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Key Points of Social Implementation in Healthcare Development

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Introduction

This paper is my third work on ecosystem research in the healthcare field, including life sciences, following "Structure and Ingenuity of Ecosystem Formation in Life Science: System Formation in Belgium and Challenges in Japan" (2023) and "Formation and Evolution of Life Science Ecosystems: Social Implementation Process and Human Resource Development" (2025).

The first work featured international comparisons, and the second work featured examples from overseas, mainly Belgium. This work focuses on the Japanese environment. Theoretical aspects of the ecosystem were discussed in the first book, and overseas situations were covered in the second book; therefore, these topics will not be addressed in detail here.

I have touched on the situation in Japan in passing, but the direct impetus for this article to focus on the Japanese environment itself came from the increased opportunities I had to have conversations with young and mid-career Japanese scientists. While describing the situation overseas in my previous works, an increasing number of scientists showed interest in the content, and I had opportunities to have discussions with them. During these conversations, many constructive ideas emerged regarding how the Japanese environment should evolve, which gave me more opportunities to examine the Japanese context from this viewpoint.

In this article, I present the Japanese ecosystem related to healthcare, including life sciences, to young and mid-career scientists and those who support them, with the hope that it will help them solve problems and plan their career paths.

The foundation for the preparation of this article was discussions centered on the seminars held at the Research Institute of Capital Formation (RICF) in Development Bank of Japan Inc. (DBJ). The core question of this paper is "the essence of social implementation" but the answer was reached early: "sharing practical perspectives toward an exit". Therefore, rather than exploring the reasons for this, the emphasis is placed on sharing perspectives. I believe that such sharing, or repeated discussions stemming from this, will lead to intergenerational metabolism, which is the basis for revitalizing innovation. The contents are as follows.

Chapter 1 describes that although the number of researchers and the scale of research funding in Japanese academia remain at a certain level, and a variety of research activities are being developed mainly at universities and public research institutes, challenges such as a decrease in the number of young faculty members, a rigid career path, and a decline in the number of international publications have become apparent. In particular, it describes the necessity of fostering excellent young researchers, ensuring mobility, and strengthening the

ability to disseminate research results internationally.

In this paper, the term "academia" refers specifically to universities and public research institutes.

Chapter 2 describes that in this field, it is essential to take initiatives that focus on basic research, clinical applications, and social implementation as products and services. It also clarifies that collaboration between experts and stakeholders is required at each stage, including strengthening evidence, regulatory responses, patent strategy, and insurance reimbursement.

Chapter 3 describes the business process. In this phase, clarification and differentiation of needs, and construction of an implementation system are the basis for commercialization. Practical perspectives are essential for collaboration between academia, companies, and venture capital (hereafter referred to as VCs) and for exit planning. In particular, VCs play a multifaceted role, including not only funding but also development progress management, team composition, and data package construction. It is also necessary for universities and research institutes to be aware of this perspective.

Chapter 4 summarizes the latest trends in the fields of drug discovery, medical devices, nursing care devices, and health tech, as well as technological innovation and investment diversification in each field. In all of these trends, it is necessary to establish the credibility of the business plan and the support of figures from the viewpoint of social implementation and market expansion.

Chapter 5 focuses on the importance of human resource development to drive these activities. The examples of the United States, Belgium, and Singapore show that human resource development that emphasizes diversity and practice is the key to innovation creation, and that exit-oriented educational programs greatly contribute to the development of human resources who can contribute to the field.

In Japan, a system for supplementing talent from external sources has been implemented for the first time, but it will become more important to appropriately build in human resources who understand both development and business within academia, and to create a framework for this.

Based on this, in the final chapter, measures to promote the vitalization of the healthcare field, especially in academia, are reviewed from the perspectives of individuals, organizations, and society. Individuals are required to delve deeper into science, visualize career paths, recognize their roles as supporters, and strengthen educational systems. Organizations are required to develop specialization and core facilities, and collaborate with industry and overseas

institutions. For society, it is important to diversify education and organizations, return overseas human resources, and strengthen international collaboration.

These divisions of individuals, organizations, and society complement each other. At the same time, individual growth leads to the revitalization of organizations, and organizational collaboration promotes the development of society. Also at the same time, society supports organizational collaboration, and the form of organizations supports individual growth.

This paper was prepared based on the many opportunities for discussion described at its end, and I would like to express my strong gratitude to those who contributed.

Chapter 1 The State of Academia

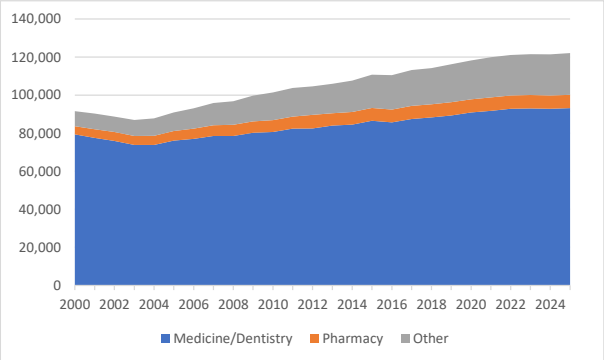
- In the field of medicine and life sciences in Japan, approximately 120,000 researchers are enrolled in academia, and research activities are conducted at various universities and research institutes, mainly at universities with 82 medical schools.
- Research funding is provided by public sources such as Grants-in-Aid for Scientific Research and Japan Agency for Medical Research and Development (AMED) in addition to the budget within academia, and supports a wide range of research from basic to applied.
- The decrease in the number of young faculty members and the decrease in the number of international publications are issues for strengthening research capabilities in the future, and is also the starting point of this paper.

1.1 Academia and Number of Personnel

To begin, I would like to address the following question: How many researchers in healthcare, including life sciences, are currently active in academia in Japan?

According to data from Survey of Science and Technology (Ministry of Education, Culture, Sports, Science and Technology, hereafter referred to as MEXT), Figure 1 shows the number of university researchers specializing in "Natural sciences _ Health"[1]. In academia, the actual number of researchers in the medical field in Japan is approximately 120,000, without taking into account the ratio of research hours.

Figure 1 Trends in the Number of Full-Time Researchers at Universities and Other Institutions (Natural sciences _ Health)[2]　Unit: people



Created by the author from MEXT's Survey of Science and Technology.

1 Medicine, dentistry, pharmacology, nursing, and others (nutrition, etc.)
2 Researchers in general are defined as those who are primarily engaged in internal research.

As shown in Table 1, there are 82 medical schools in Japan. In addition, there are more than 120 life science departments (excluding medical schools) in total, although there are various ways of calculating the number, and there are many researchers in engineering who conduct life science research in collaboration with these departments, so the range is very wide.

In addition, there are research institutions by the national and local governments that specialize in diseases or research fields, and the main ones are shown in Table 2.

Table 1 List of Japanese Universities with Medical Schools

Hokkaido area		Tokyo Medical University	(Tokyo)	Kansai Medical University	(Osaka)
Asahikawa Medical University	(Hokkaido)	Jikei University School of Medicine	(Tokyo)	Kindai University	(Osaka)
Hokkaido University	(Hokkaido)	Tokyo Women's Medical University	(Tokyo)	Kobe University	(Hyogo)
Sapporo Medical University	(Hokkaido)	Nihon University	(Tokyo)	Hyogo College of Medicine	(Hyogo)
Tohoku area		Yokohama City University	(Kanagawa)	Nara Medical University	(Nara)
Hirosaki University	(Aomori)	Saint Marianna University of Medicine	(Kanagawa)	Wakayama Medical University	(Wakayama)
Iwate Medical University	(Iwate)	Kitasato University	(Kanagawa)	**Chugoku Area**	
Tohoku University	(Miyagi)	Tokai University	(Kanagawa)	Tottori University	(Tottori)
Tohoku University of Medicine and Pharmacy	(Miyagi)	**Hokuriku and Chubu areas**		Shimane University	(Shimane)
Akita University	(Akita)	Niigata University	(Niigata)	Okayama University	(Okayama)
Yamagata University	(Yamagata)	Toyama University	(Toyama)	Kawasaki Medical School	(Okayama)
Fukushima Medical University	(Fukushima)	Kanazawa University	(Ishikawa)	Hiroshima University	(Hiroshima)
Kanto area		Kanazawa Medical University	(Ishikawa)	Yamaguchi University	(Yamaguchi)
University of Tsukuba	(Ibaraki)	Fukui University	(Fukui)	**Shikoku area**	
Jichi Medical University	(Tochigi)	Yamanashi University	(Yamanashi)	Tokushima University	(Tokushima)
Dokkyo Medical University	(Tochigi)	Shinshu University	(Nagano)	Kagawa University	(Kagawa)
Gunma University	(Gunma)	Gifu University	(Gifu)	Ehime University	(Ehime)
National Defense Medical College	(Saitama)	Hamamatsu University School of Medicine	(Shizuoka)	Kochi University	(Kochi)
Saitama Medical School	(Saitama)	Nagoya University	(Aichi)	**Kyushu and Okinawa area**	
Chiba University	(Chiba)	Nagoya City University	(Aichi)	Kyushu University	(Fukuoka)
International University of Health and Welfare	(Chiba)	Aichi Medical University	(Aichi)	Fukuoka University	(Fukuoka)
University of Tokyo	(Tokyo)	Fujita Medical College	(Aichi)	Kurume University	(Fukuoka)
Institute of Science Tokyo	(Tokyo)	Mie University	(triple)	University of Occupational and Environmental Health	(Fukuoka)
Kyorin University	(Tokyo)	**Kinki Area**		Saga University	(Saga)
Keio University	(Tokyo)	Shiga University of Medicine	(Shiga)	Nagasaki University	(Nagasaki)
Toho University	(Tokyo)	Kyoto University	(Kyoto)	Kumamoto University	(Kumamoto)
Nippon Medical School	(Tokyo)	Kyoto Prefectural University of Medicine	(Kyoto)	Oita University	(Oita)
Juntendo University	(Tokyo)	Osaka University	(Osaka)	Miyazaki University	(Miyazaki)
Showa University	(Tokyo)	Osaka Public University	(Osaka)	Kagoshima University	(Kagoshima)
Teikyo University	(Tokyo)	Osaka University of Medicine and Pharmacy	(Osaka)	Ryukyus University	(Okinawa)

Created by the author.

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Table 2 Main Public Research Institutions (Related to the Medical Field)

Name	Position of Administration	Year of Establishment
Japan Agency for Medical Research and Development (AMED)	Cabinet	2015
Institute of Physical and Chemical Research（RIKEN)	MEXT	1917
National Cancer Center	MHLW	1962
National Cerebral and Cardiovascular Center	MHLW	1977
National Center of Neurology and Psychiatry	MHLW	1978
National Center for Child Health and Development	MHLW	2002
National Center for Global Health and Medicine	MHLW	1993
National Center for Geriatrics and Gerontology	MHLW	2004
National Institute of Infectious Diseases	MHLW	1947
National Institute of Advanced Industrial Science and Technology	METI	2001

Created by the author.

On the other hand, it should be kept in mind that physicians in the medical field are engaged in both research and clinical work. Although this is somewhat old data, in the calculation of Full-Time Equivalent (FTE) values, the ratio of research time to total work time for researchers was 0.302 (2018) in the health field (based on all universities).[3]

In Figure 1, the number of researchers is shown as 120,000, but when considered on a research basis, it should be considered that the overall situation is multiplied by this coefficient.

1.2 Funding for Research

Next, I would like to look at what kind of funding has been invested in the field centered on healthcare.

First, R&D expenditures at universities and other research institutions have changed in the following manner. As of 2023, the most recent figure was 1.3 trillion yen in the health sector.

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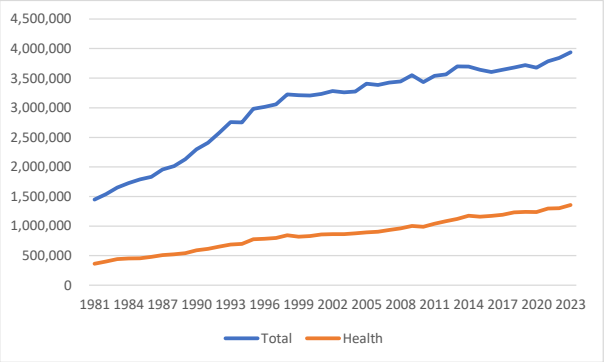
3 Yumiko Kanda, Masanori Igami (2020) "Detailed Analysis of Research and Development Expenditures and the Number of Researchers at Japanese Universities Considering the Full-Time Researcher Conversion Factor" National Institute of Science and Technology Policy (MEXT)

Figure 2 Trends in R&D Expenditures at Universities by Academic Discipline

Unit: 1 million yen



Created by the author from 'Science and Technology Indicators 2025' included in MEXT's National Institute for Science, Technology and Academic Policy.

Grants-in-Aid for Scientific Research (hereafter referred to as KAKENHI) is the largest category of basic research funded by the government in academia. The framework has undergone various changes, but the current framework is roughly as follows.

—Role and overall composition of each research category under KAKENHI—

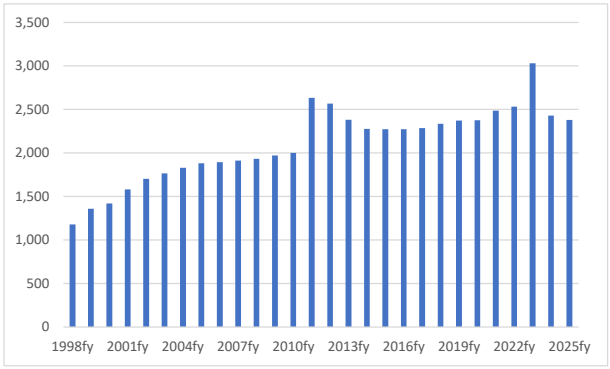
- Specially Promoted Research
- "Basic Research" category groups
  Basic Research (A, B, C, S)
- "Academic Transformation Research" category groups
  Academic Transformation Area Research (A, B)
  Challenging Research (pioneering and sprouting)
- International Joint Research Acceleration Fund
  International Leading Research
  Returnee Developmental Research
  Overseas Collaborative Research
  Strengthening International Research Collaboration
- "Young Researcher" Category Group
  Young Researcher
  Grant-in-Aid for Research Fellows
  Support for Starting Research Activities

As shown in Figure 3, the recent annual budget for KAKENHI is approximately 240 billion yen. However, looking at the amount for fields directly related to this paper, the amount for newly

selected items was more than 20 billion yen as of 2025 (Figure 4).[4]

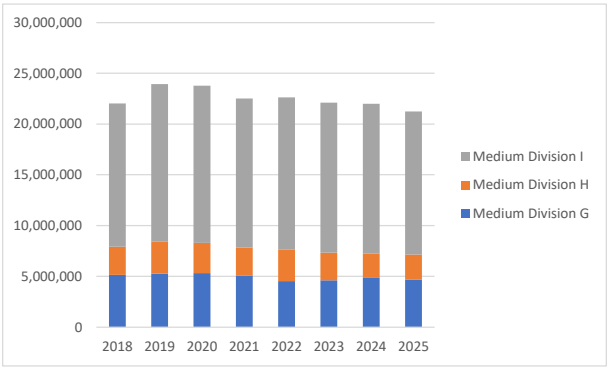
According to the "List of Allocations by Research Category and Gender (FY 2025)", the amount for newly selected items for KAKENHI as a whole was 58.7 billion yen, and the amount for new and continued items was 169.2 billion yen, which is approximately 2.9 times the amount for newly selected items.

Figure 3 Changes in the Amount of KAKENHI Budget Unit: 100 million yen



Created by the author from 'Trends in Budget Amount' (Japan Society for the Promotion of Science).

Figure 4 Trends in KAKENHI: Major and Middle Categories (Newly Adopted) Unit: 1,000 yen



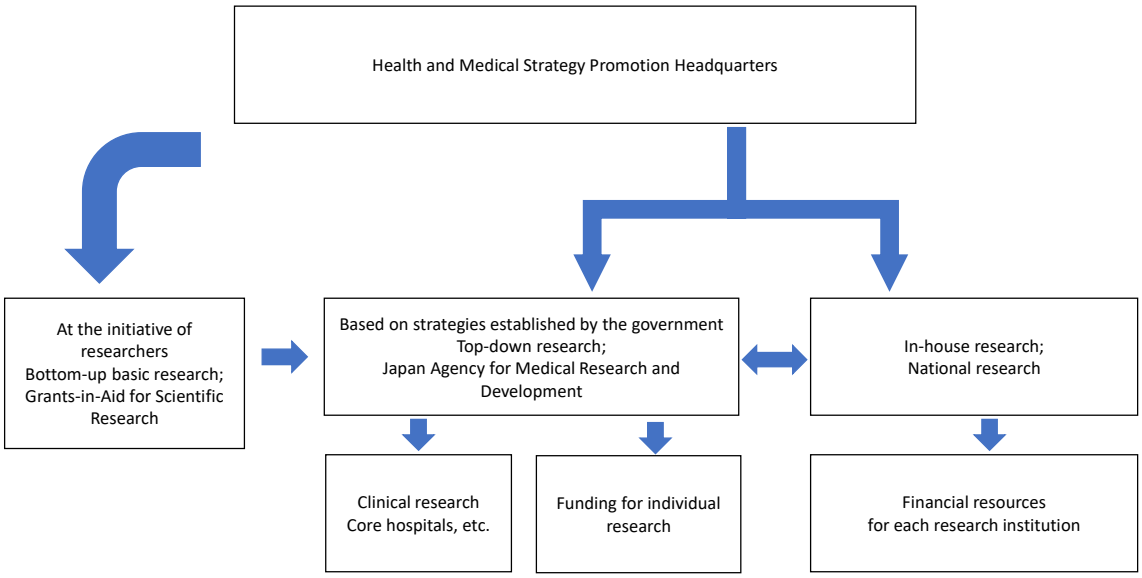
Created by the author from 'Allocation of KAKENHI' (Japan Society for the Promotion of Science).

KAKENHI is defined as bottom-up basic research initiated by Japan Agency for Medical Research and Development (AMED), which was established in 2015. However, other

4 Middle Division G: Biology at the Molecular and Cellular Levels, etc.
Middle Division H: Pharmacology, Biological Structures and Functions, Pathology, Infection and Immunology, etc.
Middle Division I: Oncology, Brain Science, Internal Medicine, Surgery of Homeostatic Organs, etc.

organizations began to provide funds to research areas defined as top-down (Figure 5).[5] At this stage, the target of funding is not necessarily academia; it is also companies, including startups.

Figure 5 Image of R&D System



Source: Health and Medical Strategy Promotion Headquarters "R&D System for New Medical Fields" (August 8, 2013)

AMED's R&D expenditure as of 2024 was 180.2 billion yen, and although the portion related to social implementation is also included in this budget, it was 141.9 billion yen (79%) for the academia categories of "Universities, etc." and "Independent administrative agencies/national research institutes".

