Biotechnology Equipment

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Overview of the Bioindustry

1. The Concept of Biotechnology

In Japan, the term "biotechnology" means technology for utilizing the biofunctions of microorganisms, animals and plants, and their chemical reactions in the living body.

An organism decomposes and synthesizes or produces materials in moderate amounts with minimal energy and has a production system for adapting to the environment. This delicate and accurate phenomenon of living organisms was recently attributed to genetic information. Watson (U.S.)and Crick (UK) clarified the molecular structure of germs in 1953, and Cohen and Boyer produced the first successful experiment on the recombination of genes in 1973. Since then, biotechnology has gained attention as an innovative technology expected to solve many of the problems pertaining to energy, food, and medical treatment that mankind is facing today.

2. Features of Bioindustry

a. Technology Thrives through Interaction with Science

Animal cell fusion technology now being directed at the production of monoclonal antibodies, has been applied as a research method over the process of applying basic research in immunology. Also, the recombinant DNA technology was developed instead of results from research that described the process of gene creation.

Because biotechnology was developed during the process of basic research as a means of promoting basic studies, the technology is still exerting its effect in this developing elemental science. Likewise, it is invaluable in conducting basic studies in the fields of immunology, cell division, and photosynthesis. To the degree that biotechnology has developed and improved through basic research in turn contributes to the development of a new understanding of the essence of science. Biotechnology could be defined as a technology that thrives through interaction with science.

b. Biotechnology is a Technology whose Findings, through Basic Research, are Easy to be Put into Practical Use

Mankind has been producing useful substances by using biotechnology since ancient times, but by taking the in vivo mechanism as a black box and using the in vivo functions according to an understanding of their empiric functions mankind has, additionally, gained a basic technique to produce substances using life forms. This became possible once new knowledge was acquired about the black box of in vivo mechanisms, that knowledge has often been brought quickly into practical use and integrated .IS a production process.

c. Biotechnology, a Technology that Thrives through Fusion with Technologies in Other Fields

To promote the R&D in protein engineering, which is expected to form another new field in the domain of biotechnology, it is necessary to elucidate the interrelation of structure and functions of the materials in protein. For this purpose, it is essential to utilize DNA chemical synthesis technology, molecular structure composition technology using NMR (Nuclear Magnetic Resonance), X ray, and SR (Synchrotron Radiation). Technologies in other fields, such .IS computer graphics, also play an important role.

The development of bio-devices consists of work towards clarifying the information processing functions of life forms and developing new materials which can manifest biochemical reactions, as it concerns the engineered, imitation information processing functions of life forms. It is the field which attempts to build bio-mechanisms through microelectronics.

Thus, biotechnology not only thrives through interfaces with technologies in other fields, but also contributes to technological advancement in the these same fields.

d. Technology as Diversity

Biotechnology is diverse in many aspects.

The first diversity which the technology has in itself is in the variety of species it deals with as the objects of research. Considering the variety of life forms living on the earth, the success of applying the technology to these life forms will produce diverse effects.

The second diversity lies in the variety of in vivo constituents making up a life form and is hierarchical. A life form is comprised of intracellular organelles and enzymes providing a variety of functions. An analysis of the mechanisms operative in the in vivo constituents of a life form, and the hierarchy of their interrelations, will give various results.

The third diversity is found in the range of application of the technology which is comprehensive scope, including such areas as the improvement of breeding individual life forms, the production of useful substances, and the disposal of wastewater.

The fourth diversity applies to the academic disciplines pursuing this technology. As it is obvious from the scope of applied uses, the academic disciplines utilizing this biotechnology range so widely as to include the physical sciences, engineering, agriculture, medicine, pharmaceutical science, etc.

3. Expectations for Biotechnology

Biotechnology, possessing these diverse characteristics, are expected to have a great, favorable effect on the advancement of various industries, general improvements in medical treatment, and solutions to food problems.

a. Advanced Industrial Structure

Biotechnology will play a substantial role in advancing the structure of industries in the following ways.

(1) Creation of high-value-added products

Biotechnology has made it possible to develop microorganisms and animal/plant cells which produce chemical substances hitherto not available through conventional processes, and is expected to make it possible to produce new high-value-added products such as high-grade chemicals. Recently, this line of pursuit and breeding of microorganisms has enabled the production of high-value-added chemicals such as cellulose for detergents, hyaluronic acid extracted from cockscomb, g-linolenic acid extracted from evening primroses.

Also, with the advent of these new biotechnology have come such novel developments as recombinant DNA technology, the breeding of microorganisms and animal/plant cells that produce high-value-added chemicals (such as lipase and which satisfies the requirements necessary for use in detergents), which have been hitherto unavailable. This is an improvement over conventional methods.

It is also expected that high-value-added chemicals can be created through a replication of natural substance conversion, information conversion, and energy conversion functions that all life forms possess. For instance, if the functioning of nervous tissue can be described, this will facilitate the development of bio-devices. Through the efforts of creative thought, learning, and memory functions that a human brain possesses, once elucidated, can allow the development of an artificial brain which can make its own judgments under given situations and act on it on its own.

(2) Increased efficiency of production processes

In various industries, including the chemical industry, biotechnology is expected to increase the efficiency of production processes by saving energy and processing costs. In the fermentation industry, for instance, the recombinant DNA technology is used to improve bacilli which produces amino acid, thereby increasing the efficiency of the production processes. Also, glucose isomerase is being used to increase the efficiency of isomerized the sugar production process. In the future, protein engineering will pave the way for the development of brand-new enzymes; and also, by substituting all or part of the existing processes with bio-reactors, the efficiency of production processes in the chemical industry will be dramatically improved.

In the areas of resources and energy as well, research is being conducted into a bacterium leaching technique which will allow a way of recovering metals more efficiently from low-quality ores. In addition, it has an application in the use of microorganisms for the secondary and tertiary recovery of oil. In the field of environmental preservation, research is conducted for the effective uses of microorganisms in the disposal of exhaust water and removal of bad odors.

(3) Formation of bioindustry support industries

With the progress of biotechnology, support industries which supply necessary equipment and reagents, etc. are now being created. With the progress of new biotechnology, reagents such as restriction enzymes, ligase, and serum-free culture mediums have been developed; and at the same time, new equipment such as a DNA sequencer, DNA synthesizer, and cell sorter have been developed. The bioengineering sub-industries, which produces culture containers and isolation/purification devices, is also making progress. Progress in research-specific software industry resulting in, for example, gene banks and data bases is also expected to be made.

b. Improvement in Medical Treatment

Biotechnology is expected to play a positive role in the development of pharmaceuticals and medical equipment, as in the contribution to explain the mechanism of carcinogenesis, the immune system, .and aging. Similar contributions will make it possible to produce blood sugar content sensors and pharmaceuticals, (such as interferon, the mass production of which was impossible only with conventional technologies). Take lymphocain, for instance, which is a multiple and differentiated element secreted by lymphocytes. Since it exists only in trace quantities in a human body and decomposes very fast, production of the substance on an industrial scale has been impossible. However, through the application of new biotechnology such as recombinant DNA, it is expected to make the mass production of lymphocain possible.

Also, since accelerated aging is occurring in Japan, biotechnology is expected to make a considerable contribution to the solution of medical problems to be encountered by the aged society, by helping to elucidate the cause for Alzheimer's disease, etc. In addition, the development of new medical services such as gene analysis will improve medicare.

c. Solution to Food Problems

It is hoped that biotechnology will significantly improve food production in both quantity and quality through the development of high-yield grains, crops of high resistance to vermin, crops able to be raised under conditions of severe environment, and nutritive elements and pharmaceuticals that benefit livestock. By using another culture technology (in which anthers, or the pollen sacs located at the distal end of and roeciums and have a function of producing pollen inside, is cultured so that plants with 2 sets of chromosomes of the same genetic character can be obtained), it has been made possible to develop new rice species in relatively short time. Also, by using the meristem culture technology in which the growing point on top of the bud of plant is cultured, virus-free carnation and orchid seedlings are now being produced. By using cell fusion technology, tomato plants that bear larger fruits of tomatoes will be developed; and by using DNA technology, rice resistance to chemicals and corns possessing an anti-disease characteristic will be developed.

In the food industry, by using cell fusion technology and recombinant DNA technology, a special ferment for producing fractooligo sugar has been developed (this is a feed for bifidus fungus living in the intestines and beneficial to the general health of the human body). This allows the sugar to remain in stable form in bread. Also, the development of a highly nutritious lactic acid beverage is being promoted. Biotechnology is expected to improve food quality.

4. Biotechnology R&D Trends in Japan

a. Trend in R&D Budget

The total biotechnology-related budget of the Ministry of International Trade and Industry (MITI) for FY 1990 amounts to ¥8.4 billion. Of all projects now being implemented, MITI is placing greatest emphasis on those related to the global environment, a matter of concern to the entire world. For FY1990, ¥6.1 billion has been allocated for research on global environmental measures, and for helping establish a Global Environment Industrial Technology Research Institute.

The biotechnology-related budget of the Ministry of Agriculture, Forestry and Fisheries (MAFF) for 1990 amounts to ¥7.9 billion. Notable is the allocation of ¥15 million for research consigned overseas (seed culture research budgets for foreign countries: basic research for developing useful, large, transgenic livestock). MAFF has also allocated ¥.9 billion for the R&D on advanced biotechnology for the food processing industry.

The bioscience-related budget of the Ministry of Health and Welfare totals to about ¥35 billion, the largest of all ministries and agencies. This is because the ministry is concerned with drugs, pharmaceuticals and medical treatment, and research in this field requires size able funds. Notable is an allocation of about ¥1 billion for advancing coordinated research on the problems associated with a graying society, The biotechnology budget of the Science and Technology Agency (STA) amounts 20.2 billion, second only to that of the Ministry of Health and Welfare. This represents an increase of ¥2 billion, or 11% over the previous year. The increase will help fund new themes to the explored by the Research Development Corporation of Japan (JRDC), under its Exploratory Research for Advanced Technology including management of food information, and protein accumulation. The STA will also increase its budgets for promoting public acceptance of new technologies and products.

The biotechnology-related budget of the Ministry of Environment Agency has not been increased conspicuously, and stands at about ¥300 million. It is possible that bio-related research will be funded using parts of the Agencies budget for promotion of global environment research.

The ministry of Education, Science and Culture has allocated about ¥14 billion for bioscience and biotechnology R&D, and the Ministry of Construction has allocated about ¥200 million for biotechnology R&D.

The total government budget for bio-related R&D thus amounts to about ¥90 billion. By comparison, the biotechnology-related budget of the private sector is estimated to be about ¥200 billion.

b. Patent Filings

As the result of energetic R&D in biotechnology, the number of patent applications has also shown a considerable increase every year. According to the international patent classification C 1 2N I 5/00, which roughly covers the recombinant DNA and cell fusion technologies, the number of patents filed and made public in the area of genetic engineering exceeded 800 in 1986, a 13-fold increase over the 5 years from 1981.

Table 1. Chronicle of .Japan's Bioindustry

Year	Contents
1931	Production begun for fermented acetone/buthanol
1937	Production started for fermented fuel alcohol
1956	Production begun for fermented amino-acids
1957	Production begun for fermented nucleic acid(5-inosinic acid)

1969	Production begun for L-amino acids by fixed enzymes Production begun for isomelized sugar
1985	Production begun for acrylamid(general purpose chemicals) by fixed microbes
1986	Production begun for amino acid by recombinant DNA

c. Research Facilities at Research Institutes and Universities

Recently, local governments and private companies have actively constructed biotechnology-related laboratories. Especially in the Tsukuba district, the construction of laboratories is active; in addition, high-technology laboratories such as a protein engineering laboratory have been constructed Kansai district.

Also, since 1985, university departments and sections related to biotechnology have been reorganized or established anew, in order to be ready for the time when R&D rather than mere education in

the field will be their prime function.

d. R&D Trends in Japan

As with the country as a whole, R&D in biotechnology is actively promoted by the Ministry of International Trade and Industry, the Science and Technology Agency, the Ministry of Health and Welfare, the Ministry of Agriculture, Forestry and Fisheries, and other interested public agencies. The Ministry of International Trade and Industry, to perform R&D of basic technologies essential for establishing the next-generation industries, instituted the next-generation industrial infrastructure R&D program in 1981. This started R&D into the recombinant DNA application technology, cell mass culture technology, and bioreactor technology. The ministry also entered into the R&D of bio-elements.

