

Chapter II
Making the biobank network more robust

Chapter II. Making the biobank network more robust

I. Building on the experience of others

In 2009, TIME magazine predicted that biobanks would become one of the 10 innovative scientific ideas that would change the world. Biobanks are the foundation for effectively implementing precision medicine. They also play a mediating role between biomedicine and research and industry. By collecting a variety of clinical specimens and data, we can accumulate the power of biomedicine big data and achieve personalized and precise medical services. Countries around the world have proactively established biobanks (Fig. 2-1-1). On the basis of their medical, health, and technology policies, they have established relevant laws and management regulations. Representative management models of biobanks in foreign countries are organized in Table 2-1-1.

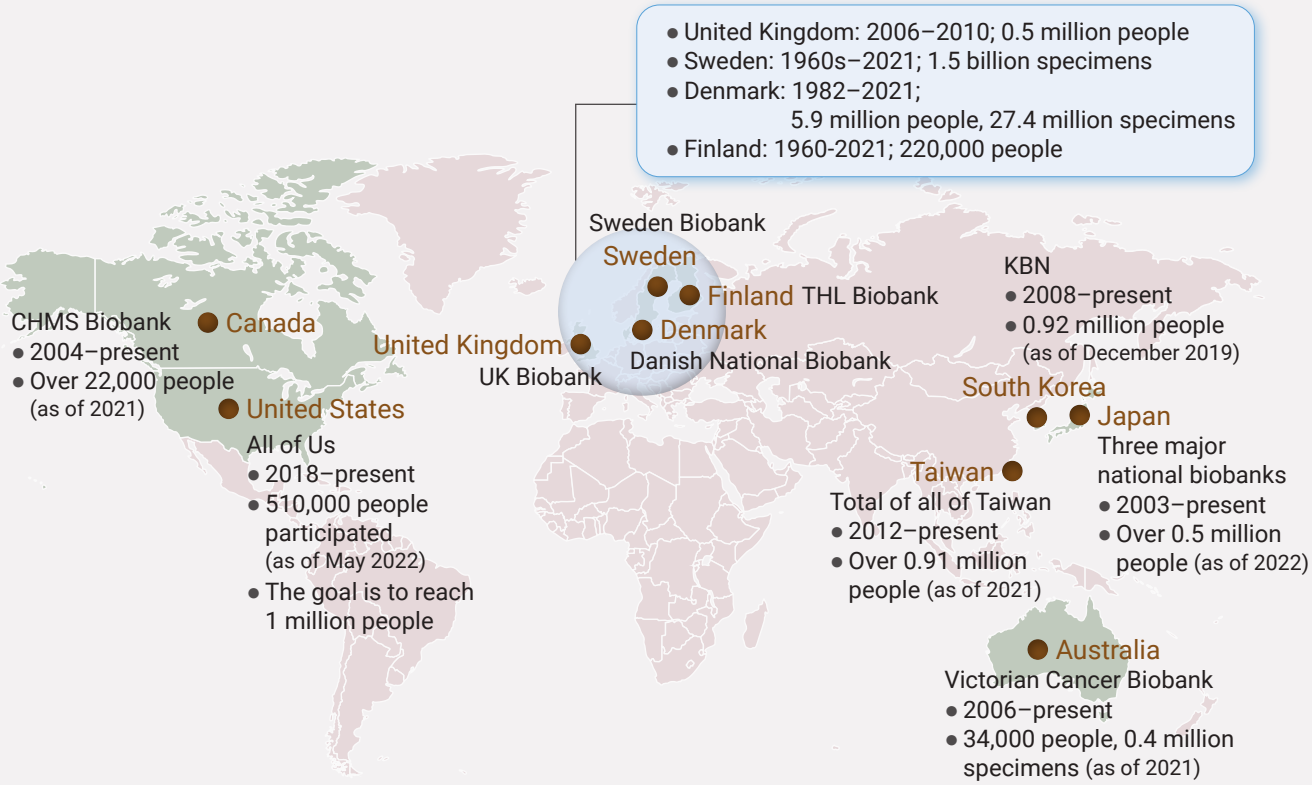


Fig. 2-1-1 Biobanks and recruitment situations worldwide

Table 2-1-1 Representative biobank ecosystems abroad

Country	Major database	Management regulation type	Establishment business model	People who can use it
Australia	Australiasian Biospecimen Network Association (ABNA)	Existing guidelines and regulations for biobanks to follow. Each state government establishes detailed management regulations.	Each state government integrates biobanks within the state. Different states exchange and share their data.	Not restricted to specific types. Domestic and foreign profit and non-profit organizations may apply to use the data.
Sweden	Sweden Biobank	Established a designated law for biobanks and conducts top-down management.	A national information integration platform was established to organize regional bio-databases. Guidance for application was provided to accelerate the process.	Domestic profit or non-profit organizations may apply for use. Foreign parties who apply to use the data must obtain a guarantee from the biobank.
United Kingdom	UK Biobank	Existing guidelines and regulations for biobanks to follow. Each biobank establishes its own management and usage framework.	A policy and special project were undertaken to promote the establishment of large-scale biobanks. Healthy people were recruited and follow-ups were conducted.	Not restricted to specific types. Domestic and foreign profit and non-profit organizations may apply to use the data. Large-scale cooperation research projects are possible.
Canada	Canadian Tumour Repository Network (CTRNet)	Existing guidelines and regulations for biobanks to follow. Each biobank establishes its own management and usage framework.	Biobanks with specific diseases were integrated using an information platform. The optimal practical operations of biobanks were shared, and education was provided.	Not restricted to specific types. Domestic and foreign profit and non-profit organizations may apply to use the data.
South Korea	National Biobank of Korea (KBN)	Established a designated law for biobanks and conducts top-down management.	Established a national large-scale biobank. It is in charge of coaching other domestic biobanks and of the information integration network.	Only open to qualified domestic research institutes and domestic researchers for research use for public benefit.

(continued)

Table 2-1-1 Representative biobank ecosystems abroad (continued)

Country	Major database	Management regulation type	Establishment business model	People who can use it
Denmark	Danish National Biobank	The regulation of biobanks is included in laws on biomedical research.	A national large-scale biobank integrates the specimens of individual organizations to centralize the management, handling, and output.	Open to domestic non-profit research institutes to apply to use the data. Other institutes must cooperate with the aforementioned institutes if they wish to apply.
Finland	FinBB	Established a designated law for biobanks and conducts top-down management.	Several regional biobanks founded a joint organization to integrate their information and services.	Not restricted to specific types. Domestic and foreign profit and non-profit organizations may apply to use the data. Large-scale cooperation research projects are possible.
United States	All of Us Research Program	Existing guidelines and regulations for biobanks to follow. Each biobank establishes its own management and usage framework.	A policy and special project were undertaken to promote the establishment of large-scale biobanks. Healthy people were recruited and follow-ups were conducted.	Not restricted to specific types. Domestic and foreign profit and non-profit organizations may apply to use the data. However, each biobank has different regulations.
Japan	Three major national biobanks; Medical colleges biobanks	Existing guidelines and regulations for biobanks to follow. Each biobank establishes its own management and usage framework.	Some of the biobanks were constructed under a national project. Some were owned by academic and research medical institutes. Under the AMED plan, their catalogue was integrated.	No regulations. Each biobank establishes its own regulations.

Different countries have different models for the establishment of biobanks, the collection and handling of specimens, the management and integration of data, and the application for data. Regarding the legal structures, some countries have established designated laws and conduct

top-down management; some countries use existing guidelines or regulations as the basis for biobanks to follow, allowing each biobank to establish its own management and usage framework. In terms of business integration models, some countries have established national or regional biobanks for integration, some governments have promoted large-scale biobank recruitment. As for data application, most countries do not restrict the types of applicants, while a small minority of countries only allow non-profit research institutes to apply for use of the data.

European countries are more comprehensive in the establishment of national biobanks and in data collection and use. They integrate existing data, and their governments lead the integration to connect with various databases. Their data research applications are also more open. Asian countries mainly establish new biobanks.

Although each country has different regulations and different medical infrastructures, they all work toward data integration and expansion of biobanks. Taiwan referenced Finland and the the Biobanking and BioMolecular Resources Research Infrastructure – European Research Infrastructure Consortium (BBMRI-ERIC) of the European Union to establish a system suitable for the domestic demands. Individual biobanks were connected and the NBCT was established for research and value-added applications. We hope to connect and integrate the existing national health insurance database, cancer registration files, and birth and death files to expand and extend bio-information and data. We also hope that in the future, we can have actual cooperation with the biobanks of different countries and enter the ecosystem of international biobanks, connecting Taiwan's biomedical industry to the world.