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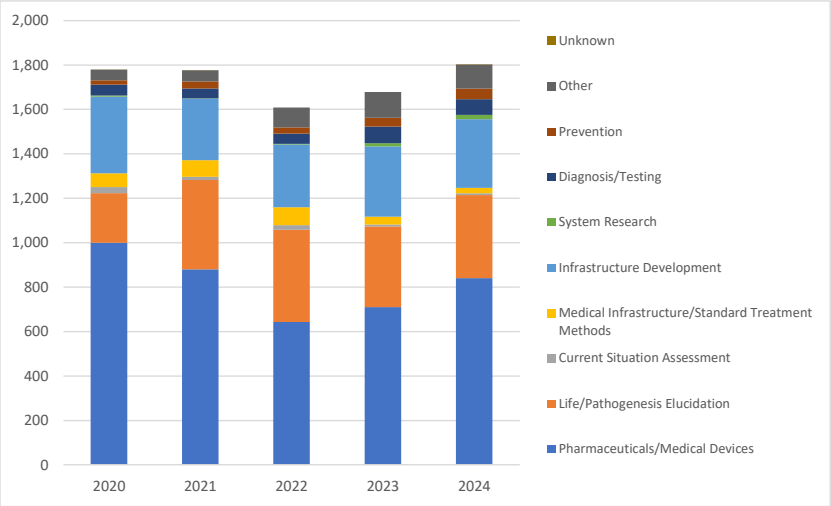
5 In 2015, the Japan Agency for Medical Research and Development (AMED) was established to integrate R&D activities in the medical field formerly carried out by MEXT, the Ministry of Health, Labour and Welfare (hereafter referred to as MHLW), and Ministry of Economy, Trade and Industry.

Figure 6 Trends in AMED R&D Expenditure　Unit: 100 million yen



Created by the author from 'AMED Data Book 2nd period'.

1.3 Career Paths of Researchers

I would like to give an overview of the careers of individual researchers in this funding structure. In Japan, the main career paths of healthcare researchers are 1) graduate students (master's and doctoral programs), 2) postdoctoral researchers, and 3) faculty positions such as assistant professors, lecturers, associate professors, and professors.

As mentioned in the previous book, Japan has traditionally adopted the *kouza* system, which differs from the principal investigator (PI) system used in Europe and the United States. This distinction is explained below.

In the *kouza* system, the research and education organization is organized in units of courses (*kouza*), and the career path posts mentioned above are included in the organization. A professor supervises the entire organization, and multiple research groups and themes exist under this. In the case of medical schools, which are also called "medical offices", clinical practice, research, and education are integrated.

Of course, the time frame within this career depends on the organization and the person, and it is difficult to calculate an average, but I would like to list some figures.

First, in the field of healthcare, the data (FY 2021) show that 48.2% of doctoral graduates exceeded the standard length of study, 24.4% exceeded the standard length of study by one year, 9.0% exceeded the standard length of study by two years, 7.7% exceeded the standard length of study by three years, and 10.7% exceeded the standard length of study by four years or more.[6]

6 'Data on Graduate School Education in the Humanities and Social Sciences' (Source: University Section, Central Council for Education, December 22, 2023)

For example, if the standard length of study for obtaining a bachelor's degree in medical school is six years, and the standard length of study for obtaining a doctoral degree is five years, then more than half of the graduates will obtain a doctoral degree in their 30s.[7] It should be noted that in Japan, there are doctors who obtain a doctoral degree without advancing to graduate school under the doctoral dissertation system.

As of 2021, the career path in the field of healthcare after obtaining a doctorate was 14.9% for university faculty and 4.6% for postdoctoral fellows. The ratio of postdoctoral fellows is quite low compared to other fields, but the category of "others (including physicians)" accounts for a high ratio, accounting for 47.8%.[8]

Since it is difficult to delineate the career path as a researcher by sector, the data is for all university faculty members. The data as of 2015 shows that the average age of postdoctoral fellows is 36.3 years old (100% with tenure), 38.4 years old for assistant professors (56.1% with tenure), 47.0 years old for associate professors (18.8% with tenure), and 57.9 years old for professors (11.7% with tenure).[9]

Data also show that the average age of postdoctoral fellows has increased since 2015. The median age for men was 35 years (2015), 36 years (2018), and 37 years (2021). The median age for women was 34 years in all three measurement years.[10] It has been pointed out in various ways that the transition from postdoctoral fellows to regular employees has become a major barrier from the perspective of all fields.

Through this process, the composition of the number of regular faculty members in national universities as of 2022 shows that professors account for the largest share (about 33%), followed by associate professors (about 27%), lecturers (about 9%), and assistant professors/assistants (about 31%).[11]

To draw a somewhat narrative view of this situation, after obtaining a doctorate through clinical experience, one is hired as an assistant professor in the medical office, and then while

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7 Under the traditional system in Japan, after graduation, students receive clinical training and continue to work as clinicians while aiming to obtain a doctoral degree at graduate school.

8 'Career Paths of Doctoral Graduates' (Human Resources Policy Division, Science and Technology Policy Bureau, MEXT, January 2023)

9 'Joint Subcommittee of the Human Resources Committee of the Council for Science and Technology and the Graduate School Committee of the University Subcommittee of the Central Council for Education (6th meeting)' July 31, 2018

10 Mari Kawamura (2024) "Careers and Challenges of Postdoctoral Fellows: Current Status of Postdoctoral Fellows in Japan as Revealed by a Nationwide Survey", STI Horizon, Vol. 10, No. 3 (National Institute for Science and Technology Policy, MEXT)

11 'School Teacher Statistics Survey 2022' (MEXT)

engaged in clinical work and research/education at the same time, one is promoted to associate professor and professor positions as posts become vacant. These personnel changes are also strongly influenced by the trends of professors. In addition, because clinical work and research/education are mixed, it can be said that there are not necessarily many career paths dedicated to research. However, the balance of the number of regular faculty by age group in the field of health is slightly different from that in other fields (the proportion of young faculty is relatively high); so, the pace of promotion and the balance of the number of faculty are assumed to be slightly different. Note that this is the case for physician-researchers. For those who choose a career centered on researchers studying overseas after obtaining a doctorate, the route is different from this “story ”.

For the sake of comparison, a simplified US/Europe style is described, in which a laboratory is managed independently by a principal investigator (PI). PIs, served by assistant professors, associate professors, professors, etc., are responsible for obtaining research funding, setting research themes, and hiring members at their own discretion. After one obtains a doctorate in one's mid to late twenties, he or she gains experience in multiple laboratories as a postdoctoral fellow and then becomes independent as a PI as early as his or her early thirties. However, mobility is high and it is common to move to other universities or research institutes.

In Japan, young researchers at the assistant professor level, as well as professors and associate professors, are increasingly taking on the role of PIs, and it is said that there is an increasing framework in which they can acquire tenured positions by accumulating research achievements as PIs. However, it is difficult to say that the results are yet to be fully realized.

1.4 Cases of Studying Overseas

In 1.3 immediately above, I looked in a somewhat schematical way at the situation in Japan. But in reality, the stage of research in the medical field is expanding globally, and it is a natural trend for researchers themselves to seek opportunities broadly for their activities.

The government also supports this trend, and has prepared several support frameworks. The main support frameworks are shown in Table 3.

The stage that researchers go overseas is a major point. But if they are young researchers trying to get a post overseas, the nationality of the research institution they belong to is largely irrelevant. As mentioned in the previous section, they will have to search for a career path under the PI system.

However, there are various challenges in this way, and one of them is the extent to which foreign nationals can get major posts at research institutions in their own countries.

Another challenge is whether these overseas moves are seamless with the environment of

Japanese universities and research institutions. Researchers who go overseas inevitably find themselves in an environment in which "it is common to move to other universities and research institutions" and the major points are whether they are able to return to Japanese academia from the same perspective and whether they can enjoy the environment they enjoyed at major research institutions in Europe and the United States when they return to Japan.

Table 3 List of Scholarship Programs for Japanese Students to Study Abroad

<table>
<tr><td colspan="2">Government-Funded Support</td><td>Support Utilizing Private Funding</td></tr>
<tr><td colspan="2">Overseas study support program</td><td rowspan="2">Tobitate! Study Abroad Initiative: New Japan Representative Program</td></tr>
<tr><td>Agreement-based dispatch type</td><td>Degree acquisition type</td></tr>
<tr><td>As Japanese universities and other institutions strive for internationalization, this program broadly supports study abroad programs based on inter-university exchange agreements, etc., in order to cultivate global human resources needed for the entire country.</td><td>This program supports students who wish to study abroad to obtain a degree at a university overseas that conducts world-leading education and research.</td><td>This program updates the "global leader image" that will shape Japan's future and the learning gained through studying abroad, fostering individuals who will contribute to solving Japan's social issues and creating new industries. The course for university students and others aims to support individuals who will become "global leaders who will bring about social change themselves" in the future.</td></tr>
<tr><td colspan="3">Japan Student Services Organization (JASSO)</td></tr>
<tr><td>FY2023 budget
4.6 billion yen (16,900 students)</td><td>FY2023 budget
1.5 billion yen (250 undergraduate students, 350 graduate students)</td><td></td></tr>
</table>

Source: Cabinet Secretariat "Initiative to Promote Study Abroad by Young People Who Create the Future (Second Proposal)"

1.5 Trends in the Number of Young Faculty Members

Here, I would like to bring the perspective of age into consideration. Although not limited to the field of life sciences, Benjamin F. Jones suggests that the peak age for research is in the late 30s and 40s.[12] Of course, this trend may change significantly in the future, depending on the state of infrastructure and trends in the technology that supports research, but it is globally recognized that younger researchers tend to produce more significant research outcomes.

In Japan, the number of young teachers under the age of 40 is shown in Figure 7 regardless of the field of study (the 2022 ratio for those under 40 is 21.2%).

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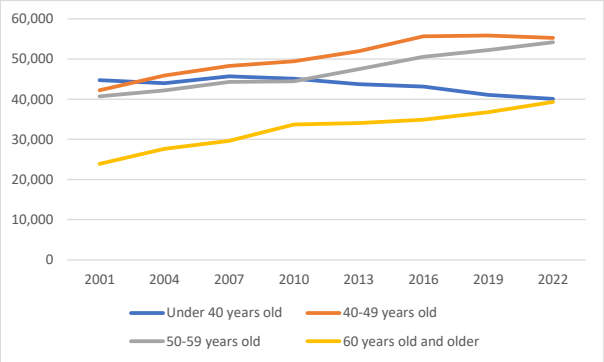
12 Jones, B.F. (2010), 'Age and Great Invention', The Review of Economics and Statistics

Figure 7 Changes in the Number of Full-Time University Teachers by Age Group

Unit: people



Created by the author from 'Statistical Survey of School Teachers' (MEXT).

As can be seen from the figure, the decline in the number of young teachers is noticeable (it should be noted that the "number of regular faculty members" is shown here, and that this figure excludes research scientists and postdoctoral fellows from the "number of regular faculty members" shown in Figure 1).

On the other hand, the health sector in Japan has a slightly different balance. This is shown in Table 4.

First of all, in the health sector, the number of teachers under the age of 40 is not so large when compared with all sectors. At the same time, despite the small proportion of postdoctoral fellows, the ratio of teachers under the age of 40 is high. In 2001, it was 43.4% (29.5% in all sectors during the same period). However, over the past 20 years, this ratio has steadily declined to 28.6%. The ratio in all sectors has also declined, to 21.2%, but the decline is much larger in the health sector. In particular, the increase in the number of teachers over the age of 50 is large even on a real number basis, showing a remarkable movement while the number of teachers under the age of 40 has remained almost unchanged.

Given the fact that the aging of the population is shifting in this way despite the characteristics of the *kouza* system, it is highly likely that the decline in the number of young teachers itself will suppress the metabolism that is originally required for organizations, such as generational replacement and revitalization. In this situation, raising the motivation of young researchers and promoting their metabolism will have a major bearing on the improvement of research output and the strengthening of social implementation, which will be discussed in the following chapters, and will have a major bearing on the whole of this paper.

Table 4　Trends in the Number of Full-time Teachers at Universities

by Age group _ Health Sciences (Top: Real number; Bottom: %)

Category	2001	2004	2007	2010	2013	2016	2019	2022
Total of full-time faculty members	46,059	49,211	54,447	57,049	61,319	65,672	67,769	69,443
Under 25 years old	84	69	76	34	40	42	33	35
25 years old and over but under 30 years old	2,144	2,115	2,536	2,264	1,974	1,893	1,968	2,001
30 years old and over but under 35 years old	7,691	7,313	7,973	7,764	7,484	7,368	7,330	7,022
35 years old and over but under 40 years old	10,056	10,070	10,652	10,895	11,614	11,668	11,072	10,815
40 years old and over but under 45 years old	9,351	9,603	9,723	9,855	11,021	12,049	12,121	11,824
45 years old and over but under 50 years old	6,166	7,380	8,343	8,670	8,941	9,914	10,342	11,083
50 years old and over but under 55 years old	4,883	5,037	5,940	6,981	7,972	8,225	8,463	9,087
55 years old and over but under 60 years old	2,772	4,084	4,937	5,050	5,982	7,198	7,708	7,671
60 years old and over but under 65 years old	2,118	2,545	2,927	4,079	4,487	5,121	6,088	6,840
65 years old and over	794	995	1,340	1,457	1,804	2,194	2,644	3,065
Average age	43.0	43.9	44.3	45.0	45.6	46.2	46.7	47.2

Category	2001	2004	2007	2010	2013	2016	2019	2022
Total of full-time faculty members	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%
Under 25 years old	0.2%	0.1%	0.1%	0.1%	0.1%	0.1%	0.0%	0.1%
25 years old and over but under 30 years old	4.7%	4.3%	4.7%	4.0%	3.2%	2.9%	2.9%	2.9%
30 years old and over but under 35 years old	16.7%	14.9%	14.6%	13.6%	12.2%	11.2%	10.8%	10.1%
35 years old and over but under 40 years old	21.8%	20.5%	19.6%	19.1%	18.9%	17.8%	16.3%	15.6%
40 years old and over but under 45 years old	20.3%	19.5%	17.9%	17.3%	18.0%	18.3%	17.9%	17.0%
45 years old and over but under 50 years old	13.4%	15.0%	15.3%	15.2%	14.6%	15.1%	15.3%	16.0%
50 years old and over but under 55 years old	10.6%	10.2%	10.9%	12.2%	13.0%	12.5%	12.5%	13.1%
55 years old and over but under 60 years old	6.0%	8.3%	9.1%	8.9%	9.8%	11.0%	11.4%	11.0%
60 years old and over but under 65 years old	4.6%	5.2%	5.4%	7.1%	7.3%	7.8%	9.0%	9.8%
65 years old and over	1.7%	2.0%	2.5%	2.6%	2.9%	3.3%	3.9%	4.4%

Created by the author from 'Statistical Survey of School Teachers' (MEXT).

1.6 Trends in the Number of Publications

So far, I have provided an overview of research personnel, funding, and career paths, with a focus on academia. At the end of this chapter, I would like to look at trends in the output generated by this structure.

The first easy-to-understand figure for output is the number of publications. Between 2021 and 2023, the number of publications in clinical medicine and basic life sciences in Japan was sixth in the world for the former and seventh for the latter, which is a step back from the 2001 – 2003 period when Japan was fourth and second in the world for both[13]. However, the number of publications itself is leveling off in clinical medicine and increasing in basic life sciences.

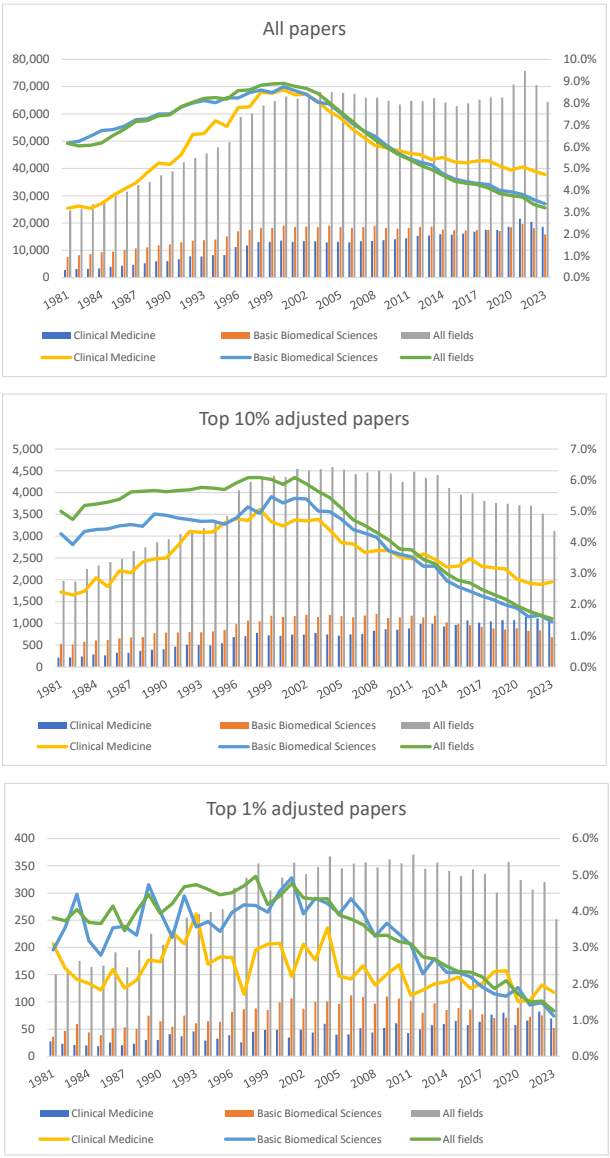
However, the position of basic life sciences has relatively declined after peaking around 2000. Clinical medicine, on the other hand, has no significant peak period, but has maintained a certain

13 Conversely, growth was mainly in China. But the former was surpassed by the United Kingdom and Germany; and the latter by Italy and India, in addition to Japan.

position.

Currently, more than 34,000 papers have been published in both fields, of which 1,700 papers, or about 5%, have been published in Top 10% journals and 300 papers, or slightly less than 1%, have been published in Top 1% journals.

Figure 8　Trends in Number of Papers (Single year, Fractional Count Method)
Left: Number of Papers, Right: Share (%)



Compiled and created by the author from 'Science and Technology Index 2025' (MEXT Institute for Science, Technology and Academic Policy).

While a decline in the share of research papers is unavoidable due to a declining population, the large decline in the share of research papers at the top 10% and top 1% levels—in other

words, the decline in the number of high-profile research papers—is a major issue that needs to be addressed. With regard to the decline in the basic life sciences in particular, the relative deterioration of the research infrastructure can be assumed to be one of the factors. At the same time, since there has been no decline in R&D expenditures or the number of researchers, it is necessary to examine the impact of changes in the age structure of faculty.