Table 2. Expected R&D Themes on Biotechnology and Schedule

Expected Year	**R&D Themes**
1994	• Development of liquid chromatographer for cell size • Development of cell control technology at condition of TOC • Development of perfect frozen storage method for breeding cells
1996	• Development of markers for recognition of differentiation and products of gene • Creation (production) of plants by application of cell control technology • Creation of superior trees by application of gene engineering technology
1997	• Establishment of high grade structural analysis technology for protein in solution • Invention of recognition function of "self" and "others" of immune cells • Promotion of social understanding for countermeasures for biohazards • Development of production technology for biomaterials using composite microbes

1988	• Establishment of structure forecasting technology from primary to completed for proteins • Development of design technology for primary structure of protein Invention of molecular biological mechanism regarding immune responses • Invention of cancering mechanism of cell • Popularization of medical treatment for viral diseases by using anti-viral agents • Development microcomputers featured with syllogism and learning functions • Realization of plant seeds produced by cell fusion and recombinant DNA technologies • Development of sensing methods for ultra small signals of biobody
1999	• Establishment of guidelines of virulence values of environmental mutation materials • Development of application methods of recombinant DNA products under the natural conditions • Invention of action mechanism for neural peptide contained materials • Development of proteins acting in pure organic solution • Development of specified ion-concentrated biomaterials
2000	• Development of introduction technology of different genes, etc. into the optional position on the chromosome • Development of automatic targeted protein synthesis machines by applying genetic information • Development of nitrogen fixation technology by bio-engineering methods • Realization of artificial excitable membranes • Development of testing technology enabling continuous/long-term/multiple/simultaneously observation of neurons • Development of portable continuous monitors for checking human health
2001	• Invention of mechanisms for clone of chromosome and cell division • Realization of synthesis of active transport membranes as same function as bio membranes • Realization of biotic membranes with information transport and conversion functions • Invention of the role of chemical materials in composite active neural • Development of new material production technology by applying bio synthesis • Development of bioreactor technology for production of new physioactive materials other than cell cultivation technology • Development of high carbon monoxide concentrated and accumulated plants • Industrialization of highly integrated biosensors • Development of character display system capable of accurate display of biodevices • Development of artificial receptors other than membrane types • Development of automatic monitoring system for biofunction

2002	• Establishment of function forecasting technology with applying composite structured protein • Development of effective anti-metastasis of cancer • Development of forecasting technology for changing of natural biological systems by activities of human being • Development of recognition technology enabling composite patterns as similar as human being
2003	• Decision of distribution of basics of human chromosome DNA • Invention of primary function (direct role) of the water for biofunctions • Establishment of operation system capable of cell generation and cell division • Invention of mechanism for organic biorythm • Development of technology capable of long-term cultivation and storage of plasts

Table 3. Biotechnology R&D Projects by Governments Ministries and Agencies

R&D Projects	**Projects**	**R&D Term**	**FY1988 Budgets**
MITI-related Projects			
1 Basic technologies for future industries	(1) Bioreactor	1985-1990	¥197 million
	(2) Cell mass cultivation technology	1981-1989	¥422 million
	(3)Recombinant DNA technology	1981-1990	¥319 million
	(4) Biodevices	1986	¥247 million
2 National R&D Program (Large-scale)	(1)Aqua Renaissance	1985-1990	¥1,757 million (Project total: ¥11 ,800 million)
	(2) Marinebio	1988-1996	¥20 million
	(3) Fuel alcohol technology	1983-1990	¥545 million (Project total: ¥4,700 million)
3 Other R&D Programs	(1) Highly efficient yeast fermentation technology for high productivity yeasts	1987-1992	¥190 million (Project total: ¥2,000 million)
4 Key Technology Center supported R&D Programs	(1) R&D on establishment of active peptide production process by gene handling and chemical synthesis, and establishment of active screening methods	1986-1991	(Project total ¥1,700 million)
	(2) Protein engineering	1986-1996	(Project total: ¥17,000 million

	(3) R&D on useful material production technology by engineering methods of plant cells		
	(4) R&D on bioreactive materials	1987-1994	(Project total: ¥2,800 million)
STA-related Projects	(1) R&D on analyzing and utilization technology for chromosome		
	(2) R&D on common base technology for utilization of bio-energy conversion functions, etc.		
	(3) Life science projects		
	(4) R&D on microorganisms specialized environments		
	(5) Bio photography		
	(6) Bio-information transmission mechanisms		
	(7) Biophoton		
Ministry of Education-related Projects	(1) R&D on molecular mechanisms of protein functions		
Ministry of Welfare-related Projects	(1) Anti-cancer projects		
	(2) Supporting to R&D on drugs, pharmaceuticals, and medical treatment technology, etc.		
MAFF-related Projects	(1) Biotechnology-2000 Projects		
	(2) Promotion of Technological innovation for food industry		
	(3) Supporting to private sector for specified industrialization of biotechnology		

Also, the large-scale industrial technologies, which are very important and are urgently needed to promote growth in the domestic economy, cannot be implemented by private companies because of the risk involved. Therefore, the government needs to formulate these large-scale industrial technology R&D programs(commonly referred to as large scale projects) in which R&D is implemented for the benefit of the entire country. From 1985, they entered into the R&D of an overall water recycling and use system(commonly referred to as Aqua-Renaissance), which is fundamentally different from its conventional counterpart, by using biotechnology in the form of film-separation technology. Further, with the purpose of promoting research on the basic technologies by private companies, the Key Technology Center was established in 1985. This is funded to establish new companies, specifically, the researching of protein engineering, the development of active peptides, plant cell engineering, and bioactive materials.

In addition, at institutes under the umbrella of the Agency of Industrial Science and Technology, such as the Microorganism Industrial Technology Institute, research into the next biotechnology themes to be exploited by the nation, are actively conducted.

Table 4. Trend in the Bioindustry Related R&D Currently Conducting and Future Planned by private Sectors

	R&D Themes	Contents of R&D	No of Company (Currently Conducting)	No of Company (Future Planned)
1	Searching technology for microbe and cells	-	60	2
2	Mutation technology for microbes and cells	-	47	3
3	Gene recombinant technology	Colon bacillus	47	5
4	Gene recombinant technology	Bacillus subtilis	14	5
5	Gene recombinant technology	Actinomycetes	9	2
6	Gene recombinant technology	Yeast	19	5
7	Gene recombinant technology	Fungi	6	3
8	Gene recombinant technology	Other microbes	13	7
9	Gene recombinant technology	Plant cells	9	10
10	Gene recombinant technology	Animal cells	19	5
11	Cell fusion technology	Animal cells	34	4
12	Cell fusion technology	Plant cells	21	17
13	Cell fusion technology	Microbe	28	14
14	Cell mass cultivation technology	Animal cells	28	10
15	Cell mass cultivation technology	Plant cells	27	10
16	Fermentation technology	-	63	3
17	Enzyme application technology	-	58	10
18	Semi syntheses technology	-	18	3
19	Bioreactor/fixation technology	-	71	9

20	Biomass conversion technology	-	18	3
21	Protein engineering (including artificial enzyme-related technologies)	-	19	22
22	Computer drug designing and polymer designs	-	16	6
23	Products separation and refining technology	-	47	9
24	Engineering technology of production plants	-	34	4
25	Biomaterials	-	10	4
26	Hybrid materials	-	5	
27	Others	-	15	2
Total		**-**	**755**	**178**

The Science and Technology Agency, while promoting projects such as the life science project at RIKEN, is also promoting basic research into such projects as microorganisms living in the special environment.

The Ministry of Health Welfare, as a part of longevity related basic research, promotes biotechnology as the basis for life sciences; and in order to support the R&D of pharmaceuticals in the private sector, it reorganized the pharmaceutical side effect victims rescue fund in 1987, and promoted this fund to address the victims needs. The Ministry of Agriculture, Forestry and Fisheries, in order to promote the development of biotechnology in the food industry, has been promoting technological innovation projects relating to the food industry since 1983. One such example of this development is the creation of a bioreactor system for the food industry. Also, the ministry is promoting a breeding technology for the 21st century based on the "biotechnological breeding toward 2001" project. In 1986, MAFF, jointly with the Finance Ministry, established an organization of technological research promotion for life form-related designated industries, and started supporting R&D in the private sector.

e. Technological Level

Although Japan lags behinds the West in basic research fields such as the recombinant DNA technology, the Nihon Keizai Shinbun poll of 1987 shows that, regarding the evaluation of "Japan's international competitiveness in biotechnology", 10.8% of the private companies in Japan thinks that Japan is on top of the world, 54.0% thinks that it is next to the USA, 26.2% thinks that it is next to the USA and Europe.

These were the findings of the "Research Report on Science and Technological Level and R&D Potentials" compiled by JETRO in 1984 on Japan's technological levels in microorganism culture technology(plant protoplast isolation, culture, and fermentation industries, and screening technology).

Trends in the Bioindustry

The bioindustry, which produces many useful substances for society and other industries by using biotechnology, is growing rapidly in Japan. In the following sections, the characteristics, present status and future prospects of the industry will be discussed with regards to each field.

1. Characteristics of Bioindustry in Japan

a. New Developments in the Fermentation Industry through Use of Biotechnology

Because of its mild climate and other favorable natural conditions suitable for the breeding of microorganisms, the fermentation industry has developed to produce high-level technologies. Pure cultures of malts and yeasts and low-temperature pasteurization were developed early on. Also, many fermented foods such as sake, miso, soy sauce, vinegar, etc., have been produced since long ago. In this way, Japan has traditionally used a technology based oil using microorganisms, and biotechnology.

Included also is the production of alcohol. Acetone-buthanol, as a fuel which started to be used in the periods before and during the Second World War, is an example of biotechnology for industrial production of specific chemical substances. After the war, the industrial production of antibiotics, amino acid, and nucleic acid using biotechnology was started. In particular the production of amino acid and nucleic acid was dramatically increased by using the metabolic control fermentation technology, a unique technology developed in Japan.

Subsequently, by introducing the new biotechnology, such as that for recombinant DNA, the industry in Japan expects a sustained improvement in production efficiency. Similarly, Japan's bioindustry features the fermentation industry with a solid industrial base of traditional fermentation techniques, which combined with the application of recombinant DNA technology to give a boost to the growth of the industry.

b. Participation of Major Companies in Various Industries

In Japan, the development of new biotechnology, such as the recombinant DNA technology, attracted the attention of many other industries in that field. Major companies in the petrochemical, synthetic fiber, soap and detergent, steel, oil refining, construction, pl.a t, electrical and electronics industries have participated or are now participating in the bioindustry. This is a way that, in Japan, not only the fermentation and chemical industries but also major companies in many other industries form the nucleus of R&D in biotechnology This trend shows a sharp contrast with the US where industrialization was started by ventures between businesses and academics, with researchers at the universities playing a central role.

c. Progress in Industrialization in Diverse Fields

In Japan, because of the participation of private companies from various industries in the promotion of research and development, industrialization is developing in many fields. In the chemical industry, for example, in addition to fine chemicals (such as amino acid, industrial enzymes, and pigment/perfume), and research reagents (such as restriction enzymes); diagnostic reagents such as monoclonal antibody have also been commercialized. Also, in the electric and electronic industry, bio-sensors have been commercialized. In the field of environmental purification, deodorant technology to remove malodorant substances by using attached activated charcoal attached to microorganisms has been put into practical use. In addition, in the pharmaceutical industry, a-interferon has been put on the market. And in the food industry, shochu (low-class distilled spirits), refined sake, and bread have been subject to this industrialization.