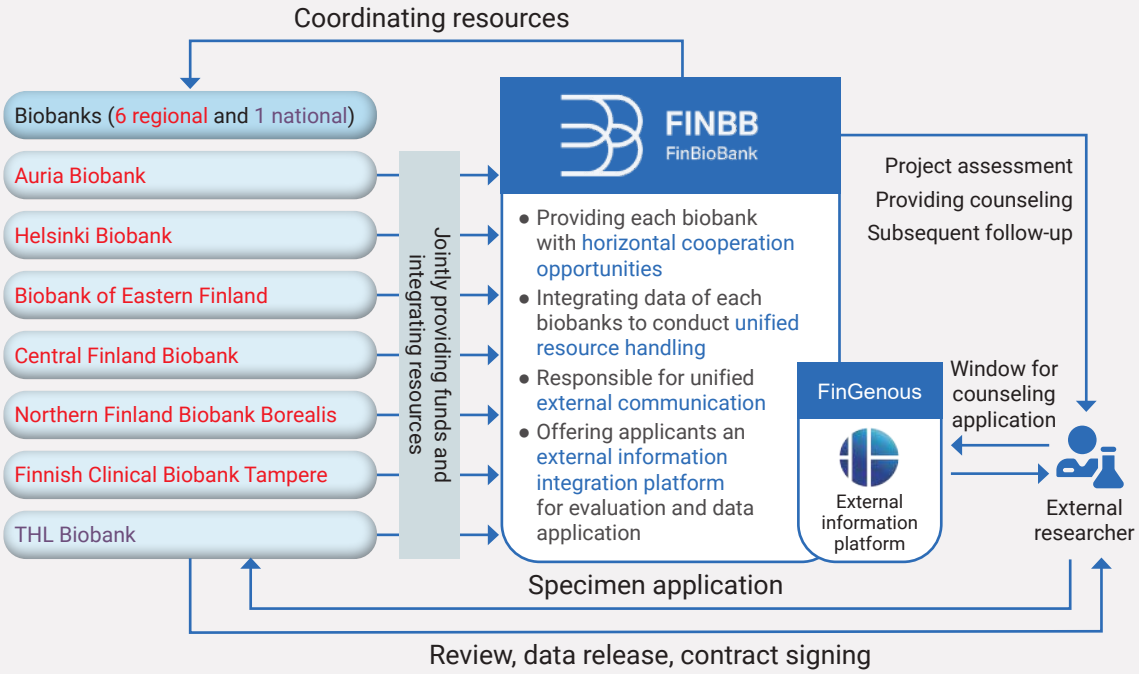


Fig. 2-1-2 Operational model of the Finland biobank integration organization, FinBB

Fig. 2-1-3 DN–TW Biobanking Collaboration Seminar, an international exchange meeting

II. Fortifying the regulatory layout

Having an environment with sound legal institutions is the first step of policy promotion. As the biomedical industry is changing with each passing day, it must be strictly regulated and monitored. The government must establish forward-looking regulations that keep up with the times and create a comprehensive environment so that industry and academia have rules to follow and that industry can thrive.

To promote the study of infectious diseases in Taiwan and to understand disease courses and causes to promote health, domestic scholars proposed in 1999 that Taiwan should have a Taiwanese biobank to precisely identify etiological agents. In consideration of that fact that specimen collection and privacy protection must follow rigorous regulations, the Taiwanese government conducted the National Research Program for Genomic Medicine Phase I in 2006. The legal status of the Precautions for the Collection of Human Specimen for Research was upgraded to facilitate the collection of human tissues, and the Draft of the Human Tissue Act and the Draft of the Genetic Information Privacy Protection Act were drafted in consideration of the demand for genetic privacy in the post-genetic era. Later, in response to doubts about the ethical, legal, and social implications brought by biomedical research across genes, medical history, family history, or information at the molecular level, multiple parties conducted debates while referencing the experiences and regulations of countries such as Iceland, the United Kingdom, and Estonia. In terms of form, a grand law structure was selected that covers all biobanks. Finally, on February 3, 2010, the Human Biobank Management Act was promulgated by presidential

decree to become the basic and special law for regulating biobanks in Taiwan. It is used to regulate the establishment, management, and use of biobanks to protect participants' rights, promote medical development, and increase people's health and well-being.

Subsequently, on the basis of this act, related regulations for all aspects of biobanks were established to create comprehensive legal procedures for biobanks. For example, the Human Biobank Information Security Specifications were established to ensure information security management; the Benefit Sharing Regulations of Human Biobanks regulate the benefits generated from commercial use to give back to the population or specific groups of the participants; the Administrative Regulations on the Establishment of Human Biobanks detail the applicants' qualifications, application procedures, conditions for establishing a biobank, review standards, regular inspections, and relevant management and other items for compliance; and the Application Instructions on the Establishment of Human Biobanks were announced as the basis for organizations to apply for establishing biobanks, extension to period of validity, altering establishment plan content, and transferring biobank databases. Moreover, to facilitate international cooperation and not hinder the interests of countries and the rights of participants, the Criteria for Review of International Transmission of Human Biobank Data or Export of Biospecimen Derivatives were announced, which stipulates that the international transmission and export of biological specimens requires applying to the competent authority for approval. The history of the regulations of biobanks in Taiwan is shown in Fig. 2-2-1.

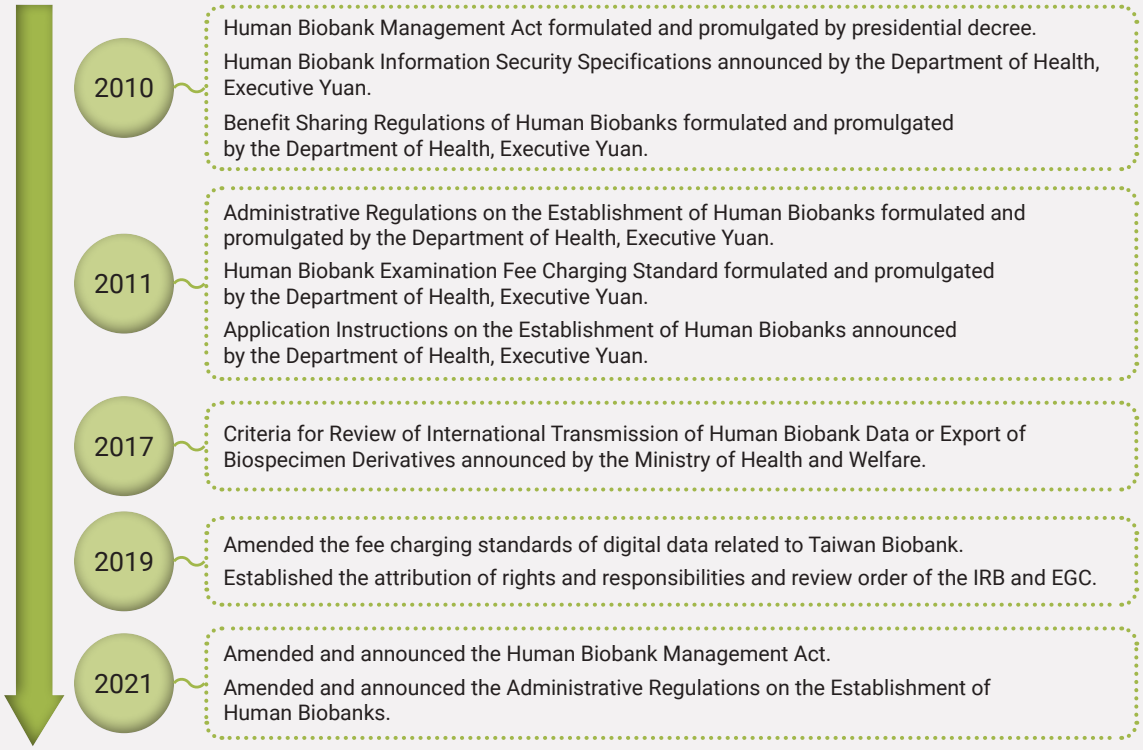
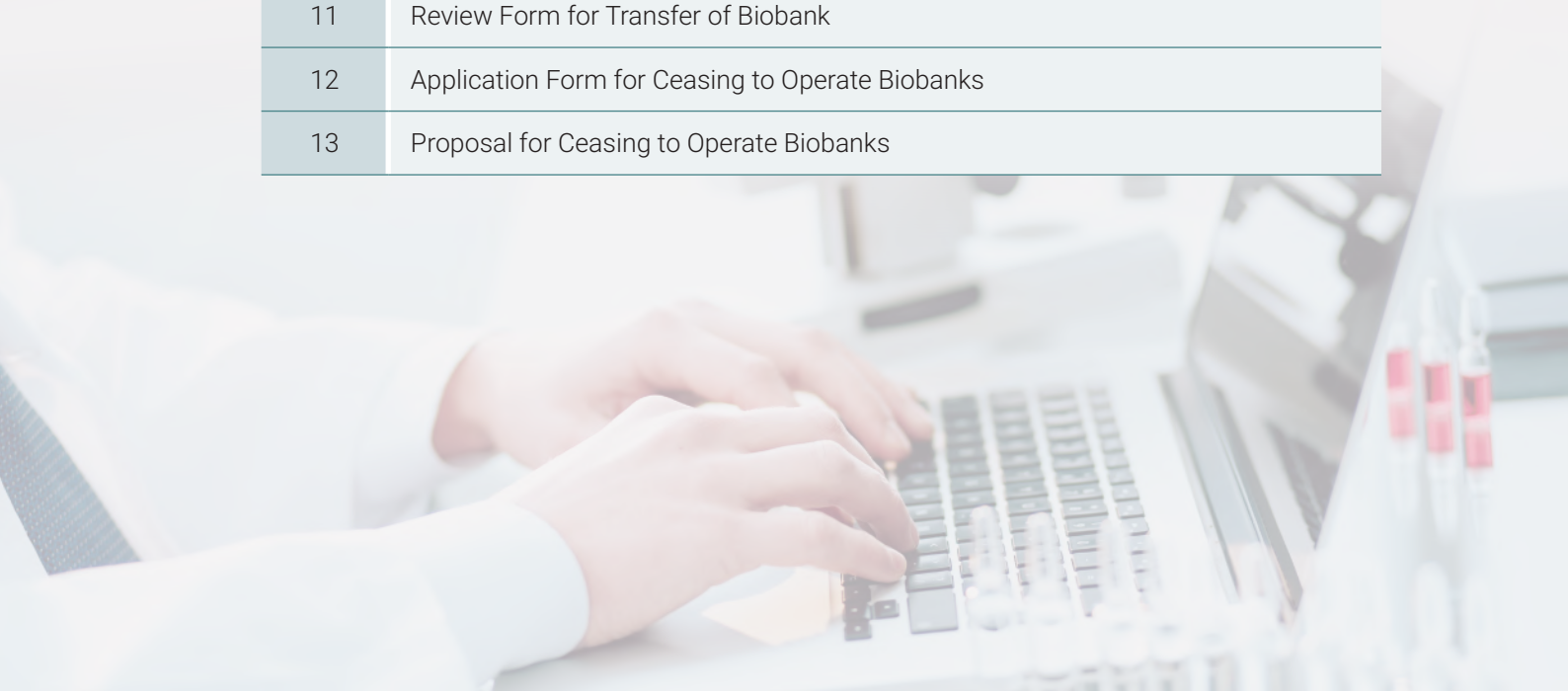