Summary

In the healthcare field in Japan, the number of researchers and the scale of research funding have maintained a certain level, and a variety of research activities have been developed mainly at universities and public research institutes.

However, issues such as a decline in the number of young faculty members, a rigid career path, and a decline in the number of international publications have become apparent. In particular, the development of excellent young researchers, ensuring mobility, and strengthening the ability to disseminate research results internationally have been long-standing issues.

Chapter 2 Evidence Construction and Development Process

- In the life sciences field, it is important both to construct evidence in science and to have a perspective that leads to social implementation.
- In order to move toward social implementation, it is necessary not only to have strong evidence but also to collaborate with specialized human resources and various processes such as regulations, patents, and insurance reimbursement in the development of pharmaceuticals and medical devices.
- Academia is also building organizations and mechanisms to respond to this trend. But it should be noted that the number of projects that actually enter this process is relatively limited.

In the previous chapter, I looked at the outline of "Research", but in order to make this field attractive, it is necessary to appropriately demonstrate the results of science and implement them into actual products and services.

Whether to emphasize science or social implementation varies by country and time. In Japan, in particular, the number of opportunities for discussion of social implementation has increased significantly.

However, in the healthcare, including life sciences, the construction of evidence when implementing social implementation is extremely important, and this chapter provides an overview of this point.

2.1 Strength of Evidence

Medical research includes basic research, disease-oriented research (DOR), and patient-oriented research (POR). In the process of social implementation, basic research delves into the mechanisms of disease states and biological phenomena, DOR is performed using bio samples, and then clinical research (i.e., POR) is conducted to investigate whether new treatments and drugs can be deployed in humans.

Clinical research also includes observational studies, which analyze information obtained in ordinary medical care, and interventional studies, which assign the contents of treatment and the presence and extent of medical treatment for the purpose of research. Among interventional studies, those that verify the efficacy and safety of new treatments or drugs or medical devices are generally positioned as clinical trials. Furthermore, evidence obtained from such clinical trials is hierarchically organized by various guidelines and evaluation organizations according to study design and reliability.

For example, the Grading of Recommendations Assessment, Development and Evaluation (GRADE) working group ranks the strength of evidence by study design. The strength of evidence itself is determined by the study design and the endpoint measured (e.g., survival rate, quality of life). Among them, a typical trial method is a randomized controlled trial (RCT). RCTs are trials that guarantee objectivity and reliability, and are considered to provide the strongest evidence to verify efficacy.

In practical terms, biostatisticians are necessary to raise the level of evidence, and they are responsible for designing appropriate study designs according to the study objectives.

At the same time, when thinking about social implementation, it is necessary to think about it from a more holistic framework, rather than the ideal form of evidence. The Consolidated Framework for Implementation Research (CFIR) published in 2009 is very informative.

The CFIR, which was revised in 2022, provides a multifaceted analysis of barriers and facilitators to the adoption and diffusion of new interventions, programs, and technologies. As we look at the CFIR, it is clear that evidence is at its core and that the business dimension, which I will discuss later, is an important part of the process. It should be noted that the points to be emphasized vary depending on the angle from which the discussion of implementation is conducted.

Table 5 Overview of CFIR

I	Innovation Domain	Source, Evidence base, Relative Advantage, Adaptability, Testability, Complexity, Design, Cost
II	Outer Setting Domain	Critical Incidents, Local Attitudes, Local Conditions, Partnerships and Connections, Policies and Laws, Finanncing, External Pressures (Social Pressure, Market Pressure, Performance Evaluation Pressure)
III	Inner Setting Domain	Structural Characteristics (Physical Infrastructure, IT Infrastructure, Work Infrastructure), Relational Connections, Communications, Culture (Human Equality-Centeredness, Recipient-Centeredness, Deliverer-Centeredness, Learning-Centeredness), Tension for Change, Compatibility, Relative Priorities, Incentive Systems, Mission Alignment, Available Resources (Funding, Space, Materials and Equipment), Access to Knowledge and Information
IV	Individual Domain	Roles: High-Level Leader, Mid-Level Leader, Opinion leader, Implementation Facilitatiors, Implementation Leads, Implementation Team Members, Other Implementation Support, Innovation Delivers, Innovation Recipients
		Characteristics: Need, Capability, Opportunity, Motivation
V	Implementation Process Domain	Teaming, Assessment Needs (Innovation Derivevers, Innovation Recipients), Assessing Context, Planning, Tailoring Strategies, Engagement (Innovation Derivers, Innovation Recipients), Doing, Reflecting and Evaluating (Implementation, Innovation), Adapting

Source: Excerpt from "Integrated Framework for Implementation Research: CFIR".

2.2 Process of Pharmaceutical Development

The research publications/papers described in Chapter 1 vary from basic research to clinical research. It is not true that all basic research should go through clinical research and be implemented in society.

It is important to put research that meets the conditions for social implementation into the necessary process. And also important is the extent to which individual researchers;

organizations such as universities and research institutes; financial agencies; supporters, including VCs; pharmaceutical companies and medical device manufacturers can have a common understanding of this judgment.

Based on this basic premise, I would like to first look at how research that is judged to "Be developed for social implementation" enters the process for product development, focusing on the field of pharmaceutical development.

The pharmaceutical field is a field with a lot of technical terms. For academic researchers, the entire process is outlined, referring to the technical terminology in the 'Handbook of Technical Terminology for Translational Research in Drug Discovery'. Although the following sections will include detailed technical terms, they provide a foundation for understanding the stages and stakeholders involved in this process.

(1) Identification and Analysis of Drug Discovery Targets

First of all, the starting point of drug discovery is to grasp unmet medical needs. To solve this problem, it is necessary to select molecules and pathways involved in the cause and progression of diseases, and to clarify the reason for selecting these drug discovery targets.

When the target molecule is clear, an assay system to measure the activity against the target (evaluation system) is constructed, and high-throughput screening[14] is performed using a compound library.

When the target molecule is unknown, measures such as using phenotype screening, which directly observes the effect at the cell or organism level, are taken.[15]

Then, target validation is performed to confirm whether the hit compounds obtained by screening act on the disease-causing target or whether the target is involved in the onset and progression of diseases.

(2) Optimization of Seed and Lead Compounds

To improve the physicochemical properties[16] of the created seed compounds, the structure of the compounds is modified stepwise (structure modification).

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14 A method to find active compounds that match a purpose by evaluating a large amount of compounds (hundreds of thousands to millions) in a short period of time using an automated system controlled by a machine.

15 A method to search for compounds that change the phenotype (phenotype) of a cell or organ, i.e., cell proliferation, cell death, or production of a specific protein, as an index.

16 Physicochemical properties of compounds, such as solubility, lipophilicity, and chemical stability

In this process, pharmacokinetics/pharmacodynamics (PK/PD)[17], dose-response relationship[18], and structure-activity relationship (SAR)[19] are analyzed, and the most suitable lead compounds are selected.

The efficacy and safety of the selected compounds are evaluated in animal disease models, and the mechanism of action on the target is clarified.

(3) Development in Preclinical and Clinical Development

Efficacy evaluation and safety testing using biomarkers[20] are conducted for optimized new compounds and compounds with new structures while ensuring reproducibility.

In the case of antibodies and biopharmaceuticals, epitope[21] identification, bioassay bioactivity evaluation[22], and cell line management are important.

Based on these data, development strategies are developed and regulatory consultation materials are prepared for the initiation of clinical trials.

(4) Conduct Preclinical Studies

Preclinical studies evaluate the safety and efficacy of a new drug candidate compound in animals and prepare for the start of human clinical trials.

Prepare information on chemistry, manufacturing and control (CMC), including synthesis, formulation, quality control, and quality assurance.

Conduct studies on drug disposition (ADME)[23], ADMET[24], and indication. Toxicity studies should be conducted according to Good Laboratory Practice (described later) to evaluate the no

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17 Pharmacokinetics (PK) involves the body's response to the administration of a drug, and pharmacodynamics (PD) involves the effect of the drug on the body. PD is often related to drug concentration and PK parameters, and the concept of these relationships is collectively called PK/PD.

18 The relationship between the dose of a compound and the response (efficacy or toxicity).

19 The physiological activity (receptor or enzyme binding activity, toxicity, etc.) of a group of compounds with the same basic backbone varies depending on the substituents attached to the basic backbone. The relationship between the strength and weakness of the physiological activity and the difference in the structure and physicochemical properties of the substituents.

20 An item that is objectively measured and evaluated as an indicator of a normal or pathological process or a pharmacological response to a treatment.

21 A molecular region on the surface of an antigen that can induce an immune response and bind to specific antibodies generated by such a response.

22 The specific function or degree to which a product exerts a specific biological effect.

23 ADME: Evaluation of the process by which a drug administered to an organism is *absorbed* (A) into the systemic circulation, *distributed* (D) to the body, *metabolized* (M) in the liver, and *excreted* (E) in the urine.

24 ADMET: ADME plus evaluation of the *toxicity* (T).

observed adverse effect level (NOAEL)[25], safety margin, and therapeutic margin.

The obtained data should be compiled as application data such as investigational new drug (IND)[26] [US], clinical trial notification [Japan], and clinical trial application (CTA) [Europe] according to the regulatory requirements of each country and region, and submitted to the regulatory authorities before starting the first-in-human (FIH) study.

(5) Clinical Development (Phase 1-3)

In clinical development, new drug candidates and drug products are manufactured in accordance with good manufacturing practice (GMP), clinical trials are conducted in accordance with good clinical practice (GCP), and the clinical trial plans are subject to ethics and safety review by the Institutional Review Board (IRB) and Data and Safety Monitoring Board (DSMB)[27].

In Phase 1, safety, tolerability[28], and pharmacokinetics are evaluated through single ascending dose (SAD) and multiple ascending dose (MAD) studies[29].

In Phase 2, proof of concept (POC)[30] are confirmed, and dose selection and initial evaluation of efficacy are conducted.

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25 NOAEL: The highest dose at which no adverse toxicological effects were observed in safety studies, including multiple-dose repeated dose toxicity studies and reproductive/developmental toxicity studies.

26 INDs are submitted to the FDA when a clinical trial for a new indication of a new drug or existing drug is initiated in the United States.

27 IRB (Institutional Review Board): An independent organization that reviews the design of a clinical trial when an institution conducts a clinical trial. It reviews the conduct and continuation of a clinical trial from the viewpoints of ethics, safety, and scientific validity. Its establishment and operation are specified by GCP ordinances.

DSMB: An independent committee that collects and analyzes data in the course of a clinical trial to evaluate adverse events and signs that one therapy is significantly superior to another, and to recommend continuation, modification, or discontinuation of the trial (subsequent development feasibility). Its establishment and operation are specified by GCP ordinances.

28 A measure of how well a subject tolerates an apparent adverse effect (side effect) caused by a drug.

29 SAD: In Phase I clinical trials, a method called dose escalation is used in which the next dose of a new drug candidate is tested as soon as the safety of a single dose of the lowest dose is confirmed.

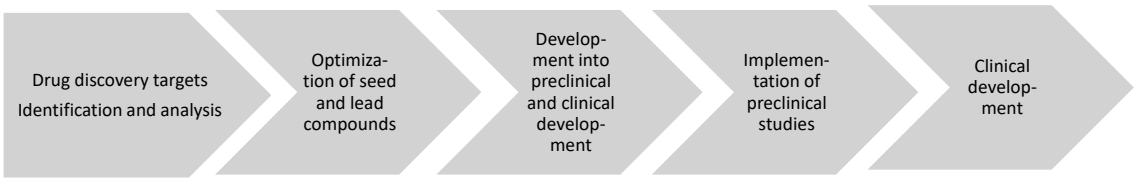
MAD: In order to confirm the safety and tolerability of repeated doses of a new drug candidate after completion of an SAD trial, the lowest dose is determined from the SAD trial. The safety is confirmed sequentially from the lowest dose to the next dose. A titration approach is often used to ensure the safety of subjects.

30 POC: A condition in which the feasibility of the efficacy and safety of a new drug candidate based on its assumed mechanism of action and therapeutic concept has been demonstrated through clinical trials, etc.

In Phase 3, confirmatory studies, mainly RCTs, are conducted. The efficacy is verified based on the primary endpoint and secondary endpoint, and the safety profile is established. In addition, the obtained data are compiled in accordance with the international standard CTD[31] format and submitted to the regulatory authorities.

When considering drug discovery from academia, the cost of the clinical development phase above does not meet the budget within academia. Therefore, it is realistic to conduct joint research with companies or establish startups and then provide funding from VCs. This point will be discussed in a later chapter.

Figure 9 Evidence Building for Drug Development



Created by the author.

Although the above figure shows the flow up to this point linearly, it should be noted that in actual drug development, there are cases in which each step proceeds iteratively and discontinuously.

2.3 Various Good Practices—"Good [x] Practice"—(GxP)

With regard to the processes outlined in 2.2, various good practices such as good laboratory practice (GLP) in preclinical studies, good clinical practice (GCP) in human clinical studies, and good manufacturing practice (GMP) in clinical studies and the manufacturing process of marketed products should be observed, and these data should be presented to regulatory authorities at the time of regulatory submission for approval[32]. These explanations are provided even though they overlap with the processes described above.

【GLP】

To ensure the reliability and reproducibility of non-clinical pharmacology studies, the study

31 Common technical document: An application form agreed upon at the International Conference on Harmonization (ICH) for the approval of drugs common to all three regions: Japan, the United States, and the European Union.

32 It should be noted that such regulatory responses are an essential process, and early consultation with regulatory authorities contributes to reducing the risk of process reversion.

design, conduct, recording, and reporting should be strictly controlled. For in vitro studies[33], activity indicators should be clearly described; and for in vivo studies[34], efficacy data using animal models should be summarized.

Dose-response relationships and duration and onset of drug effects should also be evaluated in detail, and pharmacological data supporting the mechanism of action should be presented experimentally. In addition, comparative data with similar drugs and the possibility of pharmacological interactions should be considered to predict clinical efficacy.

GLP-Tox (toxicity) studies are conducted at accredited facilities, and clinical trial applications can be submitted after completion of the GLP-Tox studies. Non-GMP active pharmaceutical ingredients that meet GLP standards are used in this study.

【GMP】

GMP is a standard for the stable manufacture and supply of drugs with consistent quality. In the manufacturing and supply method based on GMP, it is necessary to describe the synthesis method and scale of the drug substance, outline of the formulation process, GMP compliance status and manufacturing facilities, quality control methods and specifications, supply chain construction status, scale-up issues and countermeasures, manufacturing cost and cost ratio estimates, stability data and shelf life.

【GCP】

GCP is a standard for clinical trials to ensure the human rights and safety of subjects and to ensure the reliability of clinical trial data. In clinical trials based on GCP, it is necessary to clearly describe the study design outline for each development phase, primary and secondary endpoints, inclusion and exclusion criteria for target patients, rationale for dosage and administration, efficacy data (response rate, survival time, etc.), and safety data (type, frequency, and severity of adverse events).

It is essential to establish scientifically and clinically valid endpoints, and it is important to collect endpoint information from the stage of considering the indication and patient population.

Future clinical development plans and the status of discussions with regulatory authorities should also be described.

In the actual development process, the necessary application documents and study items are handled in accordance with various good practices—"good [x] practice" (GxP)—and regulations

33 "In vitro": A method of research conducted in vitro (outside the body).
34 "In vivo": Tests conducted in laboratory animals and humans.

(Pharmaceutical Affairs Law, Pharmaceuticals and Medical Devices Law, General Data Protection Regulation, etc.) in each country and region, such as those in line with various ISOs (not described in detail here). The actual number of clinical trial proposals for drugs is shown below.

Table 6 Number of Clinical Trial Proposals for Drugs

	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024
Initial Clinical Trial Plan Submission	151	127	134	136	175	162	186	194	179	161	192
Nth time Clinical Trial Plan Submission	450	530	511	557	589	512	603	614	463	377	394

Created by the author from 'Number of clinical trial proposals submitted' (Pharmaceuticals and Medical Devices Agency).

In the pharmaceutical field, the International Conference on Harmonization (ICH) has played a major role in formulating these regulations. The ICH has published dozens of guidelines in the four areas of "Quality", "Safety", "Efficacy", and "Multiple domains", and is actively reviewing them. A recent major development is the development of ICH E6 (R3) and E8[35], which reorganize the approach to GCP processes related to clinical trials.

In the process of revising E8, emphasis is placed on the introduction of the quality by design (QbD) concept, which is premised on critical-to-quality factors (CTQ factors), in the planning and design of clinical trials.

CTQ factors refer to characteristics important to quality, which are important parameters and attributes that should be especially controlled and monitored to ensure the quality of a product or process. The QbD approach states that CTQ factors should be clarified in the design of clinical trials.

E6 (R3) was developed by focusing on individual trials in this general guideline. It is formulated as a guideline for "thinking" about how to respond to the diversified objectives and design of modern clinical trials.

It is necessary to pay close attention that the trend of these guidelines will be reflected globally.

2.4 Evolution of the Development Process

Up to this point, I have described the textbook-like drug development process. In the discussion on "diversified modern clinical trials", one of the major changes in the development process is the evolution of computational approaches. This evolution has contributed to the efficiency and diversification of the development process.

35 E6 (R3) is "Good Clinical Practice" and E8 is "General Guidelines for Clinical Trials."

Here, I would like to examine the recent state of this movement, especially in contrast to the preclinical process. This is because the movement at this stage is rapidly becoming active in the development of the business side, which will be described in the following chapter, and in the trends in the areas covered by the business side.

(1) Identification and Analysis of Drug Targets—Optimization of Seed-Lead Compounds

The traditional gold standard in computational science is mainly X-ray crystallography[36] to determine the high-resolution 3D structure of proteins. Using this 3D structure information, a large database (library) of chemical compounds is quickly narrowed down to those that are likely to bind to a target protein (virtual screening).

The top candidate molecules remaining in the virtual screening are predicted to fit into the binding pocket of the target protein in 3D, and their binding affinity is evaluated (molecular docking [MD]). The overall dynamic behavior, including the stability, flexibility of the binding site, and binding dynamics of the complex obtained by docking, is evaluated (MD simulation).

In addition to these traditional processes, cryo-electron microscopy (cryo-EM)[37] has become an important method as a source of structural information for proteins that are difficult to analyze by X-ray crystallography. The obtained structures can be used as input for docking and MD simulation, depending on the resolution.

In addition to the deepening of the experimental basis, for example, 3D protein structures are predicted by AlphaFold[38], an AI-based protein conformation prediction tool developed by DeepMind Technologies Limited (DeepMind). In addition, when robust experimental structures cannot be obtained, computationally predicted structures such as AI system AlphaFold are used as a complement.