Table 5. Number of Company Participated in Bioindustry classified by Type of Industry

Type of Industry		Number of Participated Company
1.	Chemical industry	52
2	Food industry	31
3	Medical and pharmaceutical industry	23
4	Construction and plant engineering industry	11
5	Machinery industry	11
6	Oil and gas industry	9
7	Textile industry	7
8	Heavy electrical machinery industry	7
9	Shipbuilding and heavy machinery industry	5
10	Iron and steel industry	4
11	Pulp and paper industry	2
12	Non-ferrous metal industry	1
13	Mining industry	1
14	Other industry	13
	Total	**177**

Table 6. Economic Impact of Biotechnology in Year 2000

(Unit:¥1 billion, %)

No.	Products	Production value by biotechnology	Added value by biotechnology	Industrialization rate of biotechnology
01	Rice, wheat	519	381	9.51
02	Vegetables	257	164	8.70
03	Fruits	13	9	1.20
04	Potatoes/sweet potatoes	13	8	3.20
05	Produces for beverages	2	1	0.80
06	Edible produces	91	66	14.81
07	Leaf tobacco	12	9	4.10
08	Produces for feeds and others	494	400	77.70
09	Dairy	327	111	25.00
10	Meat	146	37	22.80
11	Plantation and forestry	9	7	0.66
12	Fisheries	118	71	2.97
13	Copper mining	17	13	20.00
14	Iron ore mining	15	11	9.77

15	Non-ferrous ore mining	2	1	2.00
16	Crude oil	0	0	0.00
17	Diary products	590	150	26.70
18	Bread/confectioneries	1,370	507	32.00
19	Sugar	108	13	10.00
20	Vegetable oils	0.00	0	0.00
21	Seasonings	251	73	15.00
22	Starch/starch sugars	177	30	26.02
23	Assorted feeds	637	58	30.00
24	Alcoholic liquors	1,113	662	19.84
25	Pulps	90	17	5 00
26	Ammonia	17	4	5.00
27	Ethyl alcohol	164	49	80.00
28	Methanol derivatives	52	14	16.00
29	Oil and fat products	75	19	32.00
30	Basic petrochemicals	317	44	8.32
31	Otherpetrochemicals	763	116	14.50
32	Synthetic resins fortextile materials	80	23	6.37
33	Chemical fertilizers	0	0	0.00
34	Agricultural chemicals	142	33	30.00
35	High pressure gas	64	28	11.00
36	Chemical dyeing agents	59	22	30.00
37	Other basic chemicals	73	34	41.00
38	Pharmaceuticals	3,151	1,564	40.00
39	Surface active agents/cosmetics	466	155	20.00
40	Other chemical products	479	149	12.37
41	Petroleum products	463	79	1.65
42	Electric coppers	58	4	5.00
43	Other non-ferrous metals	242	46	6.24
44	Computers/ peripherals	188	80	3.00
45	Electronics applied equipment	287	103	5.00
46	Semiconductors/lCs	98	42	2.00
47	Medical instruments	31	15	3.00
48	City gas	0	0	0.00
49	Potable water	470	303	2.40
50	Waste water	420	238	50.00
51	Industrial waste treatment	471	349	15.63

	TOTAL	15,003	6,312	11.80
52.	Biotechnology R&D support Industry	300-600	-	-

In Japan, unlike in the West, the commercialization of the biotechnology is advanced in this way to benefit various fields in addition to the pharmaceutical industry.

d. Basic Research

The DNA double helix structure, which laid the groundwork for molecular biology, was described first in the UK. The recombinant DNA technology, which is the core of biotechnology, was developed in the US. Most results of the basic research relating to biotechnology were obtained in other countries.

The Education Ministry's international comparison of papers surveyed in 1987, which compares the number of papers per million of people submitted from the US, Canada, UK, France, FRG, and Japan, shows that in the chemical category, Japan ranks fifth in both biochemistry and agricultural chemistry. In the category of medical studies, the country ranks sixth in genetics and physiology and fourth in the fundamental studies of cancer research. This indicates that the number of academic reports per million people submitted in Japan relating to the biotechnology is very low.

Also, according to the survey report on international methods to disseminate information in the sciences and technology information" ordered by STA in March 1984, the number of papers quoted in the papers on biological science published in 1977 is 1,501 for the U.S., 344 for the UK, 203 for FRG, 106 for Canada, and 72 for Japan, indicating that Japan has the least number of papers quoted, of all the developed countries.

According to this, and judging from the number of papers on biotechnology, Japan's basic research in biotechnology as a whole is still weak. Even among the people affiliated with the bioindustry, it is recognized that although in some areas of biotechnology Japan leads the world, as a whole, the country is lagging behind.

Trends for the Bioindustry Market Scale

1. General Description

The Japanese bioindustry, with a long tradition of brewing and fermentation, had a large market value in its own right, but had not been treated as a single, independent industry.

Recently, however, with rapid progress in developing the recombinant DNA technology, it has come to be used in various industries including the chemical industry. This is producing a situation prompting the recognition of the bioindustry as one independent industry. The industry is expected to make dramatic growth in the future.

According to an investigation conducted by MITI in 1988, the market value of the bioindustry (except for food and pharmaceuticals) was about ¥4,400 billion in 1987. Of this amount, the market value of items produced by the recombinant DNA technology was ¥41.2 billion and the market value of items produced by bioreactors and new biotechnology (except for the recombinant DNA technology) was ¥45 billion.

The ¥46.2 billion market for new biotechnology-related products is still not strikingly large, but according to the survey conducted by Biotechnology Industry Deve lopment Center (BIDEC) in 1985, the estimated market size for new biotechnology in 2000 may reach ¥45. 1 trillion and the bioindustry is expected to become an industry with an enormous market. For these reasons, the bioindustry is expected to become the one large industry which, together with new materials, supports the domestic economy of Japan in the 21st century.

2. Trends in Biotechnology-related Industries

Recent progress in biotechnology and applications thereof have been attracting much attention, with many Japanese firms rushing into research in this newly-recognized field of technology.

Pharmaceutical, chemical and fermentation industries have already applied it in developing new drugs and foodstuffs, their commercialization as products having created new markets in these respective areas.

Products brought forth due to applications of cellfusion, cell-culturing and genetic engineering technologies has resulted in a combined sales figure in 1989 is estimated at ¥100 billion.

In addition, there is a wide variety of biotechnology-related items being spawned, such as support equipment and chemical by-products related to enzymatic processes.

Furthermore, new R&D activities are taking place in the private sector (especially for medical products and items resulting from use of bioreactors), with new research centers being established as both individual .a d joint effort. corporate activities

Meanwhile, the budgets for biotechnology-related R&D at governmental agencies (such as the Ministry of International Trade and Industry (MITI), the Ministry of Agriculture, Forestry and Fishery (MAFF), and the Environment Agency) reflect concerns for the biosphere, as well as for medical treatments, not to mention.new areas of industrial applications such as bioelectronics

As stated in the above, in Japan, as in various industries, commercialization of the bioindustry is progressing. In the following sections, this situation is summarized with regards to each individual area and, based on the R&D trend, the future of these individual areas will be discussed.

a. Chemical Industry

Presently, the chemical products produced using biotechnology consist of amino acid, industrial enzymes, and to a degree, fine chemicals. However, with progress in biotechnology, it is expected that, as the development of high-functional enzymes progresses, the areas of applied biotechnology to the chemical industry will expand.

(1) Amino acid

According to the investigation by the Japan Essential Amino Acid Association, the estimated quantity of amino acid produced in Japan in 1985 was about 150,000 tons, and that produced in the entire world was about 680,000 tons. This indicates that the market share of Japan-made amino acid was approximately 22%. However, considering the fact that a considerable percentage of amino acid produced overseas is produced by the subsidiaries of Japanese enterprises, Japan could be named the world center of amino acid production.

Amino acid production techniques include hydrolytic retrieval, chemical synthesis, fermentation, and enzyme method. Currently the enzyme method is the central means of production. For this reason, the R&D to produce efficiently amino acid by using biotechnology is promoted actively. By 1987, eight industrial projects have been confirmed as having reached the industrial stage according to the recombinant DNA technology industrialization guidelines.

Amino acid and its derivatives possess properties of ampholytes, and that affect chelation, surface activity, sterility/bacterial resistance, and the prevention of oxidation, etc. Its polymer shows bio-affinity and non bio-degradable characteristics, etc., which do not exist in other materials.

For this reason, if mass produced, and if a low cost supply of amino acid can be made available, the progress of new biotechnology will result in new areas of application for amino acid. A new industry to be called "amino acid chemical industry" could be formed and new opportunities opened up.

(2) Industrial enzyme

Enzymes are used for the production of many different products, including glucose isomerase which was developed in Japan. This is added to the process of turning glucose into fructose without changing glucose content or calorific value, and to lipase in the process of turning fat into fatty acid through hydrolysis. Also, since enzymes have functions of decomposing fats and proteins, which sometimes form stains on clothes, loosening the structure of dirt compounds attached to fibers makes the removal and washing-off easier. Industry began to use enzymes for detergents, and production is increasing dramatically.

Enzymes possess high reaction efficiency, reaction specificity, biodegradability, and characteristics that act under stable conditions; and so these compounds are expected to be developed as a catalysts for the chemical industry. However, from an economic point of view, very few of these have, yet, reached the level of practical application. Technological development such as through the creation of high-functional enzymes by means of protein engineering will be required.

(3) Other fine chemicals

Production of chemical products through biotechnology is progressing in other fine chemical fields as well. In addition to the production of monoclonal antibodies ,IS a reagent for separation and purification, biotechnology is also used for the production of shikonin (used as a pigment for cosmetics and soap), bracil acid (used a perfume for cosmetics), and cyclodextrin (used as a stabilizer in the food, chemical, and pharmaceutical industries).

In the future, with the progress of biotechnology specializing in animal and plant cells, the production of musk will be made possible. Also by making use of the metabolism of plant cells by using biotechnology, efficient production of pigments such as anthocyanin, and cosmetics and perfume materials such as vanillin and rose oil, will also be made possible.

As for marine organisms, by utilizing their capability of producing adhesive substances (as found in acorn barnacles and violet shells), the development of shielding materials for marine structures could occur. Also, the use of viscous polysaccharide obtained from the marine algae such as "Tsunomata" for cosmetics and as a heat insulating material is also expected to be made possible.

(4) General-purpose chemical products

Of all the chemicals being produced using biotechnology, industrial alcohol is produced in the largest quantity. Its production was about 100,000 kl in FY1986. Also, acrylamide, used as a flocculating agent, was produced by bioreactor as a general purpose chemical for the first time in the world.

General-purpose industrial chemicals produced using biotechnology are still very few in number. However, in the future, with the progress of protein engineering, the development of high-functional enzymes will be made possible, which will trigger the all-out production of biotechnology in the general-purpose chemical industries.

b. Electrical and Electronics Industry

Regarding the application of biotechnology to the electrical and electronics industry, the biosensor is the most popular. Biosensors use enzymes, microorganisms, and cells to retrieve chemical changes generated by specific substances in the form of electronic signals. Also, glucose sensors which measure blood sugar levels and BOD sensors which measure BOD in exhaust liquid, have been put into practical use. In the future, it will be required to develop many high-functional enzymes for improving measuring accuracy while increasing the range of substances to be measured. Further, since the biosensor is considered to be the most promising means of enabling real-time measurement in the bioprocess, the effort to improve bio-engineering technology is also very important.

Also, bio-devices are now under development. The research and development of bio-devices is going in two different directions. One direction is to depict the operation of the brain in a circuit mapping design, and the other direction is to utilize protein molecules as a tool. Especially regarding the latter direction, since bio-devices can be integrated to a significantly higher level than the present silicon chips-the level to which integration has also been greatly effective by narrowing down the width of circuit-attention has been directed to it lately.

c. Resource/Energy Industry and Environmental Purification

In the resource/energy industry, a technique of producing methane and fuel alcohol from biomass resources is now under development. This would be applied to such areas as agricultural and forest wastes, by using ferment and bacteria.

Additionally, the bacteria leaching technique which recuperates metal traces from ores by using microorganisms, and the technique of performing secondary and tertiary recoveries of oil by using microorganisms after recovery by traditional means is exhausted, are also being discussed.