Fig. 2-2-1 History of the laws on Taiwan's biobanks

In 2020, in line with the amendments of regulations, the operating procedures and the inspection standards were reviewed while integrating the review and inspection operations of biobanks were integrated. A total of 13 related review documents and forms were standardized (Table 2-2-1) to improve the review efficiency and establish standards for compliance.

Table 2-2-1 Relevant review documents and forms

Number	Document/form name
1	Instructions for Application for Establishment, Extension to period of validity, Change, and Transfer of Biobanks
2	Application Form for Establishing Biobanks
3	Proposal for Establishing Biobanks
4	Review Form for Establishing Biobanks
5	Application Form for Extension to period of validity of Biobanks
6	Self-review and Review Forms of Biobank Extension to period of validity
7	Application Form for Change of Recorded Items in Biobank Establishment
8	Review Form for Change of Recorded Items in Biobank Establishment
9	Application Form for Transfer of Biobank
10	Proposal for Transfer of Biobank
11	Review Form for Transfer of Biobank
12	Application Form for Ceasing to Operate Biobanks
13	Proposal for Ceasing to Operate Biobanks



III. Ensuring operational quality

To ensure the operational quality of biobanks and the stability of their future development, the Taiwanese government referenced the management models of other countries, and in 2017, it commissioned the Joint Commission of Taiwan to plan and draft a biobank inspection system and conduct onsite inspection operations.

The Joint Commission of Taiwan established review criteria and grading descriptions by referencing Taiwan's biobanks establishment permits and review content for extension to period of validity and international regulations such as those of the UK Biobank, with management responsibilities of the Ethical Governing Committee (EGC), specimen quality, and information security as the framework. For the establishment, they also invited experts in the fields of law, medical ethics, biomedicine, information, and participant protection, as well as people who run biobanks, to provide practical opinions.

The inspection criteria content consists of 7 chapters (Table 2-3-1) and 32 criteria. By ensuring the quality of the relevant operations of each aspect of the biobanks, with important points including the organizational functions, operations, and written operating procedures of the biobanks and the establishment of educational training mechanisms for relevant personnel, the professionalism of the biobanks is ensured. Regarding the EGC, the composition of the members, their avoidance of conflicts of interest, and the principles for reviewing the Informed Consent Form are clearly regulated. Regarding biospecimen management, quality management of collection, storage, application, and destruction must be ensured. As for information security management, biobanks must have comprehensive policies and operational regulations for comprehensive information management and security, ensuring that information is confidential, secure, and complete, in order to protect personal data from being lost or misused. Moreover, information confidentiality measures and access control mechanisms must be clearly defined. To ensure that biobanks can operate normally and to ensure that the specimens are stored safely, the regulations should also cover the response measures to abnormal incidents and accidents as well as review and improvement mechanisms. In addition, studies using biodata be given back to the human population groups or specific population groups to which the respective participants belong . Thus, the criteria also specify that the biobank must coordinate the planning and management of the commercial application benefits that may be derived from biological samples to promote medical development.

Table 2-3-1 Biobank inspection standard

Chapter	Content	Number of criteria
1	Comprehensiveness of the operations and written operating procedures of biobanks	5
2	Biobank EGC operation management	5
3	Biospecimen management	7
4	Information security management	8
5	Rigorousness of participant protection	3
6	Abnormal incident management	2
7	Handling of biodata, results, and benefit feedback	2
Total number of criteria		32

After two cycles of inspection operations, the results showed that onsite inspection helps to improve the quality of biobanks. In the future, inspection operations will continue to be held to improve the operational efficiency of biobanks, and the results will serve as reference for extension to period of validity of biobanks. Through this, the goal of continuously improving and ensuring the operational quality of biobanks can be achieved, making the overall operation more refined.

Moreover, to ensure the quality of inspection surveyor and to reinforce the inspectors' professional abilities and attitude, allow members to understand the inspection system and their roles and functions, familiarize them with inspection skills, and to reinforce their onsite inspection surveyor communication and coordination abilities, continuing educational training courses were organized for inspectors in 2020. The content consisted of the development of the inspection system and the current implementation of biobanks, inspection criteria and key points, onsite inspection interview skills, and inspection experience sharing. By conducting an onsite observation at the Taiwan Biobank at Academia Sinica, they were able to understand the actual operation of biobanks. Case studies were incorporated for the committee members to discuss, allowing them to get a profound understanding of their roles, tasks, and values (Fig. 2-3-1)

Fig. 2-3-1 Continuing educational training courses for biobank inspection surveyor

IV. Increasing people's knowledge and capability

The biobank onsite inspection conducted in the first year collected relevant information from various biobanks, such as recruitment numbers and application numbers. The results showed that most biobanks did not operate ideally as the numbers of specimens collected and the output of research results was less than expected. Therefore, in 2018, the Ministry of Health and Welfare commissioned the Joint Commission of Taiwan to implement the Enhancing the

Utility of and Adding Values to Biobanks in Taiwan. By reviewing foreign literature on biobanks, using a questionnaire survey on domestic biobanks, and conducting forums for exchange (Fig. 2-4-1) and expert focus interviews, the challenges faced in the development domestic biobanks were organized. These challenges included the lack of stability and educational training of the employees of biobanks, the inconsistency of the quality of specimen collection and management, and individual biobanks discriminating against one another.

The cultivation of the personnel of biobanks is the foundation for long-term development. Further exploration of the educational training of personnel revealed that the educational training they received was mainly general hospital training (such as infection control and patient safety), but few of them offered training content related to the practical operation of biobanks. To enhance researchers' basic understanding of biobanks and reinforce their professional knowledge of regulations on the personnel, ethics, biospecimens, and administrative management of biobanks (Fig. 2-4-2 shows the educational training course planning workshop team), diversified biobank-related educational training courses (including workshops) are offered. In addition to providing people involved in domestic biobanks with channels to receive educational training, a serioes of courses were also offered to reinforce participants' basic concepts and to create consensus regarding operations among biobank workers.

Fig. 2-4-1 Forum on biobanks

Starting in 2019, the Ministry of Health and Welfare has commissioned the Joint Commission of Taiwan to hold biobank educational training. To date, 7 sessions have been held with a total of 852 participants, including 394 employees of biobanks, 227 EGC committee members, 124 IRB members, 59 administrative workers, and 48 researchers. (The course topics are presented in Table 2-4-1, and photos of the courses are shown in Fig. 2-4-3.)

Fig. 2-4-2 The Biobanking Training Program: Increasing Knowledge and Advancing Proficiency for Biobankers: Educational Training Course Planning Advisory Committee members

Fig. 2-4-3 Photos from biobank educational training courses

Table 2-4-1 Educational training courses for biobank-related personnel

Number	Course topic
(I) Basic courses	
1	Development history, current state, and future development trends of Taiwan's biobanks
2	Regulations related to biobanks
3	Ethical considerations for biobanks
4	Feasibility of using biobanks in business and medicine
5	Experience sharing on the application and implementation of biobank research cases
6	International trends on the regulation and management of biobanks
(II) Professional courses: biospecimen personnel	
1	Processing principles and management key points of biospecimens in biobanks
2	Biobank biospecimen treatment experience sharing
3	Biobank infectious disease biospecimen of processing principle and application sharing
4	Workshop for case discussion of biospecimen handling in biobanks
(III) Professional courses: information security personnel	
1	Biobank information security management principles and case sharing
2	Biobank information security management experience sharing
3	Physical and data management (handling and identification of data of different types)
4	Case discussion workshop for biobank information security management
(IV) Professional courses: biobank EGC members	
1	Biobank EGC job responsibilities and practice sharing
2	Biobank commercial use and benefit feedback practice sharing
3	Ethical topics related to biobank and health database research
4	Biobank case review workshop

V. Strengthening the connection among biobanks

The onsite inspection of biobanks and value-added planning projects revealed that the number of specimen collection, applications, and research cases are challenges faced by Taiwan's field of biomedicine. Over half of the biobanks had zero applications. Moreover, most biobanks had restrictions on their use (such as low usage rates or being limited to internal use). If researchers need to use a large amount of data or data across different biobanks, they need to apply individually, which is inconvenient and inefficient. To increase the efficiency of biobanks, to promote data consistency, specimen standardization, and make applications more convenient, the office of the Board of Science and Technology, Executive Yuan, invited the heads of Academia Sinica and the Ministry of Health and Welfare in 2018 for five leader meetings to plan the concept and blueprint of a human bio-database integration platform. Subsequently, the Ministry of Health and Welfare invited individual biobanks and held five coordination meetings to further discuss the preparation and operation of a national-level integrated biobank platform. In the same year, the Bio Taiwan Committee (BTC) of the Executive Yuan proposed a planning report that was approved and supported by all committee members; thus, the construction of the National Biobank Consortium of Taiwan (NBCT) and the conception of its future operating mode were launched. Through the collaboration among biobanks, consistent quality standards and clinical data content were achieved, becoming the foundation for Taiwan to develop digital medicine (Fig. 2-5-1). On October 30, 2019, the Ministry of Health and Welfare announced the establishment of the NBCT, and it was implemented by the NHRI (Fig. 2-5-2).