(2) Generation of Molecular Compounds

The structure prediction by AlphaFold has also created a flow to "design". Based on the structural information of the target protein and the information of known active compounds, completely new chemical structures are "de novo designed" using AI on a computer, and new lead compounds are created.

For example, AI models developed by companies such as DeepMind and Genentech Inc. can

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36 An analytical method for determining the atomic and molecular structures of crystals by using the property that X-rays incident on a crystal structure diffract in a number of specific directions.

37 An electron microscope method in which samples can be observed while holding water in the vacuum of an electron microscope by placing them at cryogenic temperatures (e.g., via liquid nitrogen).

38 An artificial intelligence program for predicting the structure of proteins.

predict the effects of mutations in protein and RNA sequences. Therefore, the above process is carried out after evaluating whether the designed sequence or mutant is evolutionarily acceptable or functionally acceptable and excluding mutations with high risk of pathogenicity or loss of function.

2.5 Development Process of Medical Devices and Programmed Medical Devices

I would like to briefly describe the process from research to development for the development of medical devices and programmed medical devices, although this is not as detailed as for pharmaceuticals. It should be noted in advance that the development period and funding scale are different in these developments compared with pharmaceuticals.

—Medical Device Development—

(1) Identification of Needs, Problem Analysis, Design and Development

The first step in medical device development is to identify unmet needs. After clarifying medical problems and technical requirements to be solved, the basic design and specifications of the device are formulated, a prototype is created to satisfy safety, performance, and usability, and an initial evaluation is performed. From this stage, appropriate implementation of design and development records and risk management (ISO 14971[39]) is required in consideration of regulatory requirements such as the Pharmaceuticals and Medical Devices Act, ISO 13485[40], and IEC 62304[41].

(2) Non-clinical Studies (Bench Tests, Animal Experiments, etc.)

Based on the prototype, operation confirmation and safety and performance evaluation are performed. Preclinical studies are conducted based on regulatory requirements, including biocompatibility, durability, and animal studies[42]. These studies are required to comply with GLP standards.

(3) Clinical Studies (Clinical Trials)

After safety is confirmed in preclinical studies, some medical devices are deemed to require

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39 International standard for risk management in the entire life cycle of medical devices (software, including for in vitro diagnostics) from design to manufacturing and disposal.
40 Medical Device Quality Management System
41 Medical Device Software Lifecycle Process
42 In particular, in the case of surgical devices and implants, it is important to conduct cadaver studies using human cadavers to evaluate operability, safety, and performance under actual anatomical conditions.

clinical studies on humans, with approval from an ethical review committee. Phase 1 evaluates safety, and Phases 2 and 3 evaluate efficacy and practicality. Data are submitted to regulatory authorities.

Clinical trials must also be planned, conducted, recorded, and reported in accordance with regulations and standards such as ISO 13485 and GCP.

The actual numbers of clinical trials reported are shown in Table 7 below, which indicates that the numbers reported for clinical trials are smaller than those reported for pharmaceuticals.

Table 7 Changes in the Number of Clinical Trials Reported for Machinery and Equipment

	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024
Initial Clinical Trial Plan Submission	151	127	134	136	175	162	186	194	179	161	192
Nth Time Clinical Trial Plan Submission	450	530	511	557	589	512	603	614	463	377	394

Created by the author from 'Number of clinical trial proposals submitted' (Pharmaceuticals and Medical Devices Agency).

(4) Classification of clinical trial applications and reviews

This is a review by regulatory authorities, and the classification in Japan is as follows.[43]

Class 1 (General medical devices)

Devices that are considered to pose an extremely low risk to the human body even if a failure occurs

Class 2 (Controlled medical devices)

Devices that are considered to pose a relatively low risk to the human body even if a failure occurs

43 In the United States: Class I (device that can be marketed if it meets the general regulatory requirements required for all medical devices, Class II (device whose safety and effectiveness cannot be guaranteed merely by meeting general regulatory requirements. In addition to general regulatory requirements, special regulatory requirements must be met—510 (K) or de novo filed with FDA.), and Class III (equipment used to maintain human life or prevent deterioration of health functions, or equipment that may pose a potential and serious risk of injury or disease and whose safety and effectiveness cannot be guaranteed only by the general and special regulatory requirements—PMA submitted to FDA).

In Europe, new medical device regulations were announced in 2017, and the previous European Medical Devices Directive (MDD 93/42/EEC) and the European Implantable Active Medical Devices Directive (AIMDD 90/385/EEC) were integrated into the European Medical Devices Regulation (Regulation (EU) 2017/745 Medical Devices Regulation: MDR), but the details are omitted in this paper.

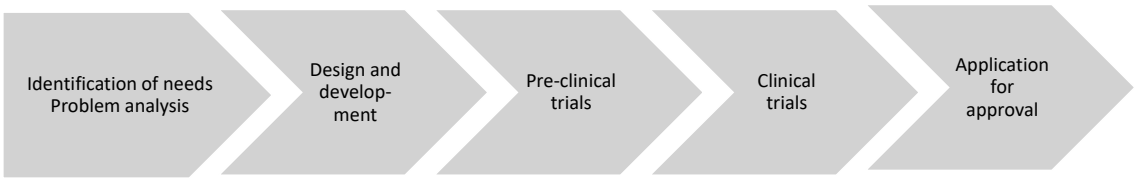
Class 3 (Highly controlled medical devices)

Devices that are considered to pose a relatively high risk to the human body if a failure occurs

Class 4 (Highly controlled medical devices)

Devices that are highly invasive to patients and may directly lead to a risk to life if a failure occurs

Figure 10 Medical Device Development Process for approval applications under the Pharmaceutical and Medical Devices Act



Created by the author.

—Programmed Medical Devices (SaMD)—

Among medical devices, the flow of digital health has penetrated in recent years, and they are grouped under the name of programmed medical devices (Software as a Medical Device, hereafter referred to as SaMD) from the viewpoint of medical devices. The development process is summarized below.

(1) Definition of Medical Issues / Requirements Analysis / Algorithm Design / Prototype Development

As with drug discovery and medical devices, SaMD development begins with the clarification of medical issues and clinical needs. Developers analyze workflows and patient issues in medical settings and organize functions, performance requirements, and regulatory requirements (classification, etc.) to be realized. Based on these requirements, they design algorithms for AI, image analysis, and diagnosis support. They develop prototypes using datasets and conduct initial performance evaluations and usability tests.

(2) Verification and Validation (Preclinical Evaluation)

Implement software validation and risk management in compliance with medical device regulations (IEC 62304, etc.), such as by verifying the performance and safety of developed software through simulations, and establish a quality assurance system.

(3) Clinical Evaluation and Clinical Trials

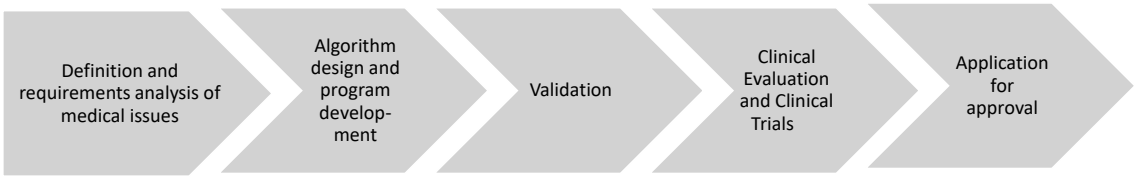
Evaluate the efficacy and safety of SaMD using real-world clinical data. Obtain approval from

the ethics review committee. Conduct pilot and clinical trials in clinical settings.

(4) Application for Approval

Apply for approval to regulatory authorities based on clinical evaluation data.

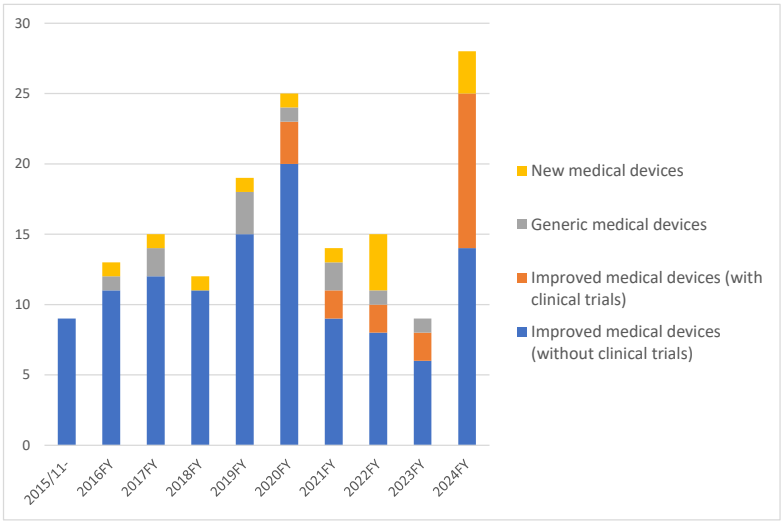
Figure 11 Program Medical Device Development Process



Created by the author.

In the process described above, primary approval is granted after basic safety and efficacy have been confirmed, followed by secondary approval based on actual clinical use data (real world data) and additional performance evaluations. This process is called "two-stage approval" (rebalance notification), and some programmed medical devices are subject to this process.

Figure 12 Trends in the Number of Approved Products for Marketing of Programmed Medical Devices



Created by the author from 'List of approved products for marketing of programmed medical devices' (Pharmaceuticals and Medical Devices Agency).

2.6 Patent Protection

So far, I have described the development process of each product type based on the

relationship with regulations.

However, patent protection is an important aspect in social implementation and commercialization of research. It is one of the difficult points in materializing research from academia, and the key point is how to apply for patent protection at the time that the evidence is obtained. Therefore, in this section, I first explain the types of patents, and then proceed to global strategies and patent application strategies.

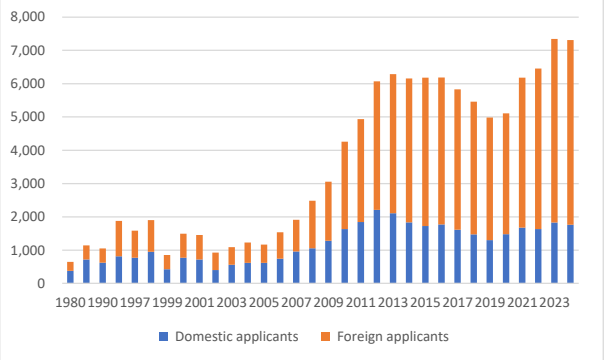
2.6.1 What Kind of Patents are There?

In terms of drug discovery, there are "substance patents", "use patents", "formulation patents", "manufacturing method patents" and "research tool patents". [44]

In addition, under patent law, software and algorithms are also subject to patent if they are "advanced inventions among the creation of technical ideas using the laws of nature". If novelty, inventive step, and industrial applicability are recognized, diagnostic support and prediction methods, systems, and programs using AI can also apply for and obtain patents.

The following shows the changes in the number of patents in the medical field.

Figure 13 Number of Pharmaceutical-Related Patents in Japan



Source: Japan Patent Information Organization, PATOLIS, JP-Net.

Created by the author from Japan Pharmaceutical Manufacturers Association DATABOOK2026.

2.6.2 Global Strategy

Given the above, it is necessary to consider international applications and global strategies.

An important aspect is the Patent Cooperation Treaty (PCT) international application system. Submitting a single application to the patent office of one PCT member country obtains the same effect as filing applications in all PCT member countries.

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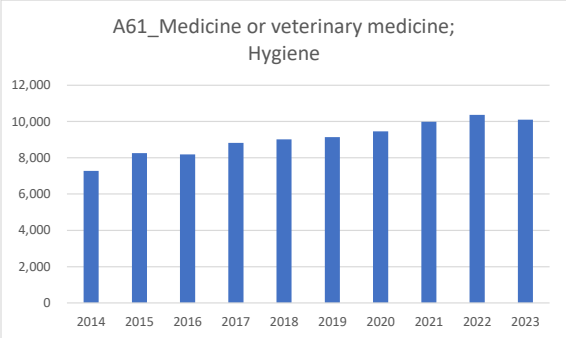
44 In the field of medical devices, it is often important to build a multifaceted IP strategy that combines patents on individual components and elemental technologies, designs, and trademarks, rather than a core material patent as in drug discovery.

The PCT system makes it possible to file applications in a single batch in a uniform format and language. The same filing date is recognized in each country. Furthermore, the novelty and inventive step of inventions can be evaluated in advance through international search and international preliminary examination, which is useful both for selecting countries in which to file applications and for improving cost efficiency. However, the final decision on the grant of a patent is left to the substantive examination of each country's patent office. After the procedures for domestic transfer, the examination is conducted in accordance with the laws and regulations of each country.

Figure 14 shows the number of international applications (PCT applications) that have been domestically transferred to the Japan Patent Office—shown according to technical field (International Patent Classification: IPC) and to the year in which documents were received. The following were extracted: 'Medicine or veterinary medicine; Hygiene'. This figure shows the trend of companies and engineers seeking to obtain patent rights in Japan mainly through PCT international applications.

Figure 14 Table of the number of domestic applications (patents),
by domestic application classification and by the year in which documents were received



Created by the author from 'The Annual Patent Administration Report 2025' (Japan Patent Office).

Table 8 shows the trends in the number of patent applications filed by Japanese based on the "Patent Application Structure in the Five Japanese Offices" in the Annual Patent Administration Report 2025.

As a whole, it can be seen that while patent applications from overseas to Japan are gradually increasing, patent applications from Japan to overseas, especially to Europe and the United States, are not increasing.

Table 8 Trends in the Number of Patent Applications Filed by Japanese[45] Unit: 10,000

	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024
USPTO	8.6	8.6	8.6	8.5	8.6	8.0	7.6	7.7	7.3	7.2
EPO	2.1	2.1	2.2	2.3	2.2	2.2	2.2	2.2	2.2	2.1
CNIPA	4.0	4.0	3.9	4.1	4.5	4.9	4.8	4.7	4.5	4.6
KIPO	1.5	1.5	1.5	1.6	1.5	1.4	1.4	1.4	1.4	1.4

Source: Japan Patent Office Annual Report 2025

2.6.3 Patent Strategy

On the other hand, from the viewpoint of academia, various issues have arisen, such as not filing patent applications early enough due to the preference for deepening research and publishing it, the lack of an appropriate scope of invention and scope of rights in the first place, and the lack of an appropriate geographical scope.

In order to avoid such situations and make use of patents in business, it is necessary to conduct prior art searches and competitive analysis, thoroughly file patent applications early, determine an appropriate scope of invention and scope of rights, and build a patent portfolio.

Specifically, it is important to grasp the application and publication number of the patent (substances, applications, manufacturing methods, etc.) of the institution, the registration status in each country, the expiration date and possibility of extension, the gist of claims, and the monopoly rights (reexamination period) under the drug approval system. At the same time, business operators will also collect information on patents and papers from other companies and conduct freedom-to-operate (FTO) analysis.

In order to implement these strategies in line with the product development strategy (timeline, indications, dosage and administration), it is necessary to draw up a target product profile (TPP) at an early stage and carefully consider the intellectual property strategy in consultation with experts.

On the other hand, from the perspective of universities and research institutions, there is a question of whether to apply for all patents. Therefore, from the perspective of researchers, it is essential to explain that the evidence is sufficient.

In this sense, the key points are to 1) consult with the business side at an early stage and 2) take appropriate measures at university technology transfer (licensing) organizations (hereafter referred to as TLO).

2.7 Consideration of Insurance Reimbursement

45 USPTO: U.S. Patent and Trademark Office; EPO: European Patent Office; CNIPO: China National Intellectual Property Office; KIPO: Korea Patent Office.

For drugs, medical devices, and programmed medical devices, a reimbursement process is essential if they are to be used in the world. This is "pricing". Not only the processes described previously, but also this reimbursement and pricing process must be completed before a product is truly ready to enter the market.

For example, in Japan, after a new product is approved and certified by the Pharmaceuticals and Medical Devices Agency, the marketing authorization holder submits a request for insurance coverage to the Industrial Information Division of the Health Policy Bureau[46]. If the product meets existing definitions and considerations, it is immediately approved for insurance coverage. However, if the product is novel and does not meet the definitions and considerations, it is approved for insurance coverage through consultation with the Medical Division of the Health Policy Bureau, specialized organizations for health insurance medical materials, and the Central Social Insurance Council, and medical fees are determined.

These methods are completely different in each country. In evaluating reimbursement values, some countries place importance on health technology assessment, and each country has set its own rules using quality-adjusted life year (QALY), incremental cost-effectiveness ratio (ICER), or both. In Japan, too, there is a system for adjusting prices to foreign average prices after they are listed in insurance, and each country has its own rules for referring to international prices in this way.

While the price of pharmaceuticals is set for each product, the price of specialty materials[47] is set for each functional category, focusing on the product's structure, intended use, and efficacy. There are approximately 200,000 specialty materials, and each product is repeatedly improved; so, the price is set for each functional category due to the high turnover of products.

2.8 Role Sharing and Support within Academia

The various processes have been described comprehensively so far, but in reality, the important point is who plays each role in this process.

Of course, it is the company that ultimately launches the product; so, in that sense, the company ultimately takes on these roles.

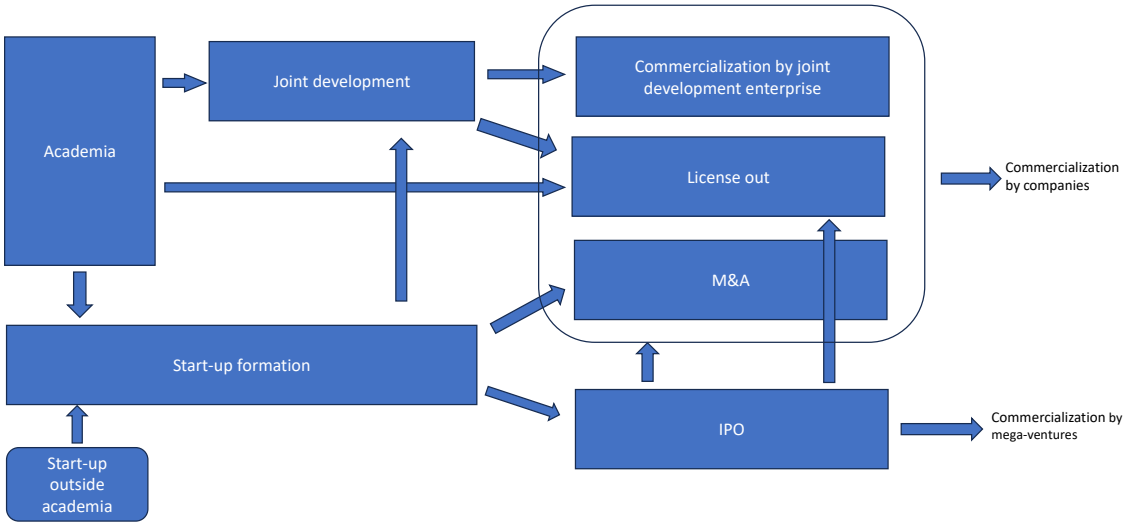
However, when considering the flow of research in academia, there are several branches before reaching that point. There are branches such as forming a startup and recruiting human resources, or conducting joint research and licensing with companies over a certain size. Figure

46 This department promotes the pharmaceutical and medical device industry, and functions not only as a place to submit a request for insurance coverage but also as a consultation counter for insurance coverage.