In the field of exhaust water disposal, waste water, tailings and sewage have conventionally been processed into activated sludge, and from this stage the decomposition function of microorganisms was used. Presently, R&D for improving the decomposition function of microorganisms in activated sludge is going on. Also, the bioreactor which fixes the microorganisms in place for efficient disposal of exhaust water while producing methane gas efficiently is likewise occurring.

Unlike in water purification, biotechnology has not been used in air purification. However, recently, the deodorant technology in which microorganisms act on malodorants has been put into use. This technology involves microorganisms attached to the surface of activated charcoal (very commonly used for removal of odors) to decompose them and results in a higher deodorant effect.

Also, the technique of using microorganisms for removal of soil contamination is also being developed.

d. Bioindustry Support Industry

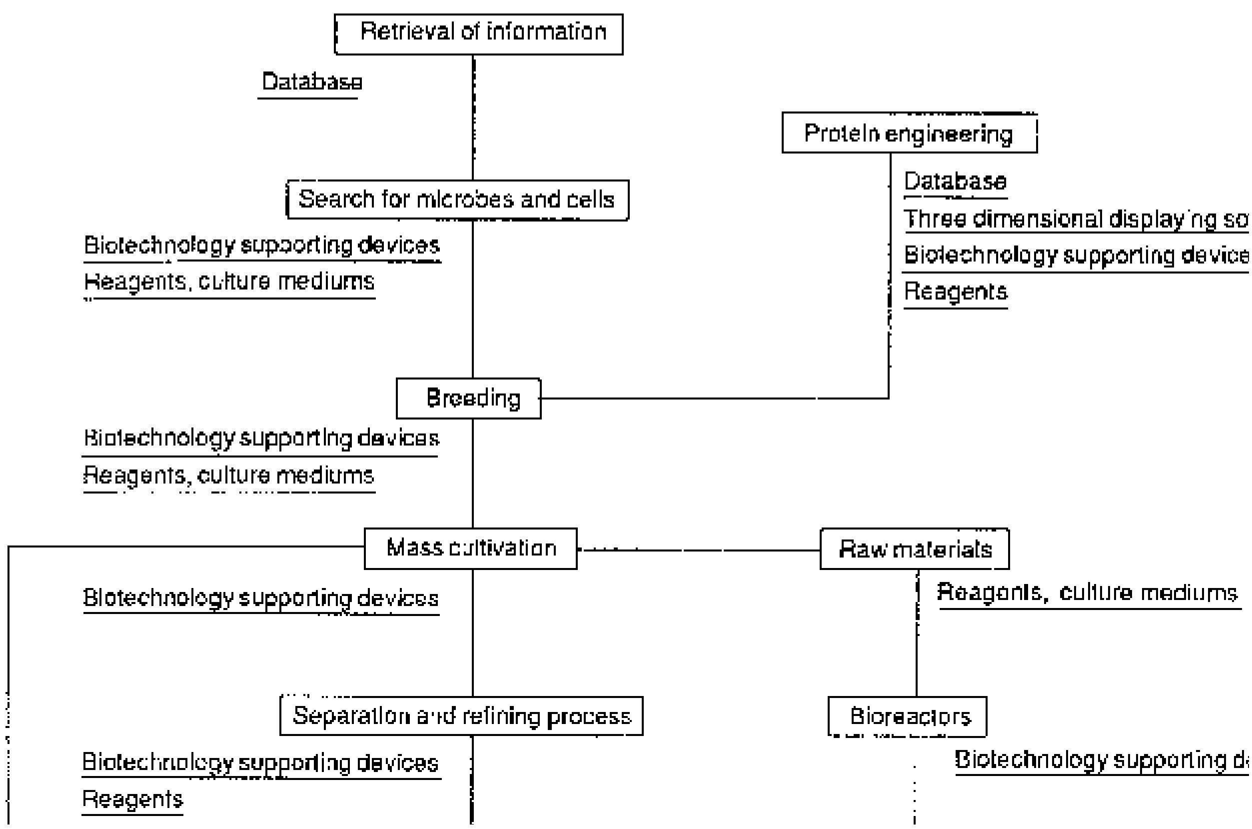
For the R&D of biotechnology, experimental equipment and reagents to satisfy specific research requirements are indispensable. This consideration is very important in bioindustry, because this field is a new technological field which handles micro-bioconstituents such as DNA and protein. Therefore functions carried out with conventional experimental equipment cannot meet these requirements and, thus, it is often the case that more advanced levels of such devices are required. Moreover, with all-out industrialization of the bioindustry, the support industries providing research software, bioengineering, and materials have come to have a increased importance.

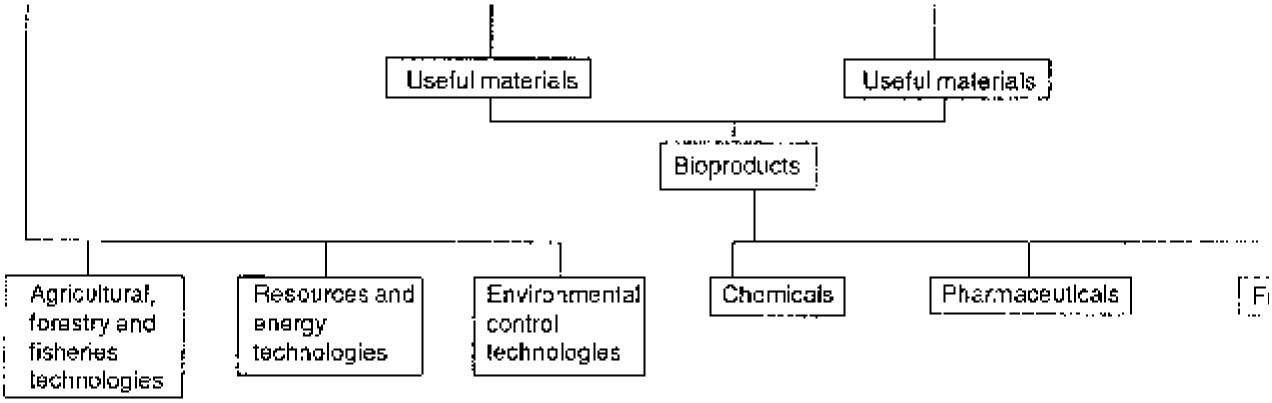
(1) R&D equipment and reagents

For the promotion of R&D in biotechnology, there is an essential need for analysis equipment such as DNA sequencers and amino acid analyzers, fermentation and culture equipment(such as jar fermentors and incubators), and reagents. Virtually all of these equipment and reagents used for the R&D of biotechnology are supplied domestically, except for very few, namely, the RI reagent. For obtaining more accurate knowledge of in vivo mechanisms, it is necessary to track down changes with the passage of time. For this purpose, the development of equipment enabling the tracking of in vivo changes while standing and in carrying out normal activities, by means such as an electron microscope which enables observation of cells maintaining daily activities, is desired.

(2) Research software

Fig. 1. **Bioindustry Support Industry for Development of Biotechnology and Bioindustr Viewpoint from Bioutilization Technology Flow**





Research software such as gene banks, which collect, store, and supply gene resources such as microorganisms and animal/plant cells, and data banks, which collect, sequence, and supply documented data and proprietary data, will greatly improve the efficiency of R&D. But unfortunately, when it comes to this area, Japan lags far behind.

For building these research software packages, will require an enormous cost in collection, classifying, and storage of gene resources and also in the collection, pigeonholing and input of data, so some voices are of the opinion that if there is already one such package in use somewhere in the world, that should be enough. However, recently, active discussions are being held on the validity of presenting this research software to other countries from viewpoints other than those that apply to the economy. A serious deliberation in this matter will be essential.

(3) Bio-engineering

After biotechnology has progressed and reached the stage of commercialization, engineering techniques such as culture propagation, separation and purification equipment will have a great effect on the success of industrialization.

The fermentation industry in Japan, as represented by amino acid fermentation, is now at a high level because of the technological accumulation supported by the long tradition. In the future, though, when new levels of engineering technologies will be required, and the applications of biotechnology expands to such areas as the production of proteins with complicated composition and easily affected properties, the process will be subject to waste and limited by the frailty of the organisms themselves. This will occur because the industrial production of animal and plant cells is more difficult than the handling of that for microorganisms in the laboratory because of their complicated nutritional requirements. For this reason, the development of equipment such as culture vessels suitable for animal and plant cells, and the development of separation and purification technologies to be used for protein and other substances of complicated composition, will become very important in the future.

The instrumentation and control technologies are also very important areas for industrialization. Japan has an advanced electronics industry, and when it comes to the biosensor, the country's technological level is also very high. Further, because of a long tradition in the fermentation industry, its technological level in the use of instruments is at a sophisticated level. However, when it comes to quality control technology in this area, Japan lags behind the United States, and it will be necessary to continue efforts to develop high-level control technologies in the future.

(4) Materials, etc.

The supply of raw materials is not a great problem if high-premium products are produced in a small quantity. However, if the mass production of items such as general-purpose industrial chemicals has been enabled by an advancement in the bioindustry, one cannot deny the possibility that problems in procuring new materials will likely be incurred.

Also, the R&D of biotechnology requires laboratory animals such as mice, rats, and dogs raised, bred, and produced to conform to specific needs. As long as mice, rats, and rabbits are concerned, Japan can provide for itself; although, it depends almost entirely upon the import of larger-sized animals, such as dogs and apes.

e. Applications to other Industries to Create Large Markets

R&D into ways of utilizing biotechnology is also actively conducted in the, pharmaceuticals, primary (agriculture/livestock/fisheries), and foodindustries. Commercialization of technology is also progressing in these industries.

(1) Pharmaceuticals and medical treatment

Pharmaceuticals are a typical example of fine chemicals and since these can be sold on a basis of high value addition, this industry is expected to become one of the major areas of application for biotechnology. In Japan, antibiotics such as penicillin, streptomycin, and cephalosporin have been produced for a long time now using the fermentation method. Also, for the R&D to apply to new biotechnology in the production of pharmaceuticals, many companies have been engaged, and a-interferon has been put on the market. However, because the development of pharmaceuticals takes a long time (10 to 15 years) for confirmation of efficacy and safety, not to mention an enormous capital investment (45 ~10 billion), the risk involved for the development is too great.

In the field of medical treatment, research has been conducted into the application of biotechnology in the treatment of hereditary diseases. However, since it involves technical and moral problems, it has remained at the research stage using laboratory animals. Also, the research to apply biotechnology to the elucidation of causes, diagnosis, and treatment of cancer, AIDS, and Alzheimer's disease, is also actively conducted.

For applying biotechnology to the development of pharmaceuticals and to the elucidation of the cause of diseases such as cancer and aides, it will be necessary, first, to give light to the mechanism of in vivo metabolism and immunity. Therefore, the promotion of research of basic medical studies will be important.

(2) Agriculture/livestock/fisheries industry

For application of biotechnology to the agriculture, livestock, and fisheries, it is necessary to handle those higher life forms at the cell level as well as individual units. Namely, it will be necessary to breed at the cell level and then culture and grow stablely up to the individual units.

Breeding plants by the recombinant DNA technology has succeeded at the laboratory level, but when it comes to animals, the research still lingers on at basic study level. The anther culture technology and the recombinant culture technology such as the growing point culture have already put into practical use, and by using these technologies, virus-free seedlings are now being produced. Also, with animals, artificial insemination and zygote transplantation technologies have been put into practical use, by which the superior ones are now being selectively bred. Furthermore, in the field of fisheries, the techniques of making female and asexual by gene manipulation have reached the level of practical application .

(3) Food industry

In the food industry, as a measure against the lactose futaisho, lactose-decomposed milk obtained by decomposing lactose through a combination with a bioreactor is being produced. And also with shochu, sake, and bread the use of malt and fermentation bred through the cell fusion technology, are being produced. This is another way that the use of biotechnology is progressing.

Since there are many traditional fermented products like sake, miso, and soy sauce, the use of new biotechnology in the food industry is expected to continue in the future, too. Problems observed include those that many of the producers producing these fermented products are small or of nominal size, and therefore cannot afford to invest in the capital and manpower necessary for R&D. Besides, food is often affected by subjective judgments such as the taste and flavor. For future promotion of the uses of biotechnology in the food industry, these problems should be addressed properly.