Fig. 2-5-1 Bio Taiwan Committee

Fig. 2-5-2 Founding conference of the Taiwan Precision Medicine and Biobank Integration Platform Alliance

The NBCT was constructed on the concept of cloud databases. The biobank specimens and data of individual biobanks do not need to be transferred or concentrated; individual biobanks still have their individual autonomy. The NBCT has a central office as the single service window for the open and fair acceptance of applications. Physicians, experts in basic organism research, medical information experts, big data and artificial intelligence application experts, and relevant legal experts were invited to form an advisory and review expert committee to provide professional opinions and to shoulder the responsibility of review and audit. In the past, due to limited budgets, individual research plans of scholars and experts could not afford a large number of specimens for large-scale research; the NBCT offers free value-added services and research funds to encourage organizations to participate and increase the willingness of clinical physicians to assist in recruiting cases, thereby expanding the scale of the database of the NBCT. (Fig. 2-5-3 shows the NBCT establishment goals; Fig. 2-5-4 presents the organization of the central office; and Fig. 2-5-5 presents the application procedure.)

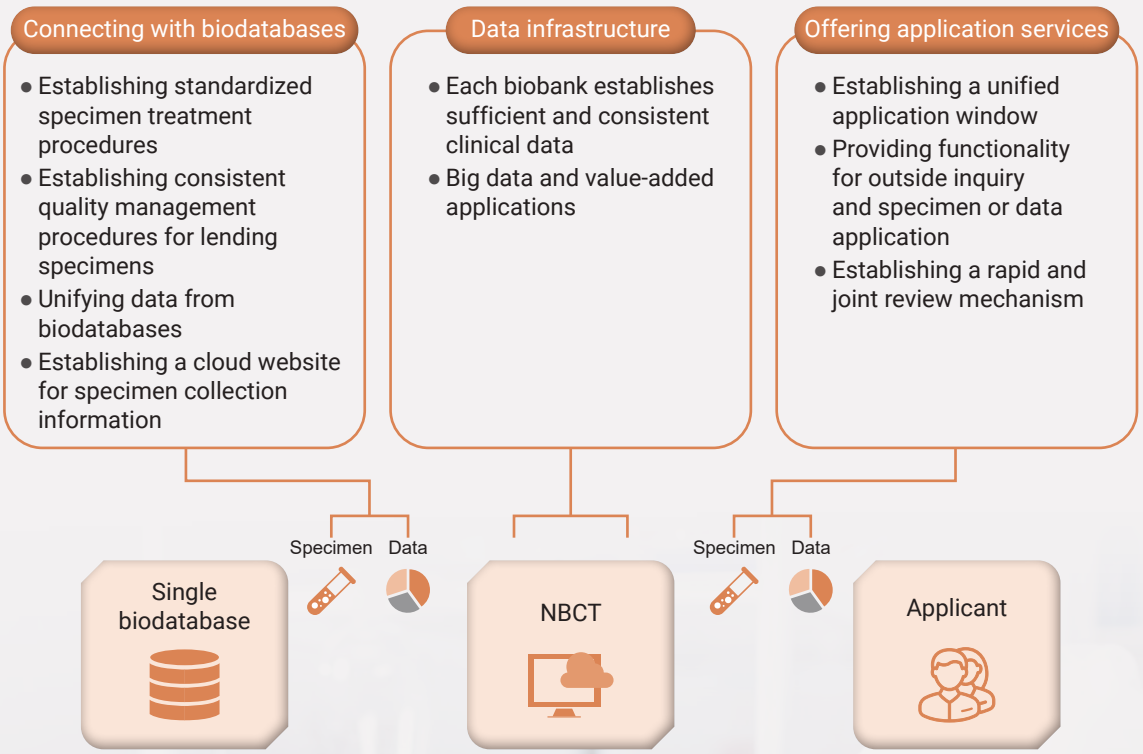


Fig. 2-5-3 Construction goals of the NBCT

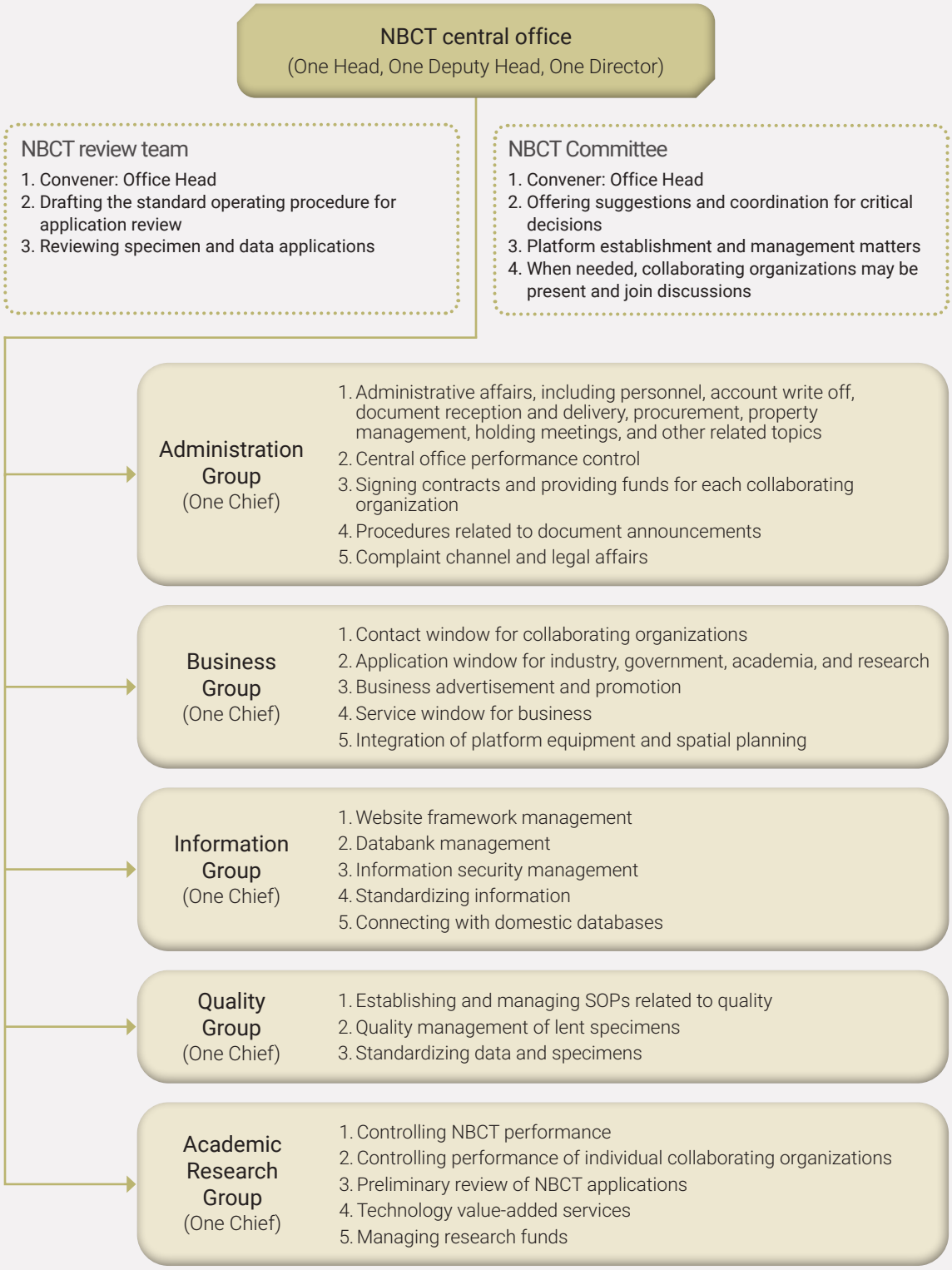


Fig. 2-5-4 NBCT central office organizational chart

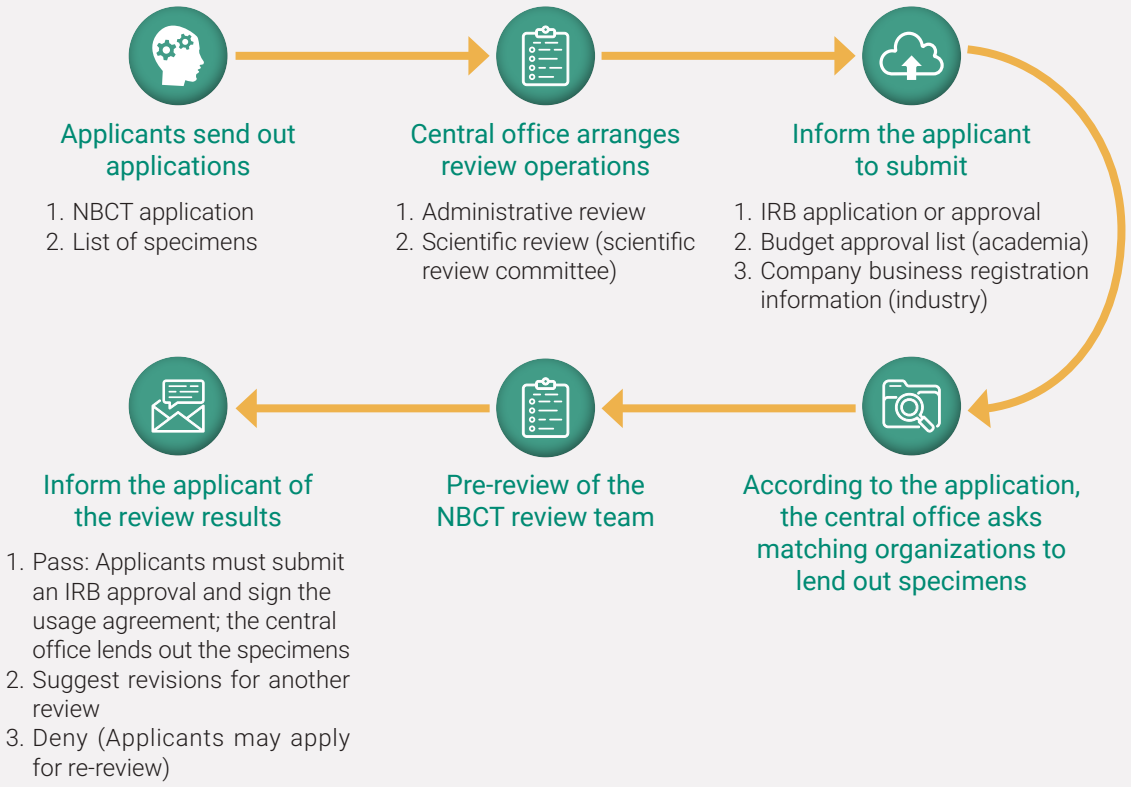


Fig. 2-5-5 NBCT application procedure

To facilitate the incorporation of data from individual biobanks and to further use the complete specimens and data, the NBCT is user-centered. It established consistent specimen quality standards, clinical data content, and charging standards (standard operating procedures are shown in Table 2-5-1). In addition, all tissues and specimens are interpreted by pathologists to ensure their quality. Specimens taken out of the databanks are irregularly inspected to understand if the quality is stable in order to ensure the accuracy of users' specimen data analysis. As for the capabilities of the NBCT website, participating biobanks can register their recruited data from their end, such as the number of disease cases and demographics. The central office can update the recruitment data in real time. The website also has functions for online application, review, and search, allowing researchers to look up specimen recruitment numbers efficiently and letting them apply directly online and track the review progress (Figs. 2-5-6 and 2-5-7).