47 An abbreviation for "specified medical materials", medical devices and materials covered by insurance as specified by the Ministry of Health, Labour and Welfare.

15 shows the branching.

Figure 15 Process to Commercialization



Created by the author.

In addition, each of the aforementioned areas, such as clinical development and clinical trials, pharmaceutical affairs and regulatory compliance, and quality control and manufacturing, requires a person in charge. Each person in charge confirms the appropriateness of the development plan and trial plan by consulting with regulatory authorities as necessary from an early stage. If the design is not efficient and the level of evidence is low as a result, it will not be able to withstand regulatory approval review. In that sense, the involvement of people who understand these processes from the goal point is essential.

However, as each regulation changes and evolves, there may not be many people who are in a position to understand the whole picture. In such a situation, it is necessary to understand who and how to consult, and to create appropriate cooperative relationships.

The government and academia have made steady progress in promoting and supporting these processes.

Approved TLOs have been established nationwide since 1998, and currently there are 30 (Table 9).

Universities are also working to enhance academic research organization (ARO) functions, and an organization called ARO Council was established in 2013 among universities with such functions.

The government amended the Medical Care Act in June 2014 to institutionalize hospitals that play a central role in world-class clinical research and investigator-initiated clinical trials as "core

clinical research hospitals" in order to promote high-quality clinical research necessary for the development of innovative drugs and medical devices. Currently, 16 hospitals are approved as affiliated hospitals of the National Cancer Center and various universities. These core clinical research hospitals have functions such as research management and data management, research consultation, investigator-initiated clinical trials promotion, regulatory response and quality control, bridging research promotion, and human resource development.

The number of investigator-initiated clinical trials that these core clinical research hospitals are expected to promote is shown in Table 10. International-level clinical research and implementation of investigator-initiated clinical trials are not linked in a unified manner, and the role of academia in each process is different. Some are led by companies, while others are led by academia. Therefore, the number of cases does not directly indicate the role of academia, but it does give a sense of the current level.

Table 9 List of Approved TLOs

Approval Year	TLO	Related Universities, etc.	Approval Year	TLO	Related Universities, etc.
1998	The University of Tokyo TLO Co., Ltd.	The University of Tokyo	2002	Kitakyushu Industrial and Academic Promotion Organization (Public Interest Incorporated Foundation)	Kyushu Institute of Technology, Kitakyushu City University, etc.
	TLO Kyoto Co., Ltd.	Kyoto University, Ritsumeikan University, etc.		Mie TLO Co., Ltd.	Mie University
	Tohoku Techno Arch Co., Ltd.	Tohoku University, Hirosaki University, etc.		Kanazawa University TLO Co., Ltd.	Kanazawa University, Kanazawa Medical University
	Nihon University Industry-Academia Collaboration Intellectual Property Center	Nihon University (including Junior College)	2003	Campus Create Co., Ltd.	University of Electro-Communications, etc.
1999	Yamaguchi TLO Co., Ltd.	Yamaguchi University		Shinshu TLO Co., Ltd.	Shinshu University, Nagano National College of Technology, Saitama University, etc.
2000	The Institute for Research on New Business Creation (TLO Hyogo)	Kobe University, Osaka University, etc.	2005	Saga University TLO	Saga University
	Nagoya Institute of Industrial Science and Technology	Nagoya University, Aichi Institute of Technology, etc.	2007	Gunma University (National University Corporation)	Gunma University
	Industry-Academia Collaboration Organization Kyushu Co., Ltd.	Kyushu University		Nara Institute of Science and Technology (National University Corporation)	Nara Institute of Science and Technology
	Tama TLO Co., Ltd.	Tokyo Metropolitan University, Kogakuin University, Toyo University, etc.	2008	Tokai University (School Corporation)	Tokai University
2001	Meiji University Intellectual Property Center	Meiji University		Tokyo University of Science (National University Corporation)	Tokyo University of Science
	Yokohama TLO Co., Ltd.	Yokohama National University, Kanagawa Dental University, etc.		Yamanashi University (National University Corporation)	Yamanashi University
	Techno Network Shikoku Co., Ltd.	Tokushima University, Ehime University, Kagawa University, Kochi University, etc.	2010	Shizuoka Technology Transfer LLC	Shizuoka University, etc.
	The Institute for the Promotion of Industrial Technology Research	The University of Tokyo Institute of Industrial Science	2016	iPS Academia Japan Co., Ltd.	Kyoto University, etc.
	Niigata TLO Co., Ltd.	Niigata University, Niigata University of Pharmacy and Applied Life Sciences, etc.	2021	Kobe University Innovation Co., Ltd.	Kobe University
			2023	Fukushima Medical University Translational Research Organization (General Incorporated Foundation)	Fukushima Medical University

Created by the author from Japan Patent Office website.

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Table 10 Publication of Registration Data for jRCTs
(Clinical Research Submission and Publication System)

	2018fy	2019fy	2020fy	2021fy	2022fy	2023fy
Specific Clinical Research	188	423	429	403	394	351
Non-Specific Clinical Research	19	65	80	112	100	135
Company-Sponsored Clinical Trials	127	219	405	608	516	525
Investigator-Initiated Clinical Trials	27	67	74	77	75	59
Other	16	34	74	275	337	446
Uncategorized	384	305	119	0	0	0

Source: Excerpt from the Ministry of Health, Labour and Welfare's 'Future Directions for Promotion of Clinical Research and Clinical Trials'.

Note: jRCT is the abbreviation for Japan Registry of Clinical Trials.

Summary

For the development of the healthcare sector, comprehensive efforts from basic research to clinical applications and social implementation as products and services are essential.

At each stage, such as strengthening evidence, regulatory responses, patent strategy, and insurance reimbursement, specialized knowledge and collaboration among relevant parties are required. It is also important to design research with an awareness of exits and to build a collaborative system between academia and industry.

Chapter 3 Response to Exits

- As business aspects, it is essential to grasp needs, differentiate, and develop an implementation system.
- For collaboration and exit design between academia, companies, and VCs, it is important to coordinate practical perspectives. In addition to providing funds, VCs play a multifaceted role encompassing functions such as development progress, team composition, and data construction.
- To what extent academia can internalize such coordination is another major issue.

In Chapter 2, I organized the processes necessary for the process of realizing products and services. In parallel, it is necessary to construct a business model. In this chapter, I will organize the difficult points involved in this process.

3.1 Business Aspects

Business considerations differ for each item, such as pharmaceuticals, medical devices, and healthcare services. In addition, as seen in Chapter 2, it is difficult to organize the processes necessary for commercialization, simply because the regulations and laws on which they are to be based differ. In this chapter, I will first organize the general contents. Then in the next chapter, I will organize the contents relevant to each field.

The theme of this paper is the development stage; so, I do not write about business based on actual results such as income. Therefore, it is important to increase the probability and persuasiveness of each aspect of business.

Here, I will first pick up some of the issues regarding social implementation.

—Identifying Needs

The biggest issue that should always be returned to is "Who are your customers and what are their needs?": the assumption of situations in which products and services are used.

In particular, this idea is widely used in the medical device field, and needs orientation is one of the major methods. On the other hand, pharmaceutical development is sometimes described as a seed-seeking type.

However, in the case of pharmaceuticals, as well as in the target product profile (TPP), which will be discussed later, how to identify needs is emphasized at the entry point, and setting unmet needs as the starting point is the central item of development.

At the same time, a sense of the scale of the needs itself is also important. In the process of

social implementation, it is important to clarify the estimated number of patients in various strata based on disease epidemiological data (prevalence, incidence, etc.) in Japan and overseas, and to estimate the number of patients considering treatment rates and other variables.

However, it is not easy to determine whether the potential patients should switch their current treatment to use the product. In order to obtain such numbers clearly, it is essential to be able to clearly envision the situations in which the product or service will be used.

—Differentiation Points

Next, while conducting prior research on technology and intellectual property, if there are competing products and services, points of differentiation become important. Clinical positioning must be organized based on the mechanism of action, efficacy, safety, and price of the main competitor.

If there are no overwhelming differences in efficacy, safety, or price, the value of the business will include how delivery is conducted.

In this sense, product development that can build a market if it has strong sales power can be imitated by someone, but it may not be attractive as a business that venture capitalists or other investors undertake as a startup.

Paradoxically, the value of a startup is importantly tied to explicitly demonstrating differentiation in efficacy, safety, and price.

—How to Execute It

I mentioned earlier that if it has strong sales power, developers often forget not only how to deliver but also how to execute the business. The assumption that someone will do it often results in no one taking that role.

Specifically, it is necessary to clarify the important conditions (milestones, exclusivity, etc.) of alliances and contracts with collaborators, including alliances and licensing, and to make the division of roles explicit.

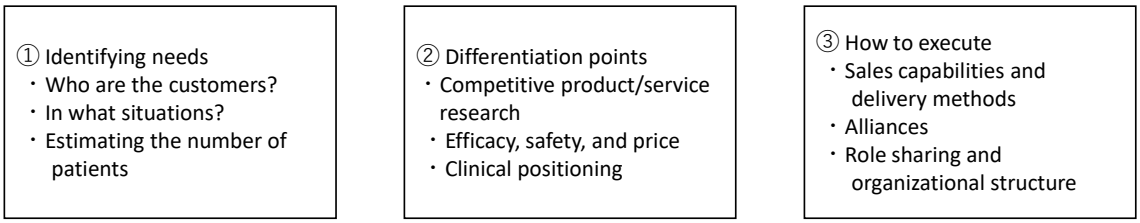
It is necessary for the business operator to control this; so, the kind of personnel and kind of organization to do this are key.

All three points listed above—identifying needs, possible differentiation points, and ways to execute the business—should always be revisited as development proceeds. The big question is "Who needs the product or service, and where?" and then we need to go back to who gets access to actual users and payers and how.

As the number of items to check relative to the business increases and collaboration progresses, the overall business tends to become less of a personal concern. It is important to

consider that the people responsible are the ones who have the desire and initiative to solve the issues at hand.

Figure 16 Points to Consider When Considering the Business Aspect



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3.2 Filling in to the Exit

In this paper, the "Exit" does not refer to a typical business exit such as an IPO or M&A. Instead, "Exit" is defined as the point at which a pharmaceutical or medical device product is finally delivered to patients and can contribute to their health. However, there are several important processes that must be completed before the product actually reaches the patient. Since the term "Exit" at those processes can sometimes be used in a narrower sense, I will specify "Exit (delivery to a company)" where appropriate to clarify its meaning.

The target product profile (TPP) is an important concept when considering the exit (delivery to a company) in pharmaceutical development. This is a concept that is mainly emphasized by pharmaceutical companies. In particular, the TPP has been arranged as a concept almost entirely on the pharmaceutical industry side until recently.[48]

In fact, the main items in the TPP are as follows.[49] These items become criteria for continuing development and making decisions on commercialization.

1. Indications, standard treatment, and clinical positioning
2. Method of administration, dosage, and dosage form
3. Number of target (potential) patients (and stratification)

48 A guideline for clarifying the image of a product to be aimed at. It is necessary to clarify issues to be solved, enable effective risk management, and objectively decide whether to continue development (go/no go) based on data. In companies, teams of experts from various fields share R&D goals using the TPP.

49 This list is based on 'Chemical and practical requirements for drug candidates targeted by companies' (Japan Pharmaceutical Manufacturers Association Research and Development Committee).

4. Scientific evidence and mechanism of action
5. Patent information/Other patents
6. Alliances and licensing relationships
7. Expected efficacy from non-clinical pharmacology studies
8. Pharmacokinetics in non-clinical studies (ADME [see footnote 23 on page 18])) and prediction of pharmacokinetics in clinical studies
9. Possible adverse reactions from non-clinical safety studies
10. Clinical study plans and results
11. Manufacturing and supply relationships
12. Competitive product information and market analysis

An important point in organizing the TPP is that the decision to continue development (go/no go) can be made objectively based on data. In fact, much of what is mentioned here is covered in Chapter 2.

From the perspective of companies, it will be difficult to incorporate research from academia into the development process if it is not consistent with the items comprehensively listed here.

However, the thinking and decision tree of companies are black box concepts, at least from the viewpoint of academia. In addition, in drug discovery, it is quite rare in modern times that academia takes the case to the end of the exit. Therefore, one of the points is how far the alignment can be made at the preclinical stage at least. Among the above TPP main items, 1, 2, 4, 7, 8, and 9 correspond to this.

In this regard, what companies point out is the difference between "good data" required for publication and data required for product development. It is also necessary to understand the thinking of companies when considering the exit. In addition to the TPP aspects pertinent to evidence building, companies' exit considerations include social implementation–related TPP main items 5 and 10 and a certain understanding of aspects related to business itself—for example, TPP main items 3, 6, 11 and 12.

It is important to have a certain level of understanding and to establish a framework in which there are no discrepancies in cooperation with the company after the fact.

In the case of medical devices and health tech, there are differences in terms of TPP main items 2 and 8, as well as consideration about the stage at which collaboration with companies becomes necessary. However, the concept of TPP covers all aspects.

3.3 Commitment and Role of VCs

At this point, the role of venture capital becomes clear. At least in the life sciences, venture

capital is not just a source of funds, but is more important than other business arrangements in terms of both expertise related to "development" and "business assembly". Here again, I would like to look at the movement of VCs related to drug discovery first, and then touch on medical devices.

There are many different stages at which VCs invest. But from the perspective of VCs involved from the beginning of project making, including company creation, one of the best timings is to commit at the stage from basic research to exploratory research (identification and analysis of drug discovery targets, optimization of seed and lead compounds, and development to preclinical and clinical development). Such timing clarifies the kind of therapeutic effect to aim for, given the particular disease, and enables early TPP engagement. "Investment intervention at the seed stage" is exactly at this stage.

It is often said that the success or failure of subsequent clinical trials depends on the quality of data at this stage. And the possibility of failure at this stage is very high.

In this sense, it is necessary to obtain sufficient data from preclinical trials. In accordance with GLP as described previously, toxicity studies are conducted to determine whether the data are sufficient to enable the submission of a first-in-human (FIH) trial application such as an investigational new drug (IND) application, and to assess whether a patent application can be filed prior to submission of a research paper.

After that, from Series B (growth-stage venture funding round) onward, Phase 1 data and Phase 2 data in line with clinical development are used as proof of concept for funding. From here on out, how to construct a decision tree is an important decision for the entire team.

The overall flow is as simple as described above. But in reality, the role of VCs is important in developing products with an eye toward an exit. The major roles of VCs are summarized below.

(1) Organizing the Direction and Creating a Strategic Exit Path

One of the major roles of VCs is to clarify the position of the product under development in the global landscape and how it can be differentiated.

Capitalists with good networks have relationships with multiple potential acquirers and can incorporate data points and milestones required by acquirers into the development process at each of the above stages. Specifically, VCs consult with investment banks early on and consider various exit patterns, including licensing agreements.

(2) Contributing to Team Up

When VCs commit, they form a startup, which requires members with various roles other than scientists.

The role of VCs is to engage from the level of "company creation" rather than mere investment, and important in that role is how to gather the necessary human resources, which will be described in a later chapter.

(3) Building Data Packages

Preclinical studies require a wide range of data, but not all studies can be done in academia or by startups. It is necessary to make a decision to comprehensively collect the data prioritized for technology evaluation within the scope of funds available.

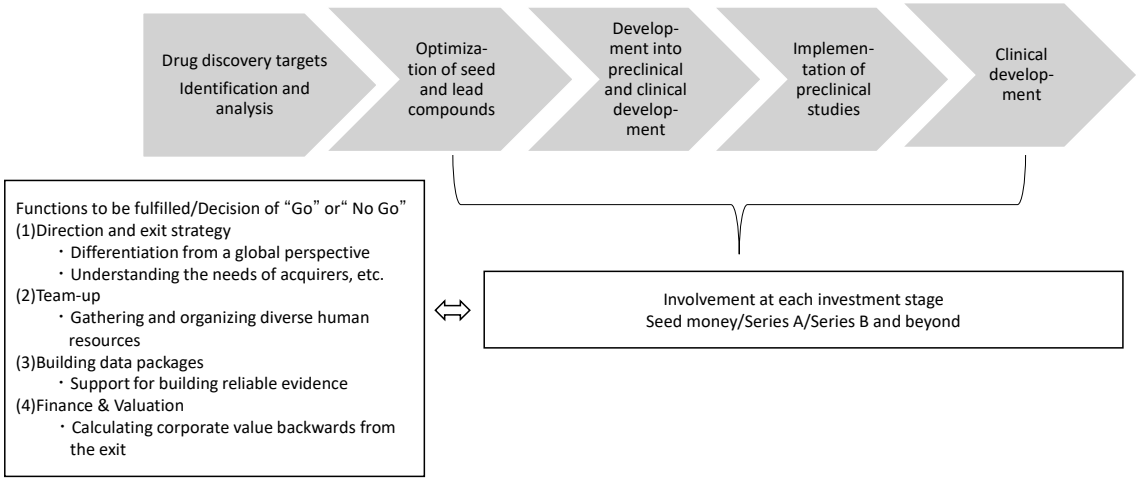
It is also important to collect reliable data that will lead to future clinical trials and to make the data package easy for each department of the company to consider. It is also necessary for VCs to team up people who can do such consideration within the VCs or in the partner company.

(4) Finance & Valuation: Calculating Backward from the Exit

Up to this point, I have sorted out how to use actual funds. At the same time, if we do not set the value of the company in an appropriate way, the perspectives of the company and the market at the time of exit (acquisition or IPO) will be far different. It is important to raise funds by making appropriate valuations while keeping in mind the value of the shares for the founding team and early committed investors and the time horizon until the exit.

As seen, VCs are deeply involved not only in funding but also in strategy building and team formation. Their primary role is to strike a balance between the progress of development and the construction of future business while communicating appropriately with the management, and they judge whether to go or not go on business progress.

Figure 17 VC Commitment (Drug Discovery)



Created by the author.

In the medical device field, the basic role is the same, but one characteristic is that the timing of commitment differs from that of pharmaceuticals.

In terms of identifying needs, as described in Section 2.5, "After clarifying medical problems and technical requirements to be solved, the basic design and specifications of the device are formulated, and prototypes are prepared and evaluated in order to satisfy safety, performance, usability, etc." One characteristic of medical devices is that it is possible to evaluate the feasibility of clinical use at this stage.