3. Number of Biotechnology-related R&D Institutions and Companies

Japan bioindustry today can be classified into enterprises intending to produce new products by utilizing biotechnology, and those enterprises which are intending to offer biotechnology equipment to those producers.

The central and local governments and private organizations involved in the development of new technologies and products on the basis of research and development of initial biotechnology are as follow:

a. Number of National and Public Research Institutions

National and Public Institutes	No. of Institutes
Ministry of International Trade and Industry (MITI):	6 institutes
Ministry of Education:	5 institutes
Ministry of Health and Welfare:	10 institutes
Ministry of Agriculture, Forestry and Fisheries:	33 institutes
Science and Technology Agency:	3 institutes
Environmental Agency:	2 institutes
Local governments:	124 institutes
Universities:	33 institutes

b. Number of Private Sector

Type of Industry	No. of Institutes
Chemical industry:	98 enterprises
Food industry:	74 enterprises
Pharmaceutical industry:	55 enterprises
Other industries:	62 enterprises

As listed above, there are 217 national and public research institutes and some 289 private sector research institutes.

Among private sector entities that have made inroads into bioindustry, chemical and pharmaceutical companies have a wealth of technologies for both synthesis and fermentation, while food processing companies have abundant technologies for fermentation. In other fields, the pulp and paper companies, oil refining companies, and machinery manufacturers have also engaged in the development of new biofuels and bioreactors.

The steps of industrialization of this field are classified into (1) basic research, (2) development of technology, and (3) development of production technology. The majority of bioindustrial ventures today are still in stages(2)and(3),and have not yet reached the industrialized stage except a small commercialized products. Biobusiness is expected to become fully operative in the immediate future.

4. Biotechnology Equipment, Instruments and Devices Manufacturing Industry

As in 1989, about 130 150 enterprises are estimated to be involved in the production and sale of biotechnology equipment.

Among these enterprises, seventeen have entered into technical collaboration with overseas companies. Biotechnology have been introduced from about 30 US companies; five FRG companies; three companies from Switzerland, France, Sweden and Denmark; and the Australian firm.

These figures indicate the total number of companies from which technologies have been adopted. Biotechnology have been introduced, from 40 overseas companies as a result.

About twenty Japanese enterprises are engaged in the import and sale of foreign biotechnology equipment. The largest equipment suppliers are 29 US companies, 21 FRG companies, eight UK companies, two companies each from Denmark and Switzerland, and one company from Israel.

As described above, biotechnological equipment and technology is supplied from foreign companies, representing an exceptional or rate phenomenon when viewed from the prevailing industrial structure of Japan.

Table 7. Manufacturers and Suppliers of Biotechnology-related Equipment, Instruments and Devices, etc.

(Alphabetical order) Name of Company	Biotechnology-related equipment, Instruments and Devices
Atto Corp.	Gel electrophoresis devices, Liquid chromatographs, Peristaltic pumps, other biotechnological devices
Beckman Instruments (Japan) Co.	Ultra-centrifuges, Amino acid analyzers, Molecularstructure analyzers, Work- station for measuring immunization, immunization robots, Violet/visible ray analyzing systems, Liquid scintillation counters, High-speed liquid chromatographs, pH meters, etc.
Biomaterial Research Institute	Cell culture methods
Chiyoda Corp.	Biological wastewater treatment systems, Animal cell cultivation systems, Malto oligo saccharide production process
Chiyoda Manufacturing Co	Bioreactors, Fermentators, Plant cultivation tanks, Sterilizing system for animal cell cultivation, P-3 mass cultivation systems

Chuo Engineering &Construction Co.	Fedbatch bioreactors, Smoke pipe system for food production, Aquatron system, Plant culturing systems
Daiseki Co.	Activated sludge wastewatertreatment plants
Dowa Mining Co.	Iron oxidized bacteria wastewater treatment equipment, Ferric ion hydrogen sulfide treatment equipment
Ebara Research Co.	Biological water, wastewater and sludge treatment systems, Biomembrane treatment technology, Bioreactors, New methane fermentation process, Microbe fixation systems, etc.
Ebara-lnfilco Co.	Activated sludge treatment Plant, Biomembrane fermentators, Biological denitration and dephosphate plant
Fiji Electric Co.	Bioclean rooms, Ammonia analyzers
Fuso Water Industries Co.	Biological wastewatertreatment facilities
Hazama-Gumi	Biocleanrooms, Biotechnology-facilities
Hitachi Plant Engineering &Construction Co.	Biohazard prevention equipment, Bioclean rooms, Plant cultivation equipment, Immobilized microorganism used wastewater treatment systems
Hitachi, Ltd.	Biotechnologysupportingequipment
Hokusan KK	Fertilized egg freezing devices, Cell freezing devices, Plant factory systems, Plant cultivation systems, etc.
Ibaraki New Technology Development Cooperative	Automatic plankton supplying and management devices
Ikeda Rika Co.	DNA and peptide related instruments, Sugar chain analyzers, Mammalian cell culture systems
Iwaki Glass K.K	Plastic tissue culture devices, Biotechnology related equipment
Japan Bio-Rad Labo., Inc.	DNA sequence analyzing workstation
Japan Organo Co.	Chromatographic separation systems, Anaerobic wastewater treatmentsystems
Japan Pharmaceutical Development Co.	Serum free mediums for human cell culture
Japan Zeus Industry Co.	Ozone applied activated cultivation devices
JGC Corp.	Bioreactors, Cell mass culture systems, Biological sewage treatment equipment
Kajima Corp.	Biological wastewater treatment facilities, Bio-deodorization facilities, Waste fluid purifying facilities by methane fermentation facilities, Biochemical vegetable plant, Fish farm facilities, Biohazard facilities
Kansai Paint Co.	Bio-immobilized systems by photo-crosslinkable resin
Kawasaki Heavy Industries, Ltd.	Biological wastewatertreatment plants, Fermentators and plants

Komatsugawa Chemical Engineering Co.	Plant-site fermentators, Jar fermentators, Computer controlled fermentators, Continuous sterilizers, Cookers, Fedbatch culture fermentators, Ultrafilters, Vacuum filters, Vacuum concentrators, Solid fermentation plant, Recombinant DNA plant, Tissue culture plant, High viscous fermentators, On-line laser turbidimeters
Koseisha Co.	Organic cultivation kits
Kumagai Gumi Co.	High-performance wastewater purifiers
Kurita Water Industries, Ltd.	Bioreactors, Fine separators (HPLC, etc.)
Marubeni Corp.	Custom DNA synthesis (Genetic Design), Normal human cell culturing kits (Imsco), Endocell (Clonetics Corp.), Rapid detection system of bacteria contamination (Imsco)
Mitsubishi Electric Corp.	Plant factory systems, Microorganism monitoring systems
Mitsubishi Kakoki Kaisha	HPLC, SCF, SCFC, Membrane separators, Centrifuges, Filters, Evaporators
Mitsubishi Petrochemical Engineering Co.	Bioreactors (Culture tanks, fermentation tanks, membrane reactors), Separation and refining plants, Bio-plant, Bio R&D facilities
Mitsui & Co.	Medical, physical and chemistry related equipment and devices.
Mitsuwa Bio Systems Co.	Enzyme sensors for analyzers
Mitsuwa Rikagaku Kogyo Co.	Fermentation equipment, pH meters, DO meters, Anti-foaming devices
NGK Insulators, Ltd.	Bioreactors for waste water treatments, biological sewage treatmentsystems
Nichimen Corp.	Hollow fiber bioreactors for Mammalian cells
Nikken Inc.	Electrostatic food processing technology
Nippon Sharyo, Ltd.	Bioreactors for wastewatertreatment, Alcohol sensors, Bioreactors for soysauce production, Glucose sensors
Nisshin Flour Milling Co.	Mushroom production mediums, Clinical diagnosis mediums
Nissui Pharmaceutical Co.	Cell culture mediums, serum free medium
Nitto Denko Corp.	MF,UF and RO membranes, Membrane bioreactors
NKK Corp.	Biological municipal wastewater treatment plants
Ohbayashi Corp.	Bioclean rooms, biological wastewatertreatment plants
Okawara Mfg Co	Evaporators, Vacuum dryers
Onoda ALC Co.	Biological wastewatertreatment plants
Orbisphere Laboratories Japan Inc.	Steam sterilize dissolved oxygen meters, Inline and portable oxygen meters
Oriental Electric Co.	Glucose analyzers, Freshness meters, DO meters, pH meters, Jar Fermentation equipment, Process controllers

Oriental Instruments Ltd.	Cultureflow TC, Colony analyzers, Zone analyzers, Elisa analyzers, Automatic colony transfer systems
Orion Machinery Co.	Biotechnology supporting equipment, Clean rooms, Clean bench, Incubators, Artificial weather devices
Osaka Gas Co.	Biological wastewatertreatment equipment
Osaka Sanso Kogyo Ltd.	Liquid nitrogen freezing and preservation containers
Research Institutes of Industrial Bio-Science Japan Co.	Microbe control system for food production, Instant tissue and cell culture mediums
Sanken Setsubi Kogyo Co.	Easy-movable clean booth, Super clean units, Biological suspended solids separators
Sanyo Electric Co.	Incubators, Clean benches, Fermentators, Cryogenicfreezers, Mushroom factories
Seiko Instruments Inc.	DNA sequence reactors, DNA extracting and refining equipment, DNA base sequence readers
Sesil Co.	High sensitive respiration analyzers, Ultra high sensitive pressure difference detectors
Shimazu Corp.	Dielectrophoretic cell fusion processors, Automatic DNA synthesizers, Micro manipulators, Bio-liquid chromatography, High density cell culture systems, Protein sequencers
Software Development Co.	Genetic information processing systems, Nutritive management systems
Sugino Machine Ltd.	Super-high pressure testing equipment
Sumitomo Bakelite Co.	Petri dish, Flask, Plate, Cell culture ware, Centrifuges tube, Freezing tube dispenser
Sumitomo Corp.	Serum free mediums, Biotechnology-related equipment and accessories
Sumitomo Heavy Industries	Membrane bioreactors, High-performance fermentators, Simulated moving bed chromatographs, Super-critical fluid extractors
Sumitomo Jukikai Environment Co.	Biological wastewatertreatment plants
Tabai Espec Corp.	Carbon monoxide incubators, Incubators, Anaerobic incubators, Deep freezers Program freezers, Bench-top fermentation equipment, Pilot scale fermentation equipment, Industrial scale fermentators, Biological shakers
Taisei Corp.	Biological wastewatertreatment systems
Takenaka Corp.	Biohazard preventing and biotron facilities, Biological wastewatertreatment plants, Water-area purifying systems using aquatic plants
The Japan Steel Works, Ltd.	High-rate composting systems, Soil-bed type depolarizing systems
Thomas Kagaku Co.	Thermostatic shaking incubators, Shaking incubators, Thermostatic shaking water bath, Jar fermentors
Tomita Iron Works Co.	Personal vegetable supplying machine farmers, Automated plant cultivation equipment
Toray Engineering K.K.	Fermentators, Membranes for separation and refining

Toshiba Corp.	Biosensor, Bioreactors for food
Toso Corp.	Aspartame, HPLC, Packed column, Random access immunoassay systems
Toyobo Co.	Clinical analyzers
Wakunaga Pharmaceutical Co.	DNA probes

Table 8. Foreign Biotechnology-related Equipment Suppliers in the Japanese Market in 1988.

Country	Name of Suppliers	Equipment	Importers
U.S.	Vitek Systems	Auto microbic detecting system	Amco Inc.
	Hull Corp.	Freeze dryer	Asahi Life Science Co.
		Bottle cleaning machine	
	Ivy Biomedical Systems	Neonatal monitors	Asahi Life Science Co.
FRG	Seits Enzinger Noll	Filters for pharmaceutical use	Byron Industries Co.

However, there are now a large number of companies participated from various type of machinery and instruments manufacturers in this fields.