Since its establishment in 2019, the NBCT has been joined by 32 biobanks (Fig. 2-5-8). It provides biospecimens including blood specimens (blood, serum, plasma, leukocyte), tissue specimens (frozen tissues blocks, paraffin blocks, paraffin sections), body fluid specimens (urine, pleural fluid, ascitic fluid, bone marrow fluid, cerebrospinal fluid), and DNA/RNA specimens (blood DNA, frozen tissue DNA, frozen tissue RNA).

Table 2-5-1 Standard operations of the NBCT

Number	Name of standard operating procedures
1	SOP-001_NBCT specimen and data application
2	SOP-002_NBCT specimen and data application review
3	SOP-003_Confidentialiy and conflict of interest avoidance
4	SOP-004_NBCT specimen: fresh and frozen tissue specimen, specimen collection, and DNA extraction procedures
5	SOP-005_NBCT specimen: tissue RNA extraction procedures
6	SOP-006_NBCT blood specimen handling procedures
7	SOP-007_NBCT blood specimen DNA extraction procedures
8	SOP-008_NBCT paraffin block and blank slice specimen production procedures
9	SOP-009_NBCT pleural fluid, ascitic fluid, bone marrow fluid, and cerebrospinal fluid specimen collection handling procedures
10	SOP-010_NBCT urine specimen collection procedures
11	SOP-011_NBCT specimen lending SOP (I) low-temperature shipping
12	SOP-012_NBCT specimen lending SOP (II) normal temperature shipping

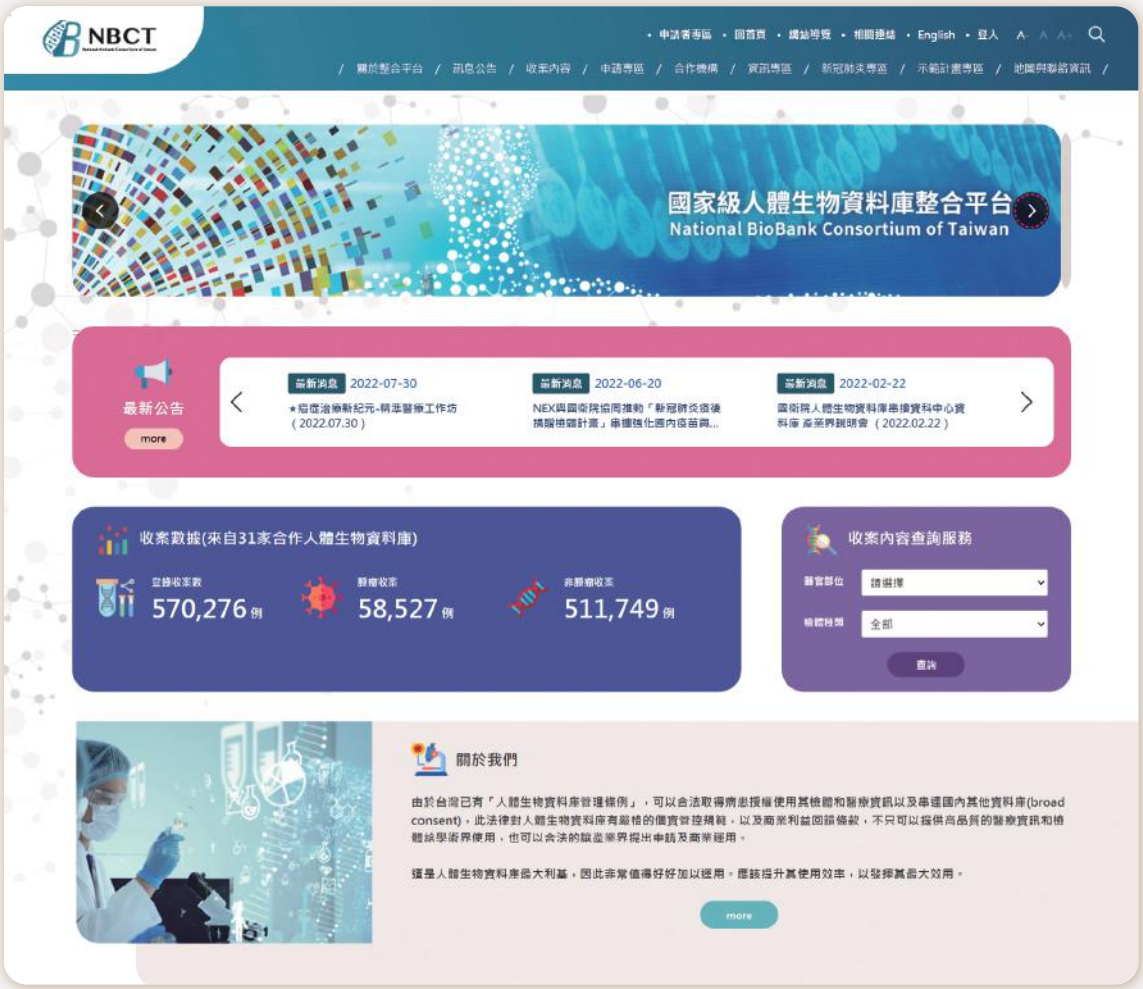


Fig. 2-5-6 NBCT website

Fig. 2-5-7 NBCT website functions

Fig. 2-5-8 NBCT contracted partners

As of June 30, 2022, the NBCT had registered 570,276 recruited cases. Of these, 58,527 were tumors and 511,749 were non-tumors. The total number of applications was 122, 104 from the medical field, and 18 from industry. The recruitment number is regularly updated on the NBCT website (Table 2-5-2). Regarding specimen recruitment numbers, the NBCT had 1,198,912 blood specimens (95%) (Fig. 2-5-9). As for individual specimen types, most blood specimens were plasma (503,313; 42%), most tissue specimens were frozen tissues (17,813; 53.6%), most DNA/RNA specimens were frozen DNA (11,915; 48.9%), and most body fluid specimens were urine (1,336; 61.6%) (Figs. 2-5-10 to 2-5-13).