Next is the process of "confirming operation and evaluating safety and performance based on prototypes at the non-clinical (bench tests, animal experiments, etc.) stage, and then moving to clinical trials". But since this time frame is faster than that of pharmaceuticals, the amount of capital required is relatively small, and the acquiring company often makes an acquisition when sales have reached a certain level; so, it is necessary to assemble a sales force by then.

In addition, compared to drug discovery, this process does not necessarily need to go through academia. One characteristic of this process is that in many cases, clinicians are invited as advisors, while serial entrepreneurs serve as management teams.

It should be noted that drug development itself requires a long period of time from the start of research to product launch, and that venture funds themselves are fixed-term funds, and that, apart from the progress of development, decisions on the progress of development may be influenced by the fund's deadline, and that there are still few capitalists, particularly in Japan, who are familiar with these activities.

As mentioned in the previous papers, Japanese venture capital investment (total of bio, medical, and healthcare) exceeded 50 billion yen in FY 2021 in a wide range outside the framework of academia, but the number of people actually involved in such investments is still limited.

3.4 Response in Academia

So far, I have described the concept of the TPP held by companies and the existence of VCs to support project creation. What is important for academia is how much of this "concept" can be internalized.

Again, there is a leap between the discussion of how to delve deeper into science described in Chapter 1 and the discussion in this chapter. Within the science that is being delved into deeper, various kinds of support should be provided for projects that are judged by people within academia to be "sufficient for social implementation at a relatively early stage", and not all projects are eligible for such support. Based on this basic premise, I would like to describe what academia should do for those "shining projects" that are eligible.

In textbook terms, universities and research institutes establish TLOs for the purpose of promoting technology transfer. They evaluate R&D projects on campus based on the technology readiness level (TRL[50]) and investment readiness level (IRL[51]), and support negotiations with technology transfer recipients. For example, if the TRL is high but the IRL is low, support will be provided for building business models, conducting market research, and formulating business plans in order to raise the IRL.

In this sense, by using levels as a common language, we can provide objective explanations to companies. On the other hand, as shown in section 3.2 in regard to the TPP, the level required by companies is that which indicates progress in line with the actual development process; and whether the company has gone through the processes necessary for commercialization is an important perspective.

In addition, in terms of the business level, there are many cases in which the commitment of VCs itself is carried out early, and the key point is how to get the project to the stage of completion before various conditions are set.

From this perspective, "Can academia proactively participate in development progress and business assumptions at the level that companies and VCs consider and commit to?" needs to be satisfied, and in fact, communication between the R&D in academia and the business development of companies is indispensable.

It is important to create an environment in which such activities can be carried out from the perspective of tech transfer (activities to transfer research results from universities and other institutions to companies and other institutions for commercialization).

At the same time, in terms of what to transfer, the primary assets are patents and datasets.

As described in section 2.6, it is essential to formulate a patent strategy in the development process, but it is necessary to be able to suggest an appropriate formulation when consulted by scientists on this point. The academic pressure on scientists can increase the likelihood of early

50 Technology readiness level (TRL) is an index developed by NASA that shows how close a technology or research result is to commercialization. It is usually rated on a 9-point scale, from 1 (basic research stage) to 9 (commercialization stage). Specific key levels are TRL1: observation and reporting of basic principles, TRL4: technology verification in a lab environment, TRL7: prototype demonstration in a real environment, and TRL9: demonstration and commercialization in an actual operating environment.

51 Investment readiness level (IRL) is an index that shows how ready a technology or business idea is to receiving funding from investors or companies and being commercialized. There is no clear international standard, but it is indicated by IRL1: business idea generation, IRL4: business model validation, IRL7: negotiations with investors, and IRL9: completion of financing and commercialization.

publication of the relevant technology; so, it is important to find a balance. Not all research applications can be submitted at the same time; so, selection is an important role.

In this process, it is necessary to evaluate intellectual property appropriately (there are cases where academics value their own IP excessively) and to have a perspective that anticipates the exit (realization of corporate value).

Since these judgments require expertise, it is a great advantage to have human resources who have not only legal background such as patent law but also medical science background. Whether such human resources can be incorporated as staff is also important from the perspective of intellectual property (IP) protection.

Through these activities, it is also possible for universities to invite international support through asset visualization. From the perspective of social implementation, it can be said that the activities that universities must carry out are how much they can assemble themselves and how they can expand their networks.

Summary

The commercialization of healthcare requires a multilayered process to enable research results to proceed to social implementation. Clarification and differentiation of needs and the construction of an implementation system form the foundation of commercialization, and practical perspectives such as the TPP and the patent strategy are essential for collaboration between academia, companies, and VCs and for exit planning.

VCs play a multifaceted role not only in funding but also in development progress management, team composition, and data package construction. Universities and research institutions also need to implement technology transfer and asset visualization, as well as tech transfer and IP protection, while being aware of this perspective.

Chapter 4 Issues in Social Implementation in Each Field

- In the drug discovery field, as the diversification of modalities and platform technologies and investment in basic technologies advance, it is necessary to discuss the exit, and the earlier the stage the better.
- In the medical device field, needs in the field are more emphasized, and improving the resolution of the exit is key.
- In the nursing care device field, the various issue include, for example, the complexity of systems and regulations, the definition of the quality of nursing care, and cost-effectiveness. Therefore, it is necessary for business entities to fully draw up the overall picture.
- In the health tech field, the process of building evidence and identifying payers is important; and both setting a business plan with an eye to the exit and committing to the business are required.
- In each field, the key to social implementation is to support the validity of the business plan and the figures based on appropriate building of evidence, understanding of field needs, and establishment of exit strategies.

4.1 Drug Discovery

4.1.1 Drug Discovery as an Object of Support and Investment

Describing innovation in drug discovery comprehensively is not a realistic endeavor, but I would like to provide some perspectives.

First, in terms of modalities, which are types and forms of treatment, various types of drugs are being developed, such as small molecule drugs and antibody drugs have traditionally been at the core of the market. Then, in addition to regenerative medicine products (cell medicine, gene therapy[52], etc.), drug development is progressing in various modalities, including peptide drugs[53], nucleic acid drugs[54], and mRNA drugs[55], which are mainly classified as macromolecules.

In addition, drug development based on new platform technologies has been active, such as microbiome drugs that target the intestinal microbiota, mitochondrial drugs that control intracellular energy metabolism, and nanomedicines that utilize nanoparticle technology.

In the field of existing small molecule drugs, new trends have emerged in recent years, such

52 Using viral vectors to repair and replace genes in the body.
53 Therapeutic drugs using natural or synthetic peptides (e.g., GLP-1 receptor agonists).
54 Using DNA or RNA fragments to suppress gene expression to treat disease.
55 Drugs that express a desired protein in the body by administering mRNA.

as drugs targeting protein-protein interactions (PPI) and proteolysis-targeting chimera (PROTACs) that induce the degradation of target proteins.

In the field of antibody drugs, in addition to conventional monoclonal antibodies[56], there are developments in drug discovery using NANOBODY®[57], development of antibody-drug conjugates (ADC) using bioconjugate technology[58] to expand the function of antibodies, technologies to selectively deliver drugs to target cells, and antibodies that simultaneously recognize multiple targets, such as bispecific antibodies and multi-specific antibodies.

【Example disease areas】

Cancer; lifestyle-related diseases (diabetes, hypertension, dyslipidemia, etc.); autoimmune diseases (rheumatoid arthritis, multiple sclerosis, etc.); neurodegenerative diseases (Alzheimer's dementia, Parkinson's disease, and amyotrophic lateral sclerosis [ALS], etc.); cardiovascular diseases (chronic heart failure, etc.); digestive diseases (Crohn's disease, ulcerative colitis, etc.); respiratory diseases (severe asthma, COPD, etc.); rare diseases

The term "platform technologies" is used above, but in recent years the term "platform" has come to indicate a large category of major investment targets for biotech VCs.

Platform technology serves as a "common platform" that can be applied not only to individual drugs and treatments but also to a wide range of applications. In fact, it is fundamental technology that supports the "type of treatment" embodied by the modality.

Examples include " VHH antibody production technology", "antibody engineering technology (antibody-drug conjugate [ADC] design and binding technology, bispecific antibody production technology, etc.)", "mRNA synthesis and modification technology", "peptide synthesis and modification technology", "viral vector and non-viral vector gene transfer technology", "gut microbiota analysis technology (metagenomic analysis, etc.)" and "mitochondrial isolation, purification, and administration technology" among many others, including drug discovery platforms that utilize AI and bioinformatics.

While there are VCs that invest in companies that have such platform technologies, there are also investments in startups targeting individual diseases mentioned above as usual.

Of course, there are many cases in which platform technologies are used for technologies that respond to such diseases, and there is a difference between focusing on the fundamental technology and focusing on the target disease. However, the fact that fundamental technologies

56 Antibodies made from clones derived from a single antibody-producing cell.
57 VHH (variable domain of heavy-chain-only antibodies) derived from camelids such as llamas.
58 The formation of a stable covalent bond between two molecules, at least one of which is a biomolecule.

themselves become investment targets indicates that fields close to basic research are becoming investment targets.

In addition to direct drug discovery, investment in drug discovery platforms that utilize AI and bioinformatics up to the preclinical stage, as described in Chapter 2, has also grown into a major field (called "bio computing"), and the scope of investment in the same bio field continues to change from a global perspective.

4.1.2 Response to Technological Diversification

In the previous chapter, I discussed how much academia includes the perspectives of companies and VCs. In fact, the newer a technology is, the harder it is to easily add it to the existing TPP. From the academia side, discussions with the business side, including VCs, become more important. Collaboration with companies will also start early.

The time axis is important in this regard. Considering the career path of a scientist, the tenure of the person in charge at a company, the investment period of a fixed-term fund, etc., the larger the themes and categories listed here, the less likely it is that individuals will be directly involved in the entire process. This is especially true when considering the timing at which they can be involved in the period from the formulation of a new technology to the launch of a drug.

Therefore, at the time of product launch, the essential needs of who will use the drug, at what time, and in what form will be separated, and as a result, the fluctuation range of the actual corporate value calculation will become large. What is important is to go back to the basics.

It is true that some epoch-making businesses will become "mega-businesses" in the future. But from that perspective, it is important not to trivialize the current individual development, but to steadily assemble it in accordance with the principles.

As for platform technology, it is not always possible for a company to understand the effective use of the technology. At present, the mainstream is that venture companies become mega-companies and promote collaboration with major companies. From that perspective, it is also necessary to keep in mind that the embodiment assumption of product utilization will be different from the conventional framework.

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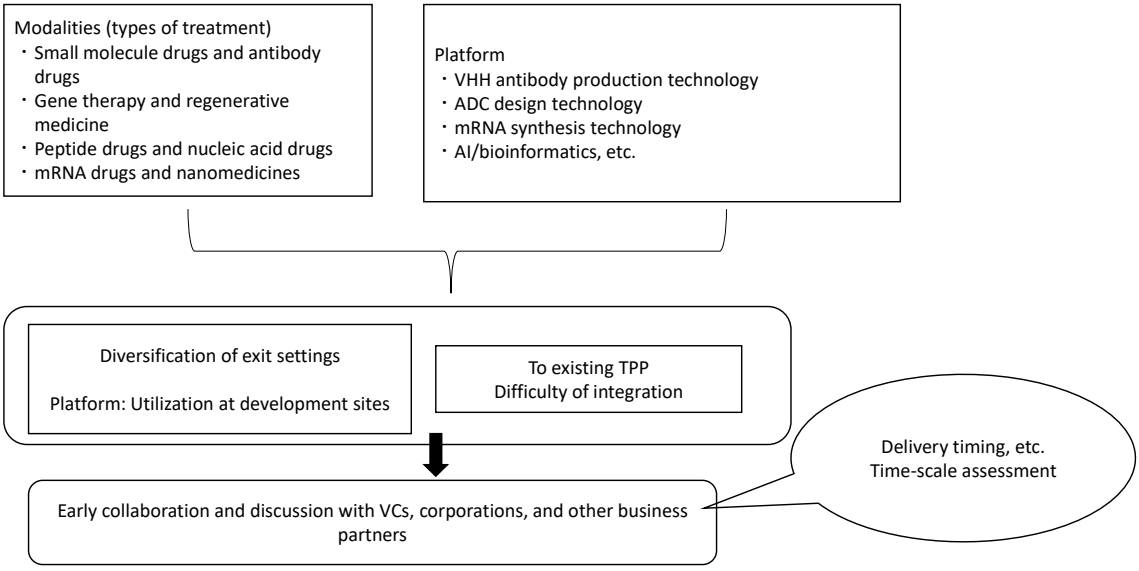
Figure 18 Perspective on Social Implementation (Drug Discovery)



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4.2 Medical Devices

4.2.1 Medical Devices as Targets for Support and Investment

In the medical device field, the number of disease areas directly targeted for treatment is narrower than in the drug discovery field described above, and the period from development to market launch is generally shorter.

In addition, there is a wide variety of devices used not only for treatment but also for medical diagnosis and monitoring including at home, and this is an area where engineering and information technology are actively utilized.

—Therapeutic Equipment—

Cardiovascular system (stents, catheters, pacemakers, prosthetic valves, etc.); orthopedics (artificial joints, spinal implants, etc.); diabetes-related equipment (glucose meters, continuous glucose monitoring (CGM), insulin pumps, etc.); surgical support/robotic surgical equipment (surgical robots, navigation systems, endoscopes, etc.)

—Diagnostic Equipment—

Diagnostic imaging equipment/AI image analysis (MRI, CT, ultrasonic diagnostic equipment, AI image diagnosis support software, etc.); high-precision diagnosis and screening of early cancer; early diagnosis and progression management of dementia (Alzheimer's disease, etc.)

—Home Medicine—

Home mechanical ventilation for patients with severe respiratory failure; home dialysis equipment for patients with chronic renal failure (miniaturized and simplified); home monitoring and preventive management for patients with heart failure; home management and preventive support for chronic obstructive pulmonary disease (COPD)

【Disease areas】

Lifestyle-related diseases (diabetes, hypertension, dyslipidemia, etc.); cardiovascular diseases (chronic heart failure, etc.); respiratory diseases (severe asthma, COPD, etc.); orthopedics, etc.

4.2.2 Enhancing the Resolution of the Exit

As I mentioned earlier, the medical device field is an area in which engineering and information technology are actively utilized; so, it is easy to develop new technologies with a technology-push approach.

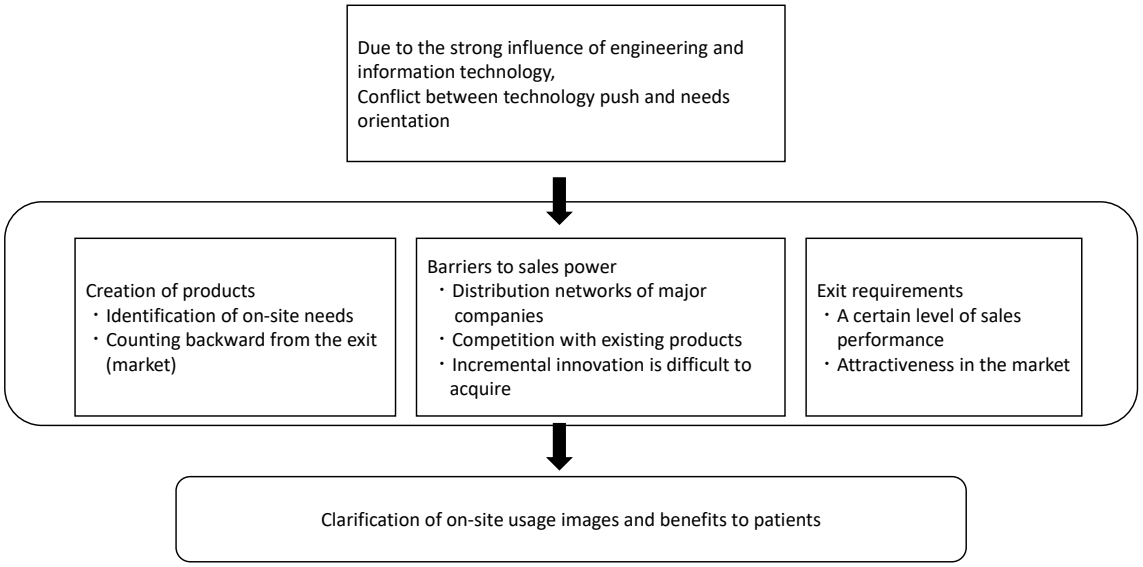
This point itself is not problematic, and it is easy to imagine that development has been carried out in this way since the dawn of time. There is a culture in which device development originally started in garages, and development that inherits this lineage is probably still being carried out both inside and outside of companies.

However, it is important to be able to carry out efficient and patient-first product development as existing technologies advance greatly and the area covered increases. The idea of "biodesign", which is mentioned several times in this paper, originated at Stanford University in the United States and spread throughout the world. It is the idea of identifying and narrowing down needs on the ground, and considering the end market first.

Another difficult point is the understanding of "sales power". If the area covered by existing technologies is large, it is natural to assume that major companies already have global distribution networks in each field. In this case, there is a strong possibility that incremental innovation will not be seen as attractive by the target company, because innovation is always accompanied by a struggle to improve existing products. In the case of medical devices, a startup-acquiring company generally requires the startup to first generate a certain amount of sales. This may be because companies with limited sales power want proof that they will be attractive in the market.

Ultimately, "exit orientation" boils down to raising the probability of how a product will be used in the field and what benefits will be brought to patients. It is necessary to raise this resolution.

Figure 19 Perspective on Social Implementation (Medical Devices)



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4.3 Nursing Care Devices

4.3.1 Innovation in the Nursing Care Market

Largely due to the existence of nursing care insurance, the nursing care market is a focus area in Japan, although it is typically positioned as a type of medical device. In the first place, medical care is focused on curing, while nursing care is focused on maintaining a certain health level. At the same time, it has been judged that it is more efficient in nursing care to utilize human resources, and as a result, pricing has been restrained. However, while demand for nursing care itself continues to increase, the shortage of human resources has become a topic, and innovation in this field is inevitable.

The system of nursing care remuneration is divided into two categories—at-home services and facility services—and the system is designed in a highly segmented manner. Various innovations have been devised, such as nursing care robots, monitoring services, and IT services for business support, but these require responses to a segmented market. The following product groups can be classified according to drug discovery and medical devices.