In Japan, the biotechnology-related equipment, instruments and devices manufacturing industry is now under "not classified" by the standard industrial code, and their production, export and import statistics are included in other industries such as chemical machinery, analyzers, electronics equipment and measuring instruments manufacturing industries. Consequently, there is no data or statistics for production, exports and imports of biotechnology-related ones.

However, we are capable to introduce the names of manufacturer, including foreign manufacturers and suppliers, with their products or the established industrial properties of biotechnology-related equipment, instruments and devices shown in Table 7.

5. Biotechnology and Bioindustry-related Equipment and Devices

As mentioned previously, the biotechnology industry of Japan is still in the initial development stage. Therefore, the supply of equipment and materials for research and development occupies a large portion of bioindustrial activities, rather than the supply of equipment and chemicals for commercial scale production lines.

The fact indicates that a large portion of R&D funds allocated to national and public research institutions, universities, and private research institutes goes to biotechnology equipment makers.

At present, roughly 130-150 enterprises have made inroads into this field. These firms supply equipment to national and public research institutes; private research institutes; as well as hospitals, pharmaceutical, foodstuff, chemical, tobacco, and other companies in the private sector. In addition, public inspection institutes, machinery manufacturers, etc., are also considered as users of biotechnology equipment.

In light of the fact that the biotechnology industry has not entered the practical full-scale production stage, Japan's biotechnology equipment market can be said to be still small in scale.

According to the results of a survey conducted in 1985, a total of ¥300-600 billion was allocated for biotechnology out of the total R&D budget of the respective enterprises. Out of this total amount, 30% is assumed to have been allocated for procurement of equipment and materials. A total of ¥100-180 billion was estimated for the biotechnology equipment market, including government budgets. On the other hands, MITI has estimated for the 1989 sales of biotechnology-related equipment, instruments and devices to about ¥1 00 million. Accordingly, the market scales for the biotechnology-related equipment, instruments and devices is to be estimated to about ¥100 -180 billions.

6. Trends in R&D Investments by Industry

The preceding sections have described the capital investment trends of Japan 's leading industries, their existing production capabilities, product supply potentials and various other situations concerning these industries. Judging from these trends, capital investments are being actively by all industries as are investments in research and development. According to MITI's data, R&D expenditures in Japan have increased by an average of 8-9% over the last three years. In 1987, the R&D expenditures of 776 enterprises belonging to the manufacturing industry and 121 enterprises belonging to the non-manufacturing industry a total of 897, totaled ¥3,917.2 billion(an average of ¥1,367 billion per enterprise overall, ¥4,503 billion in the manufacturing industry and ¥1,092 R&D expenditures of 667 enterprises in the manufacturing industry and 114 enterprises in the non-manufacturing industry, a total of 781, decreased to ¥2,292.8 billion(an average of ¥2,943 billion per enterprise overall but is estimated to have actually increased to ¥4,300-4,500 billion).

The ratio of R&D expenditures to total capital investments will differ with each industry, but on the average they are in the range of 15-25%, of which 40-50% is estimated to be for the purchase of R&D systems and equipment, attracting attention as a new market. In monetary terms, these R&D expenditures totaled ¥2 trillion, which is equivalent to 50% of the investments used for improving the production capability of the respective industries.

Table 9. Trends in R&D Investments, by Industry Type

(Unit: ¥100 million)

Type of Industry	No. of Company	1987	1988	No. of Company	1989
Manufacturing Industry	776	34,921	41,461	667	22,357
Textile Industry	55	680	699	52	628
Pulp and Paper Industry	34	217	267	30	169
Chemical Industry	109	3,781	4,123	91	2,583
Oil Refining Industry	26	417	362	24	385
Ceramics and Stone Industry	79	1,208	1,357	65	1,204
Iron and Steel Industry	41	1,418	1,502	32	581
Nonferrous Metal Industry	52	840	877	44	891
General Machinery Industry	86	2,956	3,193	79	2,516
Electronic Machinery Industry	43	6,083	6,492	38	1,922

Electric Machinery Industry	38	10,584	11,859	27	3,309
Automobile Industry	54	7,176	7,888	42	5 864
Other Mfg. Industries	189	2,626	2,842	142	2136
Non-Manufacturing Industry	121	1,231	1,353	114	571
Mining Industry	13	34	45	14	48
Electric Power Utilities	19	835	906	16	112
Gas Utilities	14	263	287	14	330
Wholesalers and Retailers	19	7	9	17	0
Service Industries	56	89	105	53	66
Total	**897**	**36,152**	**42,814**	**781**	**22,928**

Technological Level Required for Biotechnology Equipment, Instruments and Devices

The industrialized biotechnology is now undergoing for actual applications for various bio-related industry. However, it is difficult to distinguish equipment for R&D from equipment for commercial production under the present situation.

Even though microorganism and culture technology are extensions of fermentation engineering technology, it should be noted that their equipment and technology are different from the new fermentation engineering technology, based on the substances dealt with and the nature of the technology.

Promoted in the field of analysis technology is the establishment of a technology for improving the functions of the primary arrangement, through higher structural analysis or evaluation based on light activation of biopolymers and measurement of supermicro contents.

In light of the present state of the biotechnology industry in Japan, the types of biotechnology equipment that are required are for: (I) recombinant DNA technology, (2) cell mass culture technology, (3) cell fusion technology, and (4) enzyme fixation technology in bioreactors.

1. Equipment and Devices Required for Experiments on Recombinant DNA

a. Cell adjustment

Cell crusher, cooling centrifuge, and supercentrifuge.

b. Adjustment of m-DNA

Dry sterilizer, autoclave, cooling centrifuge, supercentrifuge, chromatograph riffle sampler, spectro photometer, fluorescent/fluorometric spectro-photometer, electro-phoresis device, UV-lamp photographing device, densidometer, and density gradient preparation riffle sampler.

c. Adjustment of c-DNA

Constant temperature bath (thermostat), autoclave, high-speedmicro-centrifuge, spectro-photometer, electro-phoresis devices, density gradient preparation riffle sampler, concentration centrifuge, liquid scintillation counter, automatic developing device, dupe freezer, and cryogenic temperature bath.

d. Culture of microorganisms

Dry sterilizer, autoclave, culture shaking devices, incubator, and spectro-photometer.

e. Crushing of cells

Cell crusher, supersonic crusher.

f. Purification of plasmid

Cooling centrifuge, supercentrifuge, density gradient preparation riffle sampler, electrophoresis device, and spectro-photometer and refraction analyzer.

g. Determination of the arrangement of protein amino acids

Peptide sequencer, amino acid analyzer, highspeed liquid chromatograph, spectro-photometer, and liquid scintillation counter.

h. Synthesis of DNA

DNA synthesizer.

i. Purification of DNA

Centrifugal separator, concentration centrifuge, and chromatograph riffle sampler.

j. Sequencing

DNA sequencer, electrophoresis device, automatic developing device, gel scanner, liquid scintillation counter, high-speed liquid chromatograph, dupe-freezer and incubator.

J. Insertion (integration) into vector

Constant temperature bath, autoclave, high-speed micro-centrifuge, and safety cabinet.

k. Transformation

Constant temperature bath, incubator, turntable, agar-agar plate preparation device, colony counter, and safety cabinet.

1. Analysis of plasmid and recombinant DNA

Constant temperature bath, dry heat sterilizer, electrophoresis device, uv-lamp photographing device, high-speed micro-centrifuge, transfer plotting device, concentration centrifuge, electron microscope, and DNA sequencer.

m. Fixation of manifestation protein

Spectro-photometer, chromatograph riffle sampler, immunity electrophoresis device, amino, peptide sequencer, and glutamic acid analyzer.

n. Efficient manifestation of protein

DNA synthesizer, etc.

o. Mass culture of cells

Jar fermentor and continuous centrifuge.

2. Equipment and Devices Required for Use in Research and Experiments on Animal and Plant Cell Cultures

a. Culture of Animal Cells

(1) Separation of cells from animal tissue

Sterilizer [dry (hot) air], high pressure, boiling, filtration, ultra-violet ray, X-ray and gas; water purification device (reverse osmosis, distillation and deionization); clean bench; air-conditioning equipment for germ-free laboratory; vacuum freezing dryer; refrigerator; freezer; inverted and erected optical microscopes; low-speed centrifuge; pH meter; magnetic starter; cell filter; cell counter; and test device washer.

(2) Monolayer culture of cells

Incubator, C02 incubator, multiple-stage culture device, micro-carrier culture device, constant temperature culture room, electron microscope, spectro-photometer, various shaking devices, micro-injector, micro-manipulator, cell sorter, dissolved oxygen meter, and radiation gauge in addition to the devices listed in Paragraph (1) above.

(3) Culture of floating cell

Spinner culture device, tank culture device, and sterilization system including those listed in Paragraphs (1) and (2) above excluding incubators and multiple-stage culture device.

(4) Separation and purification of cell products

Devices (excluding clean bench, optical microscope, starter, and coal tar counter) listed in Paragraph (I) above, as well as cold room, chromatograph riffle sampler, high-speed cooling centrifuge, continuous centrifuge, density gradient preparation device, riffle sampler, cell crusher; electrophoresis device, densidometer, high-speed liquid chromatograph, fluorophotometer, immunity electrophoresis device, amino acid analyzer, peptide sequencer, gas chromatograph, GC-MS fraction collector and freezing dryer.

(5) Adjustment of clinical samples

Devices in Paragraph (1) above (excluding microscope, centrifuge, pH meter, cell filter, and coal tar counter), and automatic rime sampler and vial rolling machine.

(6) Preservation of cells

Programmable low temperature cooling preserver in addition to the devices listed in Paragraph (1) above.

b. Plant Culture

(7) Separation of organs and cells and plants

Same as Paragraph (1) above.

(8) Culture of organs

Devices listed in Paragraph (1) above, as well as culture shelf with lighting, positive low temperature culture device, rotary shaking culture device, culture bath sterilization system, measurement system (pH, temperature, DO, liquid level, and glucose).

(9) Organ culture

Devices listed in Paragraph (I) above.

(10) Fixation plant cells

Devices listed in Paragraph (2) above.

(11) Purification and separation of cells and products

Cell crusher, centrifugal separator, cooling centrifuge, dryer (ventilation and vacuum freezing), chromatograph riffle sampler, highspeed liquid chromatograph, spectrophotometer, and gas chromatograph.

(12) Seeds and seedlings

Devices listed in Paragraph (1) above, as well as net room, green house, and cold room.

3. Equipment and Devices Required for Research and Experiments on Cell Fusion

a. Animal Cells

(1) Culture of immunity and lymphocytes (immune lymphocytes)

Dry heat sterilizer, autoclave, shaking culture device, incubator, cloth cabinet, cold box, C02, incubator, and spectrophotometer.

(2) Cell fusion

Table centrifuge, cooling centrifuge, incubator, and phase contrast microscope.

(3) Selection and cloning of hybridoma (selection and sorting of culture medium)

Agar-agar plate preparation device, colony counter, optical microscope, electron microscope, and cell sorter.

(4) Test-tube cultures

(5) Separation and purification of antibodies

Affinity chromatograph, high speed liquid chromatograph, chromatograph riffle sampler, spectrophotometer, fluorescent spectrophotometer, infrared spectrophotometer, GC, SIMS, FDMS, and NMR.

b. Plant Cells

(6) Apostasis of cell and formation of protoplast

Same as Paragraph (2) above.

(7) Cell fusion

Same as Paragraph (2) above.

(8) Formation of cell walls

(9) Differentiation culture mediums

Same as Paragraph (3).

(10) Confirmation of variety and separation and purification of products

Same as Paragraph (5) above.

c. Required Equipment and Devices for Research and Experiments on Microorganism Cells

(11) Fixation of microorganisms

Same as Paragraph (1) above.

(12) Formation of protoplast

Same as Paragraph (2) above.

(13) Cell fusion

Same as Paragraph (3) above.

(14) Formation of cell walls

(Same as Paragraph (3) above.

(15) Cultures

Same as Paragraph (4) above.

(16) Separation and purification of products

Same as Paragraph (5) above.