Table 2-5-2 NBCT number of recruitment and number of research cases

Item		2020	2021	As of the end of June 2022	Total
Number of collaborating biobanks		25	6	1	32
Number of recruited cases registered on the NBCT		420,000	140,000	10,000	570,000
Number of applications on the NBCT	Number of applications from academia and research	39	63	2	104
	Number of applications from industry	9	6	3	18

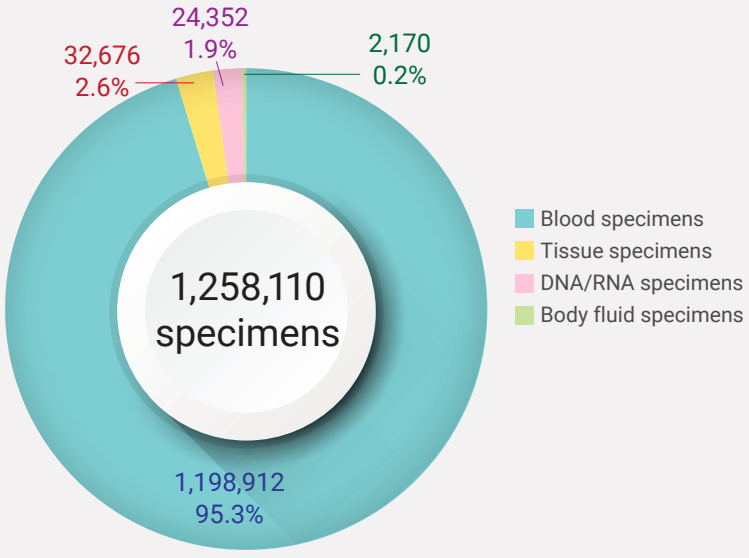


Fig. 2-5-9 NBCT specimen recruitment number

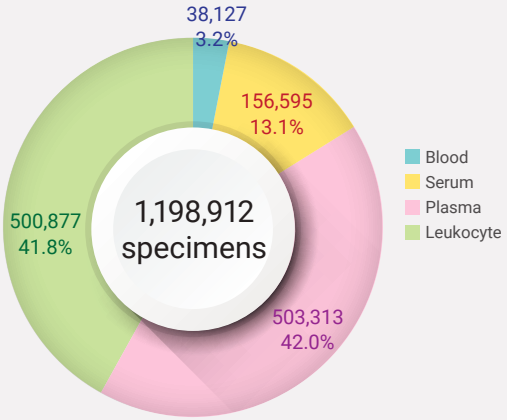


Fig. 2-5-10 NBCT blood specimen recruitment numbers

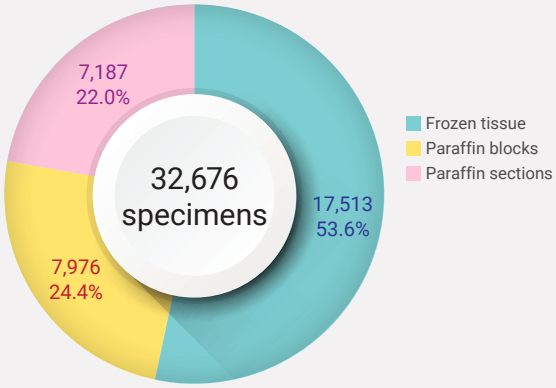


Fig. 2-5-11 NBCT tissue specimen recruitment numbers

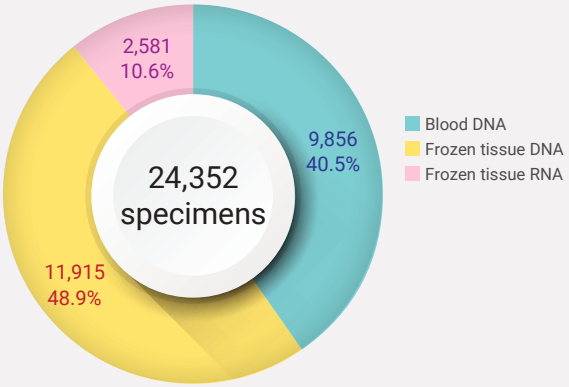


Fig. 2-5-12 NBCT DNA/RNA specimen recruitment numbers

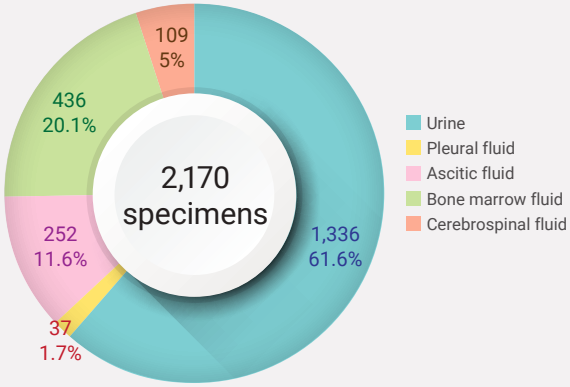


Fig. 2-5-13 NBCT body fluid specimen recruitment numbers

In 2020, Coronavirus Disease 2019 (COVID-19) pandemic became the greatest threat to human health. To gain further understanding of COVID-19 to facilitate the research and development of industry, academia, research, and medicine for pandemic prevention, the Ministry of Health and Welfare commissioned the NHRI to establish the Taiwan COVID-19 Biobank. By using the network of the NBCT, when meeting the conditions of the biosafety operating standards, specimens and clinical data from patients with COVID-19 from collaborating hospitals across the nation were collected. To date, 26 hospitals have participated. A large-scale biobank and database was established to openly share relevant information that domestic industry, academia, research, and medicine could apply to use. This database accelerated the overall pandemic prevention research and facilitated the collaboration of domestic academia and research and medical institutes regarding basic research for pandemic prevention and treatment strategies.

Currently, Taiwan's biobanks focuses on the front-end of specimen data confirmation and establishing a centralized integration platform and establishing a consistent standard for storage

and quality control for biobanks that used to be independent. In the future, we will continue to increase the operational capacity for experiments and provide value-added services such as specimen treatment and gene sequencing. In addition, we expect to start connecting existing databases such as the national health database, cancer registration, and death files. By discussing the feasibility of collaborations, we hope to introduce industry resources to assist them to develop and utilize feedback mechanisms to reuse data and research results of different sizes and scales, thereby promoting the vitalization and growth of the overall resources (Fig. 2-5-14).