—Transfer and Movement Support—

Devices for safe transfer and movement support from beds

Systems for higher precision in terms of fall prevention and detection

Devices for burden reduction during bathing (e.g., bathtub lifts)

Devices for prevention and management of pressure-induced ulceration

Measures for supporting walking (e.g., robots, power assist suits)
Devices of lift support, to reduce burden on caregivers

—Excretion and Bathing Support—
Wandering detection and monitoring system for elderly people with dementia
Excretion care (automatic excretion treatment, toilet guidance support)

—Watching and Communication Support—
Communication support devices
Remote monitoring and emergency call system for home care

—Medication Management and Life Support—
Eating assistance and swallowing support devices
Medication management and automatic medication support system

—Automation and Efficiency System—
Creation of care records and care plans

In terms of approval and authorization for such care devices, there are primarily two regulation and certification sources: the Pharmaceutical and Medical Devices Act and the Long-Term Care Insurance System.

Nursing care devices are classified according to their impact on the body. Electric wheelchairs, high-function mattresses, and transfer assistance robots are medical devices that require approval, certification, and notification under the Pharmaceutical and Medical Devices Act. On the other hand, walkers, canes, and bathing products are treated as welfare equipment and are not regulated by the Pharmaceutical and Medical Devices Act. However, they must meet the standards set by MHLW to be covered by nursing care insurance.

4.3.2 Bottlenecks in Market Building

The need for each of the above categories is understandable. However, it seems that there is still no consensus on the extent to which they are effective.

Improving labor efficiency is only a means. Essentially, the important theme is how to maintain or improve the quality of care. However, what "quality of care" entails is still unclear. Techniques for measuring quality have been discussed in various professional fields. However, compared to the field of medical care and treatment, where evidence is clearly available, it is difficult to share the same theme at the field level compared to responses to various issues such

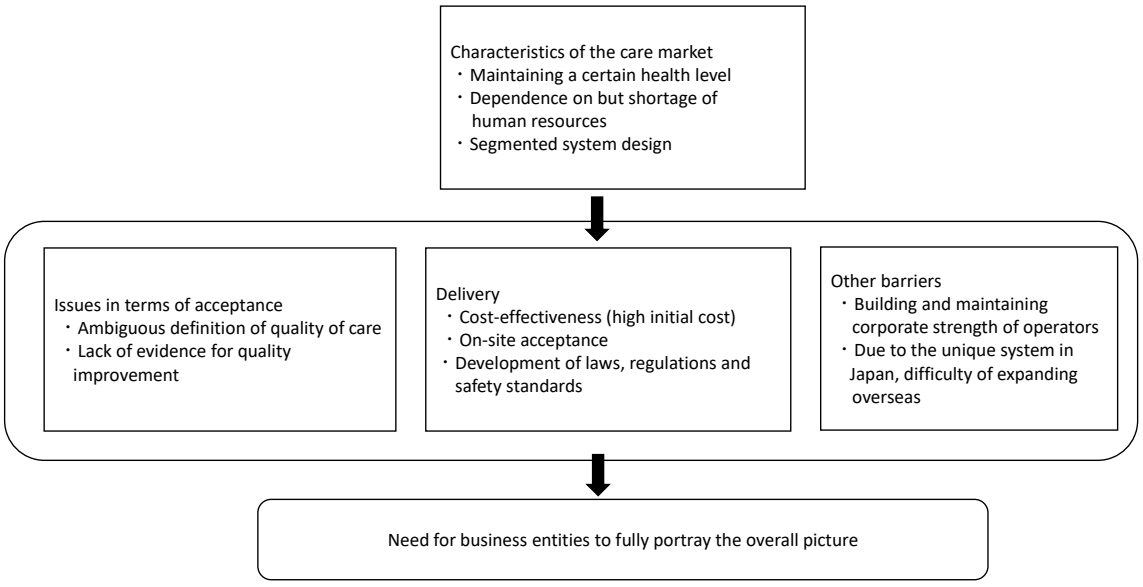
as resolving human resource shortages and improving profitability.

In addition to these essential issues, there are also issues such as cost-effectiveness (initial introduction costs are high, and the burden on care providers and individuals is high), acceptance and education in the field (fostering the understanding and trust of care workers and users in the equipment, and enhancing operation training, etc.), and the development of laws, regulations, and safety standards (certification, standardization, and international standardization). A difficulty of this field is that it must comprehensively demonstrate these points.

In light of these difficulties, the opportunity to show "what to solve" and "how to improve quality" through innovation in the field of care will be an opportunity to demonstrate the impact of innovation.

Even if these barriers are overcome, there are still a number of bottlenecks, such as building and maintaining the strength of companies that use the products and services, and overcoming the difficulty of grasping overseas markets due to Japan's unique system. Business entities are needed to fully draw up the overall picture.

Figure 20 Perspective on Social Implementation (Nursing Care Equipment)



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4.4 Health Tech/Healthcare Services

4.4.1 Markets Created by Health Tech

Efforts to utilize digital technology in medicine and healthcare in general have been ongoing for a long time, and actual products and services are undergoing changes as the technological

aspects of digital technology change. Various vocabulary terms are also used, and they are defined in various forms, such as digital health, medical diagnosis, and health tech.

Naturally, when it comes to the level of products and services, there are a wide variety of players who enter the market. Given that each player assumes a different market size, level of evidence, time frame, etc., there is not necessarily a unified view, and there is an aspect that those who are vocal are strong. However, at the moment, the needs related to the medical field are narrowed down to some extent. For example, the main needs are as follows.

—Improving the Efficiency of Medical Care, etc.—

Improving the quality and safety of remote medical care

Reducing the workload of medical practice

Interoperability and integrated management of medical data

—Disease Prevention and Management—

Behavioral change support for disease prevention and health promotion

Individualized optimization of chronic disease management

Digitization of mental healthcare

There are a variety of products and services that support these technologies, including online consultation platforms, AI interview systems, integrated management software for data from multiple health apps and devices, health promotion apps, and software as a medical device (SaMD) related to chronic disease management and mental health.

In addition to these developments, it is worth mentioning how AI is being applied. In the field of diagnostic prediction, AI analysis of diagnostic imaging (CT, MRI, pathology images, etc.) and genome analysis data is making it possible to detect diseases at an early stage, assess their progression, and predict their prognosis with high accuracy. These technologies assist doctors in diagnosis and contribute to determining the optimal treatment plan for each patient. In the field of clinical response prediction, AI analysis of various data, such as a patient's genetic information, biomarkers, and electronic medical records, makes it possible to individually predict the efficacy of a drug and the risk of side effects. This is bringing about more precise personalized medicine.

4.4.2 Evidence and Delivery

In the case of pharmaceuticals and medical devices, even new innovations are based on the market for existing products.

In many cases, substitutes are the starting point. But in health tech, the idea of substituting something is somewhat rejected, and there is a tendency to emphasize the point of being able

to do something that was not possible before.

In this sense, it is certainly a field that requires more attention to determining "what can be solved" by transforming processes.

However, this field also has issues that overlap with the fields of medical devices and nursing care devices described previously. And in many cases, it ends up being a product-out service. The discussion from the perspective of who ultimately pays for the service becomes ambiguous.

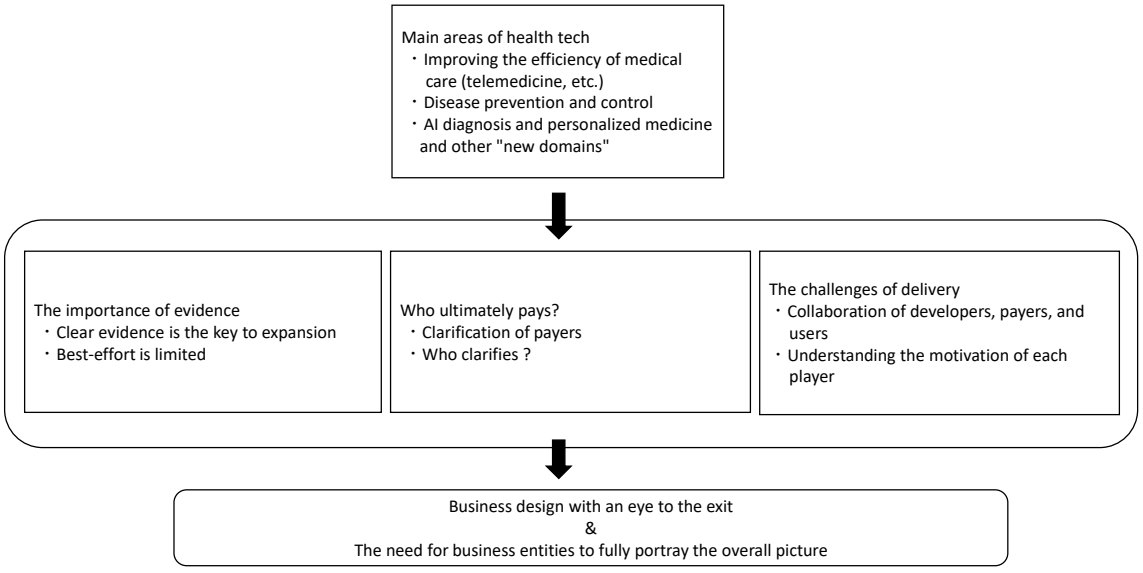
This ambiguity is closely linked to the level of evidence, and the degree of spread will naturally differ between products and services with clear evidence and those with best-effort levels. Conversely, there are quite a few cases where people talk about market changes based on wishful thinking without building evidence.

From the perspective of the ambiguity over who ultimately pays, in many cases, there is a possibility that there will be a different company or some kind of collaborator between the developer and the payer who makes the payment. But there are quite a few cases where this point is lax and the various parties think about building the evidence, but then they discard the discussion about who will commit.

Only when there is credible evidence will the person who commits take action, and much time and cost are required to acquire the evidence that is appropriate and widely credible. On top of that, it is important to understand who will take action and what motivation they will have, and whether or not it is possible to build a business and anticipate the market.

An important point is to determine how to avoid continuing development with a technology-push idea without being able to achieve this alignment, making it difficult to see an exit.

Figure 21 Perspective on Social Implementation (Health Tech/Healthcare Services)



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4.5 The Likelihood in Business

Normally, the latest trends based on technology should be described in a "trends in each field" category. But many fields are described in an abstract manner because they are destined to become obsolete the moment their definitions are written.

To begin, I would like to emphasize that not all research and development related to medicine is becoming huge. As a matter of course, the cost of the drug discovery process is ballooning, including the progress of AI, and there are an increasing number of fields that cannot be realized without the use of a huge amount of infrastructure. However, it is unreasonable to dismiss all of them as "a view of the history of biotech becoming huge", and even in each of the fields mentioned in this chapter, there are both "fields that may become huge" and "fields that can be established as local projects".

In addition, in the form of a business plan, the amount of investment required for development is taken into account, and the presence or absence of a need is reduced to "quantity". Factors that bring about differentiation are reflected in "unit price" etc. And "sales" are calculated by multiplying the "quantity" figure by the "sales" figure.

On the other hand, costs after launch are divided according to the method of delivery, and the "time axis" associated with the penetration of products and services is inevitably linked to the amount of procurement required.

A "business plan" represents a relatively simple conclusion, but it is sometimes difficult to reach this point in technology-oriented thinking. However, a business plan with a high degree of probability—that is, a plan based on figures with feasibility and evidence—is necessary.

Figure 22 shows an image of how these points are reflected in figures, but naturally the figures themselves will change to some extent as the business progresses. However, without a certain logic, these figures themselves cannot be assembled, and having a system to continuously review them is an important point for business continuity.

Here, I mainly describe the contribution to the profit and loss statement. But in actual business, it is necessary to reflect items related to investments in the balance sheet and to the management of cash flow, which convey a different meaning from the profit and loss figures.

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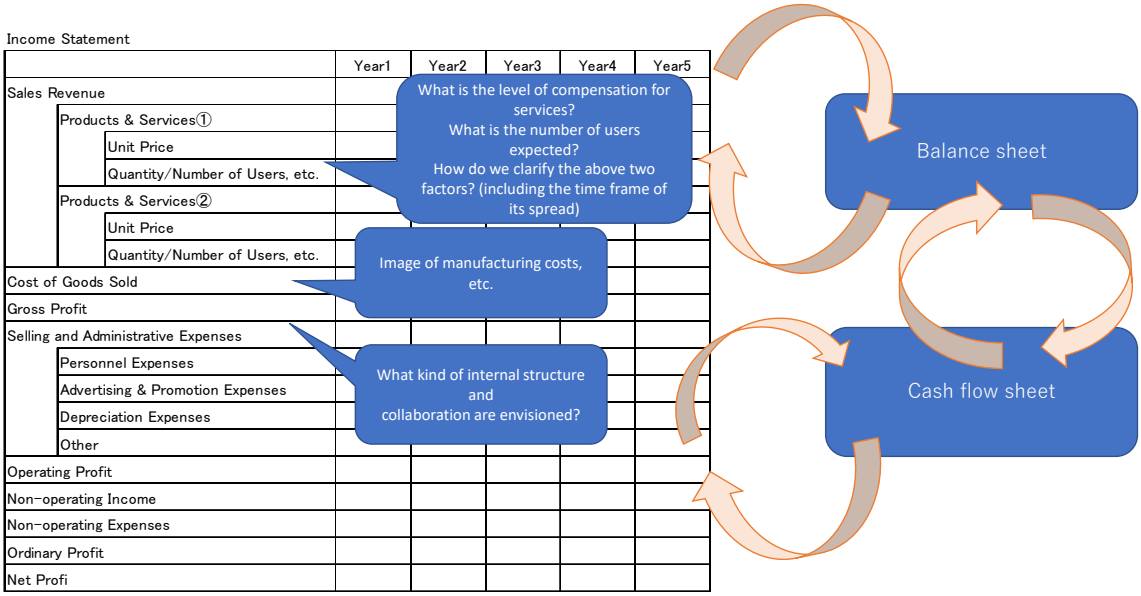
Figure 22 Reducing to Figures Image



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Summary

This chapter summarizes the latest trends in the fields of drug discovery, medical devices, nursing care devices, and health technology, as well as the diversification of technological innovation and investment in each field.

Also in each field, exit strategies, evidence building, grasping on-site needs, and solving issues for commercialization are essential. In particular, the probability of business plans and the support of figures determine the success or failure of social implementation and market expansion.

Chapter 5 Required Human Resources and Direction of Improvement

- In the United States, Europe and Singapore, as well as in other countries, programs to develop diverse practitioners and international human resources have been developed, and practical education with an eye toward exit has been emphasized.
- In Japan, external systems have been implemented by government agencies and Japan Agency for Medical Research and Development (AMED). But in the future, it will be important to appropriately build in human resources who understand both development and business within academia, and to create a framework for this.

5.1 Human Resources Required for Social Implementation

The characteristics of human resources required for social implementation will be considered. Below, I organize the image of human resources required for each function. In this context, it is easiest to illustrate the required human resources by considering the formation stage of a startup.

At the initial stage, the main human resource components comprise the following two types:

- Team Management
  Vision and strategy formulation and sharing ability
  Team management and leadership
  Interprofessional coordination and decision-making

- Research and Development
  Expertise and practical skills in drug discovery, biotechnology, pharmacology, engineering, and medical device design
  The search for new technologies and products and an orientation toward innovation
  Collaboration and communication with other fields

In practice, the following responsibilities are required according to the process described in Chapter 2. However, the need depends on the stage and can be satisfied or supplemented by outsourcing. However, when outsourcing is performed, it is extremely important not to leave the function entirely to the outsource company, but rather to handle it as an internal responsibility and to ensure that management has comprehensive knowledge of the activity.

- In Charge of Clinical Development and Clinical Trials
  Design, conduct and monitoring of clinical trials

Cooperation and coordination with clinical trial facilities and clinical research organizations
Patient recruitment data management

- In Charge of Pharmaceutical Affairs and Regulatory Compliance
  Ability to develop and implement pharmaceutical strategies
  Knowledge of regulations and application processes in each country, ability to negotiate and communicate with regulatory authorities
  Ability to develop common technical documents (CTDs [see footnote 27 on page 19])

- In Charge of Legal Affairs
  Competitive patent analysis
  Knowledge of intellectual property law and experience in patent applications, rights, and license negotiations
  Competence in contract drafting and legal risk management

- In Charge of Quality Control and Manufacturing
  Knowledge of quality control and manufacturing processes and experience in plant and production line management and auditing
  Competence in traceability risk management
  Ability to respond quickly in the event of a quality defect

In the context of Chapter 3, the above responsibilities apply especially in cases when prospects for actual sales and the like are in sight.

The following aspects will also be required:

- In Charge of Business Development and Marketing
  Market analysis and formulation of business plans and profit models
  Ability to formulate and execute sales and marketing strategies
  Ability to negotiate with customers

- In Charge of Finance and Administration
  Knowledge and experience in accounting, finance, and capital policies
  Ability to manage funds, budgets, and costs
  Business management and compliance capabilities

In fact, it is not realistic or necessary to have such a full team from the start-up stage. In the initial stage, it is necessary to have a person who leads the R&D and a person who coordinates the whole process, including the progress of the development.

5.2 Examples of Human Resource Development

5.2.1 Examples of Educational Programs

Human resource development linked to business in the medical field has been tried in various countries. Even in Japan, educational programs have been set up at several schools.

A representative example is the biodesign program in the medical device field. Originating at Stanford University, it aims to combine medicine and engineering, and emphasizes the process of letting developers get into the field of users (doctors, nurses, and patients), discovering potential needs, materializing those needs, and turning them into products.

Need-driven is a characteristic, but it is positioned as a discipline rather than mere know-how. At the core of education is a practical learning cycle referred to as "see one, do one, teach one". The essence of biodesign is believed to be acquired only through actual development on the ground and teaching to younger students. Awareness of exit strategies is emphasized from an early stage, and education has already been conducted to consider exit strategies at the stage of needs selection and idea generation.

Needless to say, there are some aspects that run counter to the culture that emphasizes these strategies and yet have impact. Therefore, the introduction of the Stanford biodesign system in Japan started with "teaching people who teach", preparing for its spread by establishing "Global Faculty in Training" in which Japanese teachers are thoroughly trained in Japan for six months in collaboration with Stanford. This system originated in Japan and was later expanded to other countries.

A characteristic of the Silicon Valley area is a deep pool of mentors, including an ecosystem that supports entrepreneurs, but this remains to be seen in Japan.

I have described biodesign programs in the medical device field. Similar to the biodesign programs described above, Stanford has a program for drug discovery ventures, the SPARK program, whereby many mentors gather to brush up on projects.

Although the above example programs are renowned worldwide, various other educational programs have been developed in various countries, mainly in North America.

5.2.2 Examples of Europe and Asia

The situation in Belgium described in my previous two publication is also helpful.

First, from the perspective of how to develop human resources for social implementation

within academia, I would like to reiterate an excerpt from an interview with Jo Bury, former director of Vlaams Instituut voor Biotechnologie. VIB has emphasized basic research while emphasizing the role of technology transfer offices (TTO) in bridging research to social implementation, and has taken a form of balancing various career paths of scientists. An aim is to publish basic research in top journals in pursuit of originality and novelty. Based on this movement, TTO experts who understand both scientific and business languages take charge of the part related to social implementation and work together with scientists to identify the application potential of inventions. These TTO personnel are required in order to combine scientific knowledge and business acumen and promote intellectual property protection and commercialization.