4. Equipment and Devices Required for R&D on Enzymes and Bioreactors

a. Screening of microorganisms

Screening device, colony counter automatic culture medium sterilizer, various types of microscopes, incubator, and C02 incubator.

b. Cultures

Shaking culture device, continuous synchronous culture device, shaking temperature gradient device, nephrometer, gas analyzer, enzyme sensor, DO controller, pH controller, biomass concentration controller, defoaming device, sterilizing autoclave, and clean bench.

c. Biomass separation

Centrifugal separator and MF filter.

d. Observation of biomass

Transmitter, scanning type electron microscop, fluorescent and ultrasonic microscopes.

e. Separation of cell organs

Cooling centrifuge and various types of microscopes.

f. Crushing

Ultrasonic crusher, French press, Dynomill, warning blender, and homogenizer.

g. Separation

Cooling supercentrifuge and chromatograph riffle sampler.

h. Extraction, concentration, and measurement of activity

Oxygen (O2) sensor, spectrophotometer, automatic titrator, fluorescent spectrophotometer, stopped flow device, and oxygen potentiometer.

i. Quantification of protein in raw oxygen

Spectrophotometer, fluorescent spectrophotometer, turbidimeter, refractometer, X-ray spectrometer, liquid scintillation counter.

j. Purification

Adjusting gel electrophoresis device, MF filter, freezing dryer, dialysis device, electric desalting device, and gel filter.

k. Analysis of oxygen (purity, structure, metal, glycolipid, etc.)

Cooling supercentrifuge, two-dimensional electrophoresis device, atomic absorption photometer, plasma emission photometer, chromatoscanner, densidometer, high-speed fluid chromatograph, infrared spectrophotometer (FTIR, ATR), gas chromatograph, GC-MS, MS-MS, laser Laman spectroanalyzer, amino acid analyzer, peptide sequencer, FAB-MS, SIMS. X-ray diffractometer, NMR, cooling supercentrifuge, light scattering analyzer, gel filter, ESR, liquid scintillation counter, fluorescent spectrophotometer, optical rotary dispersion photometer, circular dichronism measurement device, and spectrophotometer.

l. Synthesis of peptides

Peptide synthesizer.

m. Fixation

Light irradiation device, liquid scintillation counter, X-ray diffractometer, optical rotary dispersion photometer, circular dichronism measurement device, and spectrophotometer.

n. Stabilization

Colum chromatograph and affinity chromatograph.

o. Bioreactors

Quantification pump, UV-monitor, RI monitor, fraction collector, fluorescent monitor, and oxygen sensor.

p. Separation, concentration, and purification

High speed fluid chromatograph, ultrafilter, and chromatograph riffle sample.

5. High-Performance Biotechnology Equipment and Devices Required for the Future

The level of the various types of biotechnology equipment and devices used today has been described above. Under the "Promotion System for R&D on Basic Technology" under implementation since FY1980, R&D activities have been promoted with respect to the following biotechnology equipment:

a. DNA sequencer

This device is intended to cut the same four samples containing fragments of single-stranded DNA (at the respectively different positions marked in advance). In this case, addition and mixing of reagents, reaction temperature, discharge of waste liquid, drying, etc. during the respective fragmentation processes are controlled automatically on a minute-by-minute basis. Thereby, it has become possible to perform continuous fragmentation with high reproducibility-a task impossible by manual operation.

According to the present capacity, it is possible to treat twelve racks of samples in about three hours per one cycle.

b. Peptide sequencer

This device is intended to repeat the following three steps of chemical reactions under optimum conditions: coupling of PITC reagent to the terminal amino group of peptides; cleavage; and conversion into chemically stable and fixable amino acid. According to the present capability, it has become possible to analyze a very small amount of reproducible samples, which was difficult using previous conventional devices.

c. Micro-manipulator

In this device, hydraulic manipulators are placed upon various types of inverted microscopes, and operations required for experiments on cells can be performed using the manipulators while watching the display monitor. As it is possible to perform three-dimensional microtransfer up to 0.1 mµ or less, easy extraction of the cell nucleus and other operations formerly impossible are now feasible.

d. High-speed amino acid analyzer

With this device, the samples (40 ~ 80 pcs.) containing a very small amount of microorganismamino acid and protein hydrolyzates are set on an auto sample; injection of reagents, cleavage and elution into the respective amino acids in a constant temperature column, mixing with reagents, heating and coloring in the reactor, measurement of light absorption, and printout can all be performed automatically in compliance with a predetermined program.

Under present capabilities, it has become possible to analyze amino acid samples in about 30 minutes in contrast to 2 to 2.5 hours required using a conventional chromatograph.

e. Colony counter

This device is designed to automatically measure the number, area, diameter, etc. of a colony formed on a Petri dish after culturing according to the picture processing method. At present, it is possible to measure a colony with a minimum diameter of 0.06 mm within one second.

f. Enzyme antibody immunity measurement device

This device measures the quantity of an antibody contained in a sample according to the ELISA Method that uses an enzyme as a marked compound. The present device is superior in convenience, stability, sensitivity, etc. and permits speedy quantitative measurement in contrast to the conventional IF and RIA methods that caused various problems.

g. Cell sorter

With this device, fluorescence and scattered light are detected by irradiating a fluorescence-activated cell with laser beams. An electric charge is then applied to the intended cells based on what has been detected and the sorting of cells is performed automatically by means of a polarizing plate to which a constant voltage is applied. According to the present capacities, it is possible to sort 5,000 or more cells per second.

h. Liquid chromatograph for sampling the contents of an organism

This device separates and purifies the contents of a very small amount of a microorganism under optimum conditions while automatically changing the amount of liquid feed. According to present technology, it is possible to separate and purify highly active nucleic acid and other substances.

i. Carrier-free continuous electrophoresis device

With this device, a sample for separation is injected at a uniform rate into the buffer solution that is flowing vertically inside a migration cleavage tank; and while the sample is moving, electrophoresis is performed by applying a high voltage from the direction perpendicular to the flow. The present capacity is within a level wherein separation of the sample can be performed continuously.

j. Automatic culture medium preparation device

In this device, a large number of sterile Petri dishes that have been arranged in advance are transferred successively into specific positions, and agaragar culture media that have been sterilized are automatically sorted with accuracy.

According to the present technology, it has become possible to sort samples accurately and sterilely which had not been possible with conventional manual-sorting operation.

k. Colony transfer device

This device is designed to automatically confirm the colony on a Petri dish by picture processing, and to transplant an intended colony precisely into a desired position.

This device is still in the development stage, and is expected to make it possible to precisely specify the color, tone, shape, dimensions, and transplanting position of a colony; to enhance the construction to retrain a germ-free environment; and to improve reliability and efficiency as a development target.

1. DNA synthesizer

This device is designed to synthesize intended DNA by using reagents containing various kinds of nucleic acids, and solvent media based on a chemical synthesis process. According to the present capabilities, it has become possible for an unskilled person to finish DNA synthesis in several days in contrast to two or three months required for experts to perform the same DNA synthesis operation with easier technology.

m.. Peptide synthesizer

This device is designed to synthesize peptides by creating reaction under optimum conditions with amino acids.

According to present technology, it has become possible to automatically synthesize 50 couplings of peptide per reagent-filling, and to complete the synthesis of one coupling in about one hour.

n. Cell culture device

With this system, an AC current of about 500 kHz is applied to cell suspensions arranged between 1 mm or smaller electrodes so as to arrange the cells in suspension/liquid in one row. Then, the cell membrane is perforated by applying a DC pulse (100 V/ min. and duration of roughly 10 sec.) to these cells, thus fusing adjacent cells.

According to present capability, the fusion ratio at the time of preparing hybridoma has been improved to 20% from 2% attainable with conventional technology.

Promotion Measures for/ Laws and Regulations on Biotechnology Industry

1. Promotion of R&D

a. Promotion of Basic Research

As stated above, biotechnology has a characteristic that the results of basic research are easily translated into practical application. Also, considering the significance of the technology in the advancement of basic research and that the technology contributes to the expansion of the technological frontier for all mankind, it is very important to promote this essential research in the future.

As regards the promotion of basic research, because it is conducted in close relationship with various other industries (e.g. agriculture, forestry, fisheries, manufacturing, and mining), and because its technology complements other related ones, it will be necessary to maintain existing communication links-even strengthen them-if effective promotion of the technology is to occur.

(1) Promotion of basic research initiated by universities and national research institutes

For concrete implementation of the above goals, and for the detailed reasons, it will be necessary for universities and national research institutes to take the initiative in promoting the basic research of biotechnology while keeping close contact with each other. It is also necessary that they promote an exchange of researcher with foreign institutes as well as private companies, and to provide the necessary funding for research.

Namely, it will be necessary to expand and strengthen basic research for biotechnology in university departments, national research institutes, and private companies in and out of Japan; and to create a system in which all those organizations can keep in close contact with each other.

(2) Discussions about establishing a central organization for the promotion of basic research for biotechnology

As stated above, to radically strengthen basic research in the field of biotechnology in Japan, it is necessary to promote basic research initiated by the universities and national research institutes in the first place. In addition to this, organizations should provide an environment that allows free and creative research that can accept young and creative researchers from universities, national/public research institutes, and private companies in and outside of Japan and who are, in effect, mobile researchers. And while providing equipment and the funds necessary for the research, it is desirable that respect be paid to the spontaneity of researchers and to the selection of research themes and techniques. This will be beneficial from the viewpoint of promoting basic research. If an organization like this is established, it will serve as the center to which all technologies related with biotechnology come together, and considering the characteristics of biotechnology, that it grows through close interrelation with many industrial technologies, it will become the place of contact for all industrial technologies relating to biotechnology. It will serve Japanese and foreign researchers alike.

From this viewpoint, further discussions will be necessary regarding the expansion and strengthening of biotechnology-related basic research at universities and public research institutes, and also regarding the necessity and viability of a "biotechnology center." The administration for this joint office, thus, should be a shared responsibility of the concerned industries, academia, and the government.

b. Promotion of R&D Project for Common Base Technology

To set out a plan for the development of common base technologies, it will be essential for bringing about dramatic progress in basic research and applied research.

Consequently, it will be important to promote R&D projects for common base technology under the collaboration of industry, universities, and government, from the following viewpoints.

(1) Diversification of life forms to be studied

In the past, the main target of R&D was placed on the microorganisms that are land-based because of their relative ease of handling. At present, among the land-based life forms, interest is increasing in these higher-level life forms only. In the future, it will be necessary to expand the research focus of biotechnology to the marine organisms which have never been studied in the past.

(2) Compounding of bio-constituents

In the past, the main attention was to develop technologies that utilize functions of a single bioconstituent as represented by DNA. But in the future, it will be required to promote technological developments that utilize the functions of compound systems. Examples are the technologies that utilize constituents of compound composition (bio-membranes, intracellular organelle, etc.), and chromosome engineered which enable transformation of higher life forms in which many genes are involved. In particular, the bio-membranes are responsible for the high-level in vivo conversion of substances and information. It will be desirous for the biotechnology industry of the future to elucidate the mechanism of bio-membranes and to find ways of application of the mechanism.

(3) Diversification of application fields

In the past, utilization of the means for substance conversion in the production of industrial chemicals was the main area of technological development. Later, the development of bio-devices which utilize cellular information conversion functions in the field of the information technology industry was begun. In the future, it is desired that efforts be made to develop technologies that utilize biotechnology for resource energy and environment purification such as in the secondary and tertiary oil recovery and the removal of oil clouding pollution.

(4) Advancement of biotechnology support equipment

To promote the development and industrialization of biotechnology, the development of support equipment is also very important.

In promoting the commercialization of this field in particular, the development of separation and purification technologies is essential. The development of technologies which improve separation accuracy such as the separation of trace substances in more quantities than in the past by using the monoclonal antibody's selective bonding characteristic, and also the development of efficient technologies such as the improvements in the construction of storage containers and of liquid chromatography. Also, the development of materials required for these equipment will also be necessary.