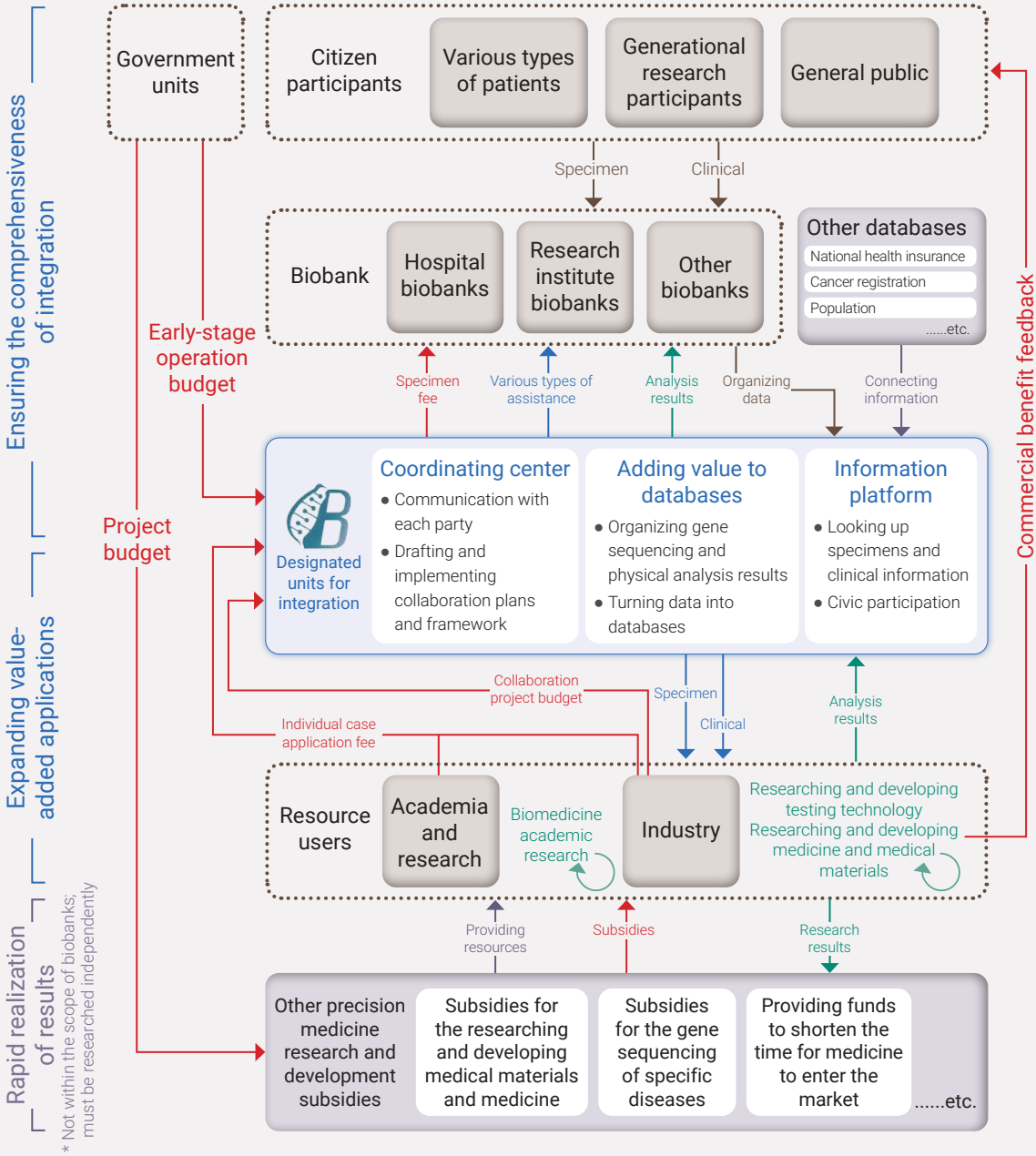


Fig. 2-5-14 Taiwan's future biobank integration and application ecosystem

Chapter III Future outlook

Chapter III. Future outlook

This annual report follows the development history of Taiwan's biobanks and leads the reader across international standards, the establishment of regulations, assurance of operational quality, personnel training, and cross-organizational integration platforms to review the evolution of the institutions related to biobanks. However, as technology keeps evolving and being innovated, the environment changes rapidly. All aspects of biobanks must keep up with the times. On the premise of protecting participants and meeting legal and ethical regulations, applications are broadened and topics are expanded.

At the present stage, the NBCT has reached a certain scale. The next step will be connecting health databases of various types to maximize the benefits of relevant information, so as to increase the value of data, promote industry applications, and increase the visibility of Taiwan's biomedical field in the world. This annual report invited experts from various fields involved in biobanks to provide their professional views and reminders about the future development of the application and ethical aspects of biobanks to serve as reference for people in different fields.

I. Expert analysis: Application of biobanks

• Application of health big data

National Institute of Cancer Research

Researcher
Yi-Hsin Yang

In recent years, precision medicine has been booming worldwide. Medical studies have been conducted to more precisely design disease treatment plans to seek maximum welfare for patients. Top research institutes worldwide have been implementing various national projects to collect data for precision medicine, such as the All of Us and CancerLinQ in the United States and the Genomics England and UK Biobank in the United Kingdom. Specifically, an innovative method is to design a set of shared data columns, allowing the electronic health record (EHR) system of each medical institute to automatically extract the information columns they need. Information is no longer obtained by manually reviewing case histories.

A key in precision medicine is to understand the correlation between multi-omics and disease treatment effects. This includes follow-up data on patients' reaction to medicines, side effects, and treatment prognoses. To obtain multi-omics data paired with specimens, the results of patients' treatment must be tracked to take full advantage of the function of multi-omics data. Thus, the current major trend of the operation of biobanks is planning the continuous organization of patients' medical information after collecting their specimens, such as treatment reactions and side effects. However, disease treatment data is patients' personal data. To collect this data, one must inform the patients and gain their consent. During the storage process,

medical institutes must protect patients' privacy and ensure information security. Achieving this while collecting enough data to meet the demands of precision medicine research is a challenge we must face.

In light of this challenge, the National Biobank Consortium of Taiwan (NBCT) information team designed the NBCT common data model (CDM). It enables interoperable collaboration and data across institutions, including patients' demographic information, diagnosis and stages, treatment process, test data, out-of-pocket items, and disease treatment tracking. To date, researchers related to biobanks in Taiwan are familiar with the governmental database format of the NBCT CDM. However, to allow international collaboration, if the NBCT CDM is to be interoperable with international large-scale databases, the data must be further reorganized using the data format standards of the Health Level Seven Fast Healthcare Interoperability Resources (HL7 FHIR) and Observational Medical Outcomes Partnership (OMOP) CDMs that are frequently used for the international exchange of data. To maintain the international competitiveness of NBCT on medical research and to provide it with the potential to collaborate with international large-scale health databases, the NBCT must continue to face the challenge of keeping up with the times.

• The basis of precision medicine

Institute of Public Health, National Yang Ming Chiao Tung University

Professor
Ming-Wei Lin

As the human genome project launched in the 1990s, scientists worldwide have been wondering how the new technologies and information brought by the project can help people understand genetic factors in complex human diseases. Conducting research related to human disease genes requires patient DNA and RNA specimens. However, early large-scale epidemiological generational studies rarely collected or stored specimens from research participants, and the progress of personalized medicine was limited. Thus, in the post-genome era, countries worldwide have established large-scale biobanks and connected the data to relevant electronic medical histories, clinical test data, and health databases for researchers to study the genes of human diseases and environmental and other risk factors, hoping to develop superior disease prevention and treatment methods. In January 2015, Barack Obama, then-President of the United States, announced the launch of a precision medicine project. The project hoped to consider individuals' factors such as gene variations, environmental exposure, and living habits to tailor the most suitable disease prevention and treatment strategies for, hoping to resolve all human health and disease problems. In recent years, countries around the world have been establishing large-scale biobanks and health databases to serve as the critical foundation for promoting precision medicine.

The founding of the National Biobank Consortium of Taiwan (NBCT) effectively integrated the specimens and clinical data of various biobanks, providing a sufficient number of disease

cases for industry, academia, research and medicine to conduct research and to find the bio and genomic markers of various diseases. Allowing the data to realize maximum benefits is conducive to developing precision medicine for various diseases.

However, it is not just Taiwan that is establishing a platform for integrating domestic biobank resources. Internationally, cooperative biobank alliances are also being set up. By integrating the biobanks of different countries, races, and ethnic groups, we can more comprehensively understand disease causes and pathogenic mechanisms, thereby developing the most suitable prevention and treatment strategies, thus maximizing the benefits of human biobanks.

The earliest international biobank cooperation alliance is the Public Population Project in Genomics, which was founded in 2012 by Quebec's CARTaGENE, the GenomEUtwin project, Estonia's genome project, and the UK Biobank. Later, Europe founded a cooperative organization of an even grander scale, the Biobanking and BioMolecular resources Research Infrastructures - European Research Infrastructure Consortium (MMBRI-ERIC), which consists of 16 regions and one international organization. The founding of alliances promotes the sufficient use of bioresources and biomedicine facilities, providing high-quality molecular biology and medical research.

In 2019, the Global Biobank Meta-analysis Initiative was established, an international cooperative alliance spanning across four continents, 19 biobanks, and 21 million people. The Taiwan Biobank of Academia Sinica is one of the members. This alliance incorporates the genetic data and electronic health records of six major ethnic groups: African, American, Central and South Asian, East Asian, European, and Middle Eastern. Different diseases have different prevalence rates and causes among different races, ethnic groups, and regions. Large-scale cross-country and cross-race genomic correlation studies and whole genome sequencing results in recent years have revealed that genetic mutations that affect disease occurrence, exacerbation, drug treatment responses, and side effects differ in different races and in different ethnic groups. In addition to some effects of common genetic variations, the effects of unique genetic mutations in specific races or ethnic groups result in the same disease having different prevalence rates in different countries, races, or ethnic groups. They may even affect treatment choices and disease prognosis. Therefore, integrating international forces to establish cooperative biobank alliances is conducive to clarifying risk factors, pathogenic gene variants, and pathogenic mechanisms of different diseases in different races or ethnic groups, thereby improving disease risk prediction and the choice of suitable medicine for treatment, increasing disease prognosis, enhancing the health of all humans, and achieving the ultimate goal of precision medicine.

II. Expert analysis: Ethical aspects of biobanks

• Ethical governance

Institute of European and American Studies / Research Center for Information Technology Innovation, Academia Sinica

Associate Research Fellow
Chih-Hsing Ho

The establishment of the NBCT has made the standardization and sharing mechanism of data more and more mature. In the future, with the increase of application cases, how to use an efficient review mechanism to fulfill the NBCT's function of integrating and uniting biobanks, while respecting the trust relationship between biobanks and participants, will determine whether the NBCT can successfully play the role of alliance and integrate resources. In the current design of the dual review mechanism, the central ethics review committee of the NBCT is only responsible for giving pre-review recommendations for the release of data and specimens. However, the decision to actually release the data and specimens is still determined by the EGC of each hospital and institution. This mechanism is to respect the autonomy of individual biobanks in the alliance of the NBCT. More importantly, it serves to maintain the long-term interaction and trust between the participants and biobanks. Therefore, each institution is entrusted with making the most appropriate measurement and judgment on whether the release of the data and specimens can conform to the governance framework of the biobank. While increasing the benefits of using biobanks, this can also take participants trust into account.

Furthermore, with the rapid development of bioinformatics and big data technology, data sharing among biobanks will rely on the establishment of a common data model. In recent years, the legislative trends of various countries are being taken into consideration, especially the emphasis on informed consent and the privacy impact assessment in the European Union's General Data Protection Regulation (GDPR). The recruitment of biobanks is based on broad consent, meaning that participants allow their data to be used for unspecified purposes in the early stage of data collection, while some biobanks also require regular follow-up and updates of the participants' health information. Thus, how to ensure that the research of biobanks can meet the goals of biomedical research and that the encryption and decryption process of data is rigorous, and the notification and disclosure obligations of the managers of biobanks are fulfilled, will also become increasingly important for transparency and accountability of biobank governance.