On the other hand, the Advanced Master in Biotech and Medtech Ventures (AMBT) at Solvay Brussels School at the Université libre de Bruxelles has started efforts in terms of fostering entrepreneurship in business. In this program, a variety of practitioners from academia, industry, VCs, and regulatory authorities serve as lecturers, and the students are of various nationalities and backgrounds. This focus on variety is partly because of the underlying philosophy that diversity is essential to the creation of innovation and, like the biodesign program, the emphasis is on "development with an eye to the exit". Here, the exit means "delivering products to patients and the field to save many people", and the steady assembly of each process with an eye to the bottleneck is a point that is very useful for Japan as well.

In Singapore, too, a variety of human resource development and human resource invitation programs have been actively developed to support the development of cutting-edge industries, including in the life science field. These programs range from cross-industry programs to those specialized in the life sciences.

The Technology for Enterprise Capability Upgrading (T-UP) program operated by the Agency for Science, Technology and Research (A*STAR) in Singapore dispatches researchers to companies for up to two years to work as technical advisors, transferring technology and sharing know-how on site.

The Singapore Biodesign Program is a representative example of human resource development specialized in the life sciences field.

Also, SG Innovate has launched the Helix Immersion Programme as an initiative focused on the life sciences field, aiming to strengthen the human resource pipeline in the biomedical field. This program provides immersive learning opportunities to experience each stage, such as clinical development and funding, and emphasizes helping early-career human resources understand the complex processes of industry.

5.3 Japan: Supplementing Human Resources

In Japan, universities offer educational programs, but at the same time, support for "supplementing human resources" has been strengthened as a policy to strengthen businesses. Here, we will take up two Japan Agency for Medical Research and Development (AMED) projects.

- Strengthening Program for Pharmaceutical Startup Ecosystem

This project aims to solve the large-scale shortage of development funds faced by startups in the drug discovery field and raise the level of the ecosystem as a whole. The unique point is that AMED has established a "registered VC (venture capital)" system to subsidize the development and commercialization of startups in the non-clinical, phase I, phase II, and exploratory clinical trial stages on the condition that VCs who provide hands-on support specialized in drug discovery invest in them.

The subsidy target includes foreign-affiliated Japanese companies for the purpose of raising funds and commercialization in overseas markets, and the design is strongly conscious of global expansion.

AMED's subsidy supports development costs for commercialization on the condition that registered VCs invest at least one third of the total project cost. This aims to increase the leverage effect between private and public funds and promote growth in Japan and overseas.

- Medical and Engineering Collaboration Global Expansion Project (International Expansion Hands-on Support Project)

In the field of medical devices, AMED is developing projects to support the global expansion of small and medium enterprises and startups. For the development of medical devices at the preclinical and clinical stages, AMED provides development support with a view to expanding overseas, including in the United States, and experts assist in solving issues essential for international expansion, such as intellectual property, legal affairs, and regulatory compliance.

In addition, AMED is developing an environment to promote collaboration between major companies and domestic startups, and has built a system to accelerate the practical application and global expansion of innovative medical devices.

These policy supports are characterized not only by funding but also by multilayered mechanisms, such as expert support, system development for global expansion, and strengthening industry-academia-government collaboration.

5.4 Practical Measures in Japan

Looking back from Chapter 1, Japan's current level of funding for R&D in academia is

approximately 200 billion yen a year from KAKENHI and AMED, and there are 120,000 researchers, even if not all resources are allocated to research. Considering that the amount of VC investment and the number of clinical trial applications in this field have remained at the level described in this paper, not only in academia but also in Japan as a whole, it can be said that further improvements are required. These improvements are especially needed from the perspective of social implementation from academia.

The system for supplementing talent from external sources described in section 5.3 is one methodology, but in order for Japan as a whole to reach a higher level, it is necessary to build a system and human resources that can see "the whole process" on the academia side.

As for the parts of the functions described in section 5.1 that can be addressed within academia, broadly speaking, there are two aspects: one is related to the development process, and the other is management with an eye toward the exit.

In the part related to the development process, it is necessary to appropriately understand the development process as described in Chapter 2, and to bridge the process to the next stage in the form of tech transfer, and to implement intellectual property protection in that process. One of the keys is whether the person who implements this in academia can create a situation in which they communicate closely with the R&D person and make appropriate suggestions.

It is up to the judgment of the organization whether to secure such human resources through career changes from doctors and researchers, or whether to assign specialized human resources to the field and develop them. However, considering the limited number of projects that are headed toward the exit at the moment, it is not hard to imagine that good results will be difficult to achieve unless the organization sets a firm direction and prepares to develop human resources. Organizational commitment is extremely important.

On the other hand, management with an eye toward the exit is basically required, including in entrepreneurship, and it does not mean that it cannot be developed unless it is linked to an organization. As with the development process, there can be either a career change from doctors and researchers or a development as specialized human resources in the field. But conversely, it is desirable to create a situation in which the position of entrepreneur or an individual in charge of social implementation with an eye toward the exit can be considered as a career path. In this sense, it is desirable to set up a place where people from various backgrounds can gather and learn.

There are two more important points. One is the image of the target project. In this field, there are a mix of products and services that are unique to the Japanese market and that do not exist

overseas. What should be avoided as a discussion is a bias toward one side or the other. It is necessary to build a network for projects that should be developed in a way that is comparable to overseas markets. On the other hand, it is not necessary to forcibly discuss the international market for projects that are not. It is also necessary to work as a professional to build a market on one's own, even if the project is basically aimed at the domestic market. These discussions tend to get tangled up frequently, so discernment and balance are important.

The other remaining important point is the effective use of human resources who have had the opportunity to study and do research overseas, as discussed in Chapter 1.

It is easy to imagine cases in which, when returning to Japan from a country where such a framework is already in place to some extent, the lack of such an environment makes it impossible to make effective use of the knowledge and networks available. Looking at the age structure of researchers described in Chapter 1, there is a possibility that such a situation will be repeated. To avoid such a situation, not only as individuals but also as an organization, it is necessary to prepare a situation in which the overseas environment can be understood seamlessly.

Figure 23 summarizes the picture based on these issues. Since conventional methodologies ultimately lead to discussions on a "project basis", it seems that there are many cases in which individual universities and research institutes make efforts to create a project, supplement human resources externally, and discuss social implementation on a stand-alone basis within the scope of their individual knowledge. When such a project becomes visible, the result is often different from what was expected for the exit, and it is speculated that this causes the actual commercialization process to stop.

Figure 23 schematically shows measures to improve this situation. Whether it is the development process or the social implementation process, it is necessary for the support side to shift the direction to intensively cultivate human resources who can handle the project, and to seek ways to avoid having to deal with it all by one organization. When focusing on the framework of "cultivating human resources", it is necessary to make use of overseas human resources and overseas networks. Therefore, it is necessary to seriously create such a framework.

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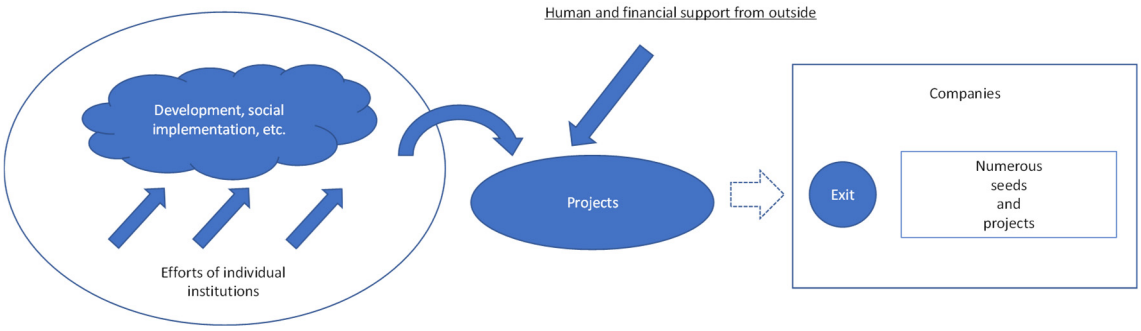
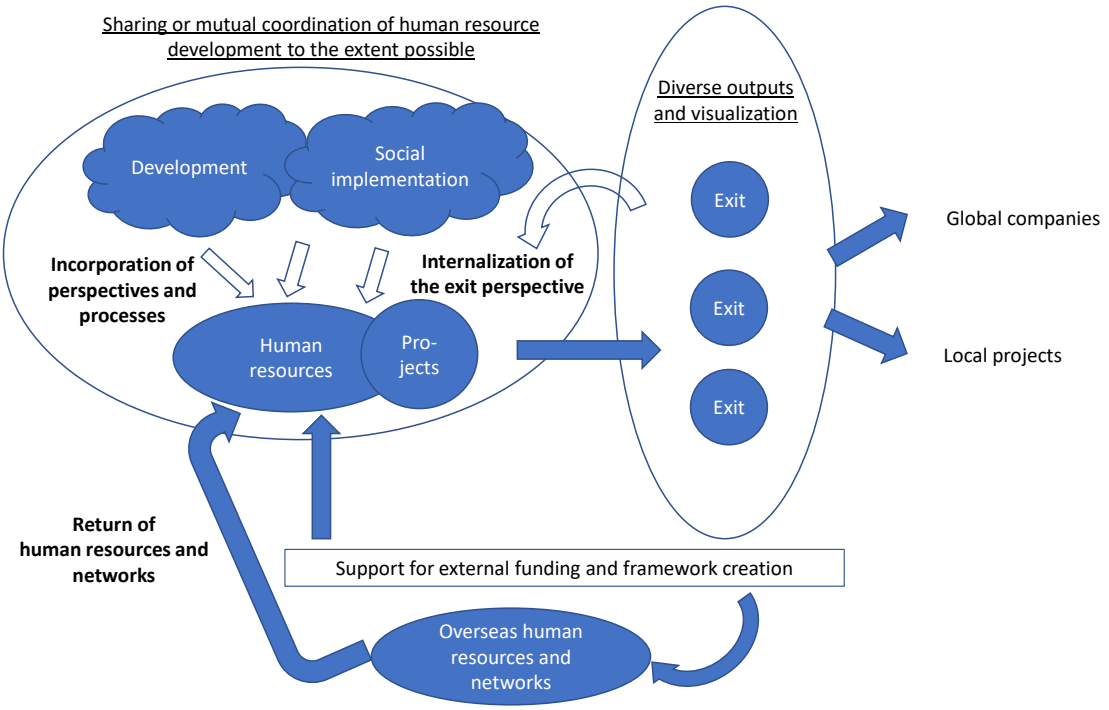
Figure 23　Measures to Improve Social Implementation

—Previous Image—



—Direction of Improvement Image—



Created by the author.

As I wrote this paper, I was reminded of the need for mentors to suggest the direction that should be included in both project-based support and overall framework consideration, based on past experiences. It is easy to imagine that the more layered an ecosystem is, the richer the presence of such mentors and the suggestions generated from them. In Japan, it is also necessary to create an environment in which various trial-and-error experiences currently being conducted will lead to appropriate mentoring in the future.

Summary

From the examples of the United States, Belgium, and Singapore, it can be seen that human resource development that emphasizes diversity and practicality is the key to creating innovation, and that exit-oriented education programs greatly contribute to the development of human resources who can contribute to the field.

In Japan, an external system has been used to conduct the projects, but it will become more important to properly build in human resources within academia who understand both development and business.

Closing Chapter Toward Strengthening Social Implementation

- It is necessary for individuals both to have the opportunity to look over the entire process while delving deeper into science and to visualize the career path for such human resources.
- As an organization, it is necessary to continue to create a form of deepening science by specialization and strengthening core facilities, and to develop end-to-end human resources and collaborate with industry and overseas institutions.
- Society should promote both international alliances and the return of human resources from overseas, while responding to the dispersion of education and organizations.
- The key to social implementation is the sharing of practical perspectives toward an exit, and steady responses to the above are required.

This paper has looked at measures to promote the vitalization of the healthcare field, especially in academia, from various angles. It is summarized as follows from the perspectives of individuals, organizations, and the whole.

1 Toward Individuals

The term "individuals" here mainly refers to researchers. However, I think that what is described in this paper is not realistic from the viewpoint of researchers who understand the research field mainly by writing papers. The starting point is that researchers themselves delve into the field and produce high-quality results.

On the other hand, as described in this paper, it is one aspect of the truth that trying to "turn research into products and services" or providing support for them may contribute to the healthcare of many people in the original sense.

Regardless of whether researchers end up in that position or not, it is important in their career to understand the process to exit and grasp the career path within it. In particular, it is not a loss to know "what kind of supporters can exist", and it is important to have an environment in which they can consider the possibility of being on the support side after looking ahead to their own career from the aspect of "ecosystem formation".

2 Toward Organizations

As in the conclusion for "individuals" above, the term "organizations" here mainly refers to universities and research institutes. As in the case of individuals, there are quite a few things that need to be addressed in order to build a system that enables them to explore science in academia, such as the division of labor among research-related specialists and the strengthening of core

facilities, although this article has hardly touched on them. In particular, considering that there is no environment in which the budget scale will increase significantly, the difficult situation will continue.

On the other hand, strengthening of social implementation is a slightly different theme from how funding should be. As mentioned in Chapter 5, it is important to deal with practical human resource education and to make decisions as an organization in that direction in order to break through the sense of stagnation created by the age balance of research personnel.

To that end, it is important to deepen the understanding of the process as an organization with an eye to the exit, to visualize one's own assets in an open manner, and to form a flat alliance with overseas institutions in that flow in order to build a foundation for promoting metabolism.

3 As a Society

Finally, in the abstract category of "society", these can be understood as measures to address issues that are difficult to overcome by a single organization.

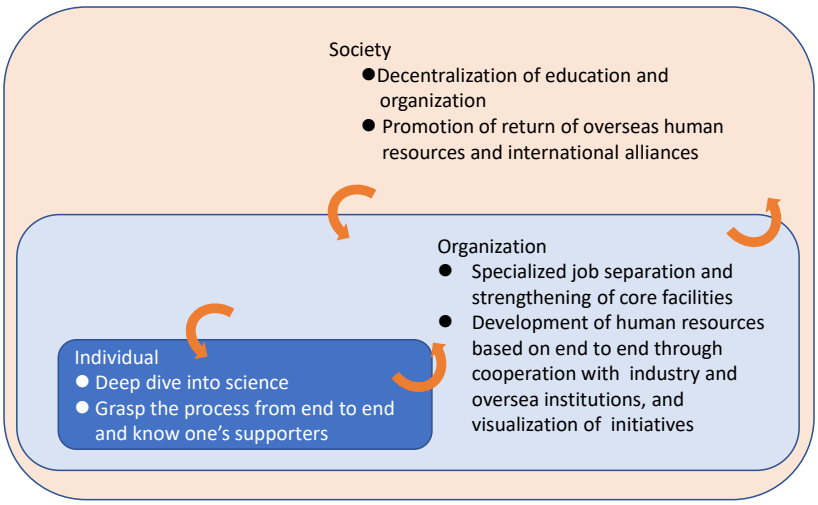
In line with this article, such measures also refer to the development of an "educational system for management personnel" as described in Chapter 5, the return (or exchange) of personnel who have left overseas, and the promotion of international collaboration based on these efforts.

As described in Chapter 4, there are issues in each field that cannot be addressed by academia alone unless there is an exchange of personnel, including those in industry. However, there is a limit to the ability of individual organizations to develop human resources who will be the backbone of resolving these issues.

The current limited number of projects for social implementation is also considered to be a bottleneck in maintaining the educational function. However, as funds for R&D continue to flow and human resources continue to exist even at this point, measures to improve this situation should be considered at a level that goes beyond individual organizations.

The categories of individuals, organizations, and society described here complement each other. The growth of individuals leads to the revitalization of organizations, and the cooperation of organizations promotes the development of society. At the same time, society supports the cooperation of organizations, and the state of organizations supports the growth of individuals.

Figure 24　Relationships among Individuals, Organizations, and Society



Created by the author.

The core quest of this paper is to determine "the essence of social implementation". And as I mentioned in the introduction, I believe that sharing practical perspectives toward the exit is essential for developing individuals and ensuring that the revitalization of organizations and society becomes a reality, rather than merely an ideal.

Personally, I have been fortunate enough to have opportunities to talk with people who are considering various developments in their career paths, and I have often felt that a "practical perspective" is essential for engaging in meaningful discussions. Therefore, in this paper, I have decided not to describe the process of reaching the conclusion that a practical perspective is essential, but rather, to the extent possible, use that conclusion as a starting point to show what a "practical perspective" is.

For this reason, much of the writing included in this paper is quite casual for a managerial economics research format, but I hope that you will understand that this is something that should be clearly communicated.

Special Thanks

As described at the beginning, this paper is prepared based on the many opportunities for discussion described at the end. I would like to express my great gratitude to those who participated in this paper. Among them are the following participants in my series of seminars (called "Practical Discussion for the Formation of Life Science Ecosystem") hosted by DBJ's RICF (personal titles were as of the time of each individual's participation in the seminars).
(2023FY)

Hidenobu Ishizaki (Director, Center for Advanced Cancer Therapy, Cancer Institute Ariake Hospital)
Naohiko Aketa (Center for Clinical Research, Keio University Hospital, Solvay Brussels School of Economics and Management)
Hiroki Shimazu (Fellow, Research and Development Strategy Center, Japan Science and Technology Agency)

(2024FY)
Fumiaki Ikeno (Senior Researcher, Stanford University School of Medicine)

(2025FY)
Kieran Mudryy (4BIO Capital Partner)

In many of these meetings, Michihiko Wada participated as an interviewer. The discussions at these seminars form the basis of this paper. Naohiko Aketa's work and various activities that form the basis of his work, which are also mentioned in the references, form an important basis for organizing this paper.

In addition, I would like to express my great gratitude to Nobuhiro Tanno and Ken Matsumoto, with whom, since the publication of my previous work, I have had the opportunity to discuss various issues that researchers have, and to Tomoko Asaoka, who introduced me to various researchers.

Then, the greatest dynamo in organizing this paper to complete a trilogy were my continuing discussions regarding the two previous works with Jean Claude Deschamps, who in November 2025 was awarded the Order of the Rising Sun, Gold Rays with Rosette, for his contributions to strengthening economic relations between Japan and Belgium. It can be said that all three of these ‘Economics Today’ works were directly influenced by his activities. I would like to express my gratitude again.

Finally, having reached the end of this paper, I would like to mention that I have always felt through my discussions with the respective experts that the underlying strength of healthcare and life sciences in Japan is strong. It is certain that technology, human resources, and the market all exist in Japan, and how to improve the design that connects them is a major theme. I would like to continue to invest my efforts in this regard.

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