Furthermore, since, in the future, it will be necessary to track down in vivo changes with the passage of time, it will be necessary to develop equipment that enables the tracking of in vivo changes over time, such as electron microscope which enables the observation of cells in activity.

c. Preparation for Infrastructure of Biotechnology R&D

Since research software for items such as gene banks (which collect, store, and present genetic resources) pertains to such life forms as microorganisms and animal/plant cells, and to data bases which collect, sequence by priority, and present proprietary data it will be urgently required to streamline these software while ensuring harmony with the systems of other countries. A database will dramatically assist this process by improving efficiency through applied R&D

Also, for smooth and efficient promotion of technological development, it will also be necessary to build research facilities that can be commonly used by researchers as the infrastructure for their research. While pursuing various subsidiary programs such as the research infrastructure streamlining program of the New Energy/Industrial Technology Overall Development Organization, it will be necessary to build technological development infrastructure such as the mining and manufacturing industries marine life form utilization technology research center.

Necessary also are a bio-engineering analysis center, as a large-scale, advanced research facility open for use by a wide scope of researchers in Japan and overseas alike.

2. Construction of Industrial Infrastructure

Since the bioindustry is still in its infancy, the infrastructure for the industry has not yet fully been built up Because the build-up of industrial infrastructure is an essential element for the development of any industry, the following measures will have to be taken quickly for biotechnology likewise, so that an industrial infrastructure can be built up

a. Promotion of Standardization

Since biotechnology is a field in which the level of technological development is visible, there is a considerable non-uniformity in quality, notation, and experiment/evaluation methods that exists with the equipment, devices, and reagents being used in the field Because equipment, devices and reagents are something which forms infrastructure, making clear definitions of the operative concepts is vital And the promotion of easing comparisons by making uniform the terms, notations, and experiment/ evaluation methods will be an essential requirement for putting the biotechnology into practical use Therefore, the promotion of standardization of equipment / devices and reagents must be done while considering the exact timing to make them, from the international point of view

b. Build-up of Statistics

In ensuring the sound progress of a new industry, it is important that the manufacturer, user, and the supplier of related materials and equipment come to accurately understand the situation facing each of them They must further determine for themselves the corporate strategies such as their own development, production, and sales. For this reason, the collection and streamlining of information concerning the trend of production/delivery, trade, and investment in plant and equipment, is important when the related businesses determine corporate strategies and also when the government formulates appropriate administration measures and performs economic analysis as is required. However, at present, since, except for a part of the fermentation industry's products, the statistics have not yet been gathered, and it is desired that this build up of the bioindustry related statistics meet its urgent need

c. Build-up of Biotechnology Information Network

Throughout the world, R&D and industrialization is progressing, and to respond to this trend, the amount of information on research equipment/reagents, for the bioindustry products is accruing at a dramatic rate For this reason, it will be necessary to build up a data base which can supply, accurately and on demand ,the information to those involved in the research and development of biotechnology and in production of bioindustry products.

d. Training and Securing Talent

A wide scope of knowledge is required for the promotion of the development and commercialization, and also great care must be taken in securing safety However, at present, there are not many people of such talents So, the government should strive to train people with these skills while noting the importance of the promotion of inter-disciplinary exchange and the cooperation of industry, universities, and the government. Also, securing talent will be aided by setting the goal for bioindustry researchers to give an stimuli for improving technology; showing the level of ability required as a bioindustry researcher to improve levels of research; and establishing the certification system to secure a certain level of ability and technology in a comprehensive scope of fields, thereby contributing to the securing a sufficient pool of talent.

e. Improvement of Patent Protections

Those who want to file a patent application for their inventions, related to microorganisms are obligated to deposit the microorganism with the Fermentation Research Institute of the Agency of Industrial Science and Technology. An exception exists in the cases where those of ordinary knowledge in the field to which the inventor belongs should be allowed easy access to the microorganism in question. The microorganism deposited with the institute is something that can be viewed as an amalgam of know-how, and so, views are divided for the conditions on providing access to the microorganism. Thus, full considerations should be given to this matter. Also, in the field where the development of biotechnology is progressing noticeably, measures should be taken for further acceleration of the examination of patent applications in addition to the implementation of conventional measures.

Further, since the further internationalization of commercial proprietary system is expected in the future, it is hoped that secure international harmony of industrial property sharing in the bioindustry will continue to occur through meetings of WIPO, etc. as is now going on.

In addition to the problems concerning the industrial property system like said in the above, the problems concerning the protection of property right of experimental somatic cells have also been pointed out which are also desired to be addressed as quickly

as possible.

f. Vitalization of the Bioindustry in Individual Districts

Despite the fact that biotechnology is expected to grow from the special characteristic of each individual field and to contribute to the vitalization of the local economy, the localities unfortunately are lacking in resources for researchers, research facilities, information on, and funds for R&D; and because of these reasons, their commitment to biotechnology, in general, has not yet fully materialized. To promote the vitalization of localities on the merit of biotechnology, it is necessary to overcome problems faced by the lack of relevant talents, information, and funds while concurrently trying to build a firm base for the R&D in the localities. For these purposes, the following measures are desired to be taken.

(1) Understanding of local biotechnology-related potentials and presentation

In individual localities, biotechnology is beginning to thrive in many sectors, but unfortunately, the fact is that most of them have not yet been put into practical use. It will be important to dig out the potentials of biotechnology latent in the localities so that the enterprises in the areas can utilize them.

For this purpose, it is desired that an understanding and clarification of local biotechnology-related potentials will be actively pursued. This would address such matters as the natural conditions for resources and life forms related to the biotechnology and social conditions. In turn, this would concern such issues as the level of operation of universities and public research institutes currently involved in the study of biotechnology. Also, it would effective to discover and show the appropriate form of bioindustry for which potentials for growth in that district are very high, based on an understanding of well defined potentials.

(2) Construction of bio-intelligence network system

It is necessary to build up the national bio-information network proposed in the section for build-up of industrial infrastructure so that the latest information can be retrieved. When the inter-local exchange is promoted, it will promote a collaboration on organic topics in the district, which will, in turn, contribute to the expansion of the bioindustry in the nation as a whole. For this reason, it will be very important to construct the bio-intelligence network system which also contains information concerning the bio-potentials for each district.

(3) Formulation of bioindustry introduction manual

To overcome the lack in personnel and information resources in the districts, it is desired that the local governments should prepare guidelines with which to guide local businesses and to which the local businesses can refer when entering the biotechnology field. For this reason, it will be necessary to formulate a bio-industry introduction manual compiling solutions to the problems that possibly may be encountered when the local businesses attempt biotechnology R&D and the points to note for efficient R&D and promoting commercialization.

Also, for continued concrete discussions for the above measures and for preparation of the manual, it will be necessary for this committee to have a sub-committee and to continue deliberations.

3. Safety Considerations

For the problem of safety assurance, OED began to be involved with this problem from earlier the beginning and in their board of directors meeting in July 1986, they adopted the recommendation titled "Observations in Safety of Recombinant DNA Technology".

The Ministry of International Science and Technology, in order to secure safety in recombinant DNA technology over the industrial processes, has just formulated and proclaimed "Guidelines for Industrialization of Recombinant DNA Technology" in June 1986, based on the discussions made by OECD and also on the report submitted by MlTl's chemicals committee of May 1986.

It is already more than two years since the guidelines for industrialization were formulated. Although the guidelines are gaining ground with respect to knowledge of their existence, it is also necessary to continue efforts to make them more widely known to the public and to appropriate administer these guidelines through an illustration of specific situations.

Since additional technological development is prominent in the field of applied biotechnology, it will be necessary to keep abreast of the latest technological developments and to incorporate the most recent additions to knowledge in the respective data banks. Through conducting surveys of development status, those concerning the safety of recombinants and safety assurance, and those on the current level of DNA technologies which have been put into practical use already, this can be achieved. Based on an accurate updated understanding, it will also be necessary to modify the guidelines, with flexibility in mind, when such changes are required. Also, with the advancement of the bioindustry, the number of applications filed for confirmation for conformance to the guidelines is expected to increase, and it will be necessary to build up a computerized data management system which assures speedy processing.

In the meantime, biotechnology with the objective of utilizing recombinants under the natural environment is developing, such as that which occurs through the disposal of exhaust water.

Under these circumstances, OECD submitted the recommendation in July 1986 that the safety assurance measures in the case of utilizing recombinants under the natural circumstances should be fully discussed. Based on the recommendation, the meetings of experts for discussing the safety assurance measures in the case of utilizing recombinants under the natural circumstances is scheduled to be held from this year.

In Japan, it will be necessary to steadily promote surveys and discussions on the safety evaluations and control techniques for the recombinants under natural circumstances (this was started in 1986), and to combine the findings with the surveys being made by OECD in order to establish the safety assurance measures for utilizing recombinants under normal conditions.

4. Expansion of Application and Education of the Public

With the high-technology field of microelectronics, the results of technological developments are put into the concrete form of IC chips and personal computers, and are used in extensive areas of the society. So it is relatively easy to have an understanding of the usefulness and safety of such technologies. However, with biotechnology, since the result of technological development thrives in areas almost detached from daily life, the fact is that the public understanding of this technology remains very poor. So it will be essential to the sound growth of the bioindustry in the future to promote dissemination of concrete and accurate information on the usefulness and safety of biotechnology, and to promote educational activities for the benefit of the general public, thereby deepening the understanding of the technology by this group.

5. Establishment of Comprehensive Import Expansion Policy

The comprehensive import expansion policy compiled by the Ministry of International Trade and Industry (MITI) this time is unprecedented from both historical and international perspectives, having the aim of establishing a taxation system to promote commodity import, to exempt customs duties on over 1,000 items and to substantially improve the budgetary and financial measures related to import expansion. This new import expansion policy may be regarded as a drastic reversal of the export promotion measures the government adopted in the 1960s, and marks a big step forward in making Japan a leading "'import-oriented country." The outline of new policies are as follows:

a. Establishment of Tax Credit Measures for Promotion of Commodity Import

    (1) Establishment of Comprehensive Taxation System for Commodity Import Promotion Compatible with Various Trading Modes

        (a) Offering incentives such as tax reduction (5%) or accelerated depreciation to manufacturers with respect to increased import amounts.

        (b) Enabling wholesalers and retailers to build up reserve funds (tax-free) for market development designed to promote sales of imported commodities.

    (2) Term of Application of Aforementioned Measures: 3 Years

    (3) Measures Applicable in Principle to Customs Duties-Free Commodities (Computers, Semiconductors, ICs, etc.), at Roughly 5% of Japan 's Total Imports, with Estimated Import Value of ¥5 Billion (US$400 Billion) Based on 1988 Statistics

b. Tax Credit Measures for Promotion of Commodity Import

(1) Objective

Substantial costs and risks will be involved in commodity prospecting, sales promotion and marketing for increasing commodity imports. The aim of this taxation system is to provide various tax incentives such as tax reduction and accelerated depreciation to alleviate costs and risks, and thereby to promote increased commodity imports.

Incidentally, this taxation system may be regarded as running counter to the export promotion taxation system the government adopted in the 1960s.

(2) Taxation System Scheme

(1) Reduction of Taxation Amount and Acceleration of Depreciation

- Target enterprises: Enterprises whose import values of commodities designated by the import promotion taxation system are increased by over 10% compared with the standard fiscal year (fiscal year with the maximum import value prior to fiscal year 1989).

- Target commodities: In principle, the commodities designated in Part 5 to Part 8 of the Standard Internal Trade Classification (SITC) and which are customs duties-exempted.

- Contents: Selective application of either of the two following systems.

(a) Tax Reduction

Tax reduction equivalent to 5% of the increased import amount of commodities designated for import promotion (Limited to 10% of corporate tax, and to 15% in case of small and medium-scale enterprises).

(b) Accelerated Depreciation

Accelerated depreciation on assets accrued during the term concerned and the two preceding years, from among the mechanical facilities possessed at the end of the business term.

Acceleration rate:

Target import promotion commodities 20%

Others I 0%

(Limited to 50% of the increased import amount of target import promotion commodities)

- Applicable term: Three years

(2) Preparatory Funds for Development of Imported Goods Markets (Tentative Name)

- Target enterprises:