In the future, if biobanks can further establish an interactive participation model with participants, the participants can truly become important stakeholders of biobanks, which will further enhance the transparency and social trust of the governance framework of biobanks. Moreover, the modes of benefit sharing for commercial applications will become more diversified in the future. In addition to traditional financial interests, taking the feedback of health information

into account enables specific groups or even individuals to proactively take corresponding health risk management measures to achieve the preventive purpose of precision health. It can also increase the willingness of participants to join biobanks. Under the development of precision health and precision medicine, biobanks can truly exert the spirit of common good and reciprocity.

● Participant Protection

Human Subject Protection Association in Taiwan

Representative director
Lu-Hung Lin

Since the promulgation of the Human Biobank Management Act in February 2010, biobanks have sprung up like bamboo after rain in Taiwan. There are considerable differences in the scope, number of specimens, and utilization of the biobanks, and the same is true for the resources invested in the biobanks or their governance frameworks. However, as far as human subject protection is concerned, specimens, data and information are provided for research purposes due to altruistic beliefs. The participants of biobanks enjoy the same protection of rights and interests regardless of the biological data they have contributed. This should be a common goal that is worth working hard and must be achieved.

In 2016, the World Medical Association issued the Declaration of Taipei on Ethical Considerations regarding Health Databases and Biobanks in Taipei. Article 4 mentions that “Health Databases and Biobanks are both collections on individuals and population, and both give rise to the similar concerns about dignity, autonomy, privacy, confidentiality and discrimination”. This concern is also a primary ethical issue for the protection of biobank participants.

First of all, in terms of respecting the dignity and autonomy of individuals, the difference and similarity with general human research lies in informed consent. The similarity is the necessity of obtaining the valid consent of the human subjects, and the difference is that the consent obtained by the biobank the broad consent of the human subjects is. Consent is given for the specimens, data and information to be provided for many times and almost unlimited use in various researches. The scope of authorized use is very different from general human research consent for use in only specific research, so the process of the human subjects’ informed consent is particularly important. At present, the consent forms of biobanks are in accordance with the Human Biobank Management Act. The consent forms of each biobank should be reported to the Ministry of Health and Welfare to ensure they are consistent. How is consent obtained in practice, and have you fulfilled the duty of explanation? As each biobank may not have a designated person to obtain consent, the establishment of a complete training and internal audit system, as well as a regular or irregular monitoring mechanism for informed consent by the EGC, will affect the protection of participants’ autonomy. However, in order to recruit participants, the phrasing “free health examination” has appeared multiple times in the past which has caused a lot of controversy. This is also worth noting.

Second, ensuring privacy and confidentiality and avoiding collective discrimination relies on good governance mechanisms for biobanks. From the perspective of the participants, the broad consent provided by participating in the biobank—despite the magnitude of the authorization given—is nothing more than based on trust in the biobank, and good biobank governance should be the cornerstone of trust. According to the Taipei Declaration, the Human Biobank Management Act, and related literature, good governance should at least include: sound management of the specimens, data, and information of the human subjects, openness and transparency in operations, participation of the public or community, and accountability. The management of data and specimens of participants is a basic procedure, and it is also the focus of biobanks at present. The openness and transparency in operations includes providing research types and research results, the conditions of specimen preservation and utilization, and EGC meeting minutes, which should be made available on channels accessible to the public. However, there are still differences in the degree of openness and transparency of each biobank. Participation refers to the dialogue and participation mechanism between the biobank and potential participants and the groups and communities to which they belong. Operating biobanks involves the collection of genetic data, not only of individuals but also of groups. The purpose of dialogue and participation is to promote understanding and form consensus—especially on the ethical issues of biobanks—and to introduce the views of the community and their diverse voices, which will help to build trust in biobanks and biomedical research. Currently there are not many biobanks that have this concern, as most of them still focus on the personal attributes of the participants in the biobank and pay less attention to group or community participation.

Furthermore, biobanks are different from general human research. Those who establish biobanks have a heavy responsibility within the framework of participant protection. They are responsible not only for the participants, but also for supervising whether all research complies with regulations, ethics and the agreement of the participants and researchers on the use of specimens and data. Therefore, the responsibility of those who establish biobanks is an extremely important factor in the protection of the participants of the biobank. However, in practice, there still seems to be a gap in the level of resources and manpower available to biobanks.

Finally, according to Article 1 of the Human Biobank Management Act, the legislative intent of the Act is to "ensure the rights and benefits of biological database participants, and promote medical development and public welfare", that is, "promoting medical development" and "protecting participants" should be balanced. Currently, biobanks for the general public are still a relatively new issue, and it is expected that the competent authorities and biobanks will have more channels for the public to correctly understand the use of biobanks and the meaning participation in biobanks holds for them and the group they belong to. This is the first step of participant protection!

• Relevant legal framework, future development trends and suggestions for domestic human biobanks

Institute of Law for Science and Technology, National Tsing Hua University

Professor Chien-Te Fan

Today, as the world is entering the big data era of precision medicine and precision health, the World Medical Association announced Declaration of Taipei in 2016, particularly emphasizing the value of "ethical considerations regarding Health Databases and Biobanks", and the International Bioethics Governance Committee of UNESCO, in its 2017 report on "Big Data and Health", especially focused on how to maintain a balance between individual and collective interests to promote collective interests in the field of health; including the paradigm shift of systems related to participant self-determination, consent, data protection, and governance related to big data. For Taiwan, although the Human Biobank Management Act leaves room for participants to agree to the use of their biodata or information links for using health data and the National Biobank Consortium of Taiwan was created in 2019, how this kind of plan can meet the exclusion license circumstances of the Personal Data Protection Act still depends on the further relaxation or adjustment of regulations. Issues that depend on the improvement of relevant laws and regulations on biobanks include using comprehensive governance to reinforce the self-determination participants should have and strengthening general consent, opt-out consent, and dynamic consent in response to diverse and cross-database utilization, as well as introducing principles such as solidarity and reciprocity, addressing the challenge of special privacy protection in the era of big data, strengthening security measures across database links, properly reconciling regulations between personal and public interests, technology and communication mechanisms, innovative data collection, management and attribution models, and the facilitation of a paradigm shift from ownership to governance and sharing. Concretely, in response to the advent of the era of health big data, Taiwan's future legal system for biobanks should actively introduce an innovative governance structure with self-determination, transparency, legality, privacy and information rights as its main content.

Looking ahead to the future, for the health of the people and the well-being of the next generation, we will combine the strengths of professional experts and the public to continue facing various challenges, to step-by-step promote Taiwan's biobanks and make steady progress towards the realization of true precision medicine.

Chapter IV Appendix

Chapter IV. Appendix

Related links

The following is the contact information of government agencies, related associations and biobanks.

Related Units

Ministry of Health and Welfare Biobank management area

National Biobank Consortium of Taiwan

Joint Commission of Taiwan Biobank inspection

National Center for High-performance Computing

Taipei

- Tri-Service General Hospital
- Taipei Medical University
- Academia Sinica
- Taipei City Hospital
- National Taiwan University Hospital
- Cathay General Hospital
- Koo Foundation Sun Yat-Sen Cancer Center
- MJ Health Research Foundation
- Taipei Veterans General Hospital
- Shin Kong Wu Ho-Su Memorial Hospital
- Mackay Memorial Hospital

New Taipei

- ● Far Eastern Memorial Hospital
- ■ Taipei Tzu Chi Hospital, Buddhist Tzu Chi Medical Foundation

Keelung

- ● Keelung Chang Gung Memorial Hospital

Taoyuan

- ■ Linkou Chang Gung Memorial Hospital
- ● Taoyuan General Hospital, Ministry of Health and Welfare
- ◆ Landseed International Hospital

Miaoli

- ● National Health Research Institutes

Taichung

- ● China Medical University Hospital
- ■ Taichung Tzu Chi Hospital, Buddhist Tzu Chi Medical Foundation
- ■ Chung Shan Medical University Hospital
- ● Tungs' Taichung MetroHarbor Hospital
- ● Taichung Veterans General Hospital

Changhua

- ● Changhua Christian Hospital

Note: Human biobank type

- ● Specific group (disease) specimens
- ◆ Population (healthy people) specimens
- ■ Specific group (disease) and population (healthy people) specimens

Chiayi

- Ditmanson Medical Foundation Chia-Yi Christian Hospital
- ■ Chiayi Chang Gung Memorial Hospital

Tainan

- Chi Mei Hospital Center
- National Cheng Kung University Hospital
- ◆ Tainan City Government

Kaohsiung

- E-Da Hospital
- Kaohsiung Veterans General Hospital
- Kaohsiung Chang Gung Memorial Hospital
- Kaohsiung Medical University Chung-Ho Memorial Hospital

Yilan

- Lotung Poh-Ai Hospital

Hualien

- Hualien Tzu Chi Hospital, Buddhist Tzu Chi Medical Foundation

Note: Human biobank type

- ● Specific group (disease) specimens
- ◆ Population (healthy people) specimens
- ■ Specific group (disease) and population (healthy people) specimens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Address : No. 488, Sec. 6, Zhongxiao E. Rd., Nangang Dist., Taipei City 115204

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Address : No. 488, Sec. 6, Zhongxiao E. Rd., Nangang Dist.,
Taipei City 115204

Tel : +886-2-8590-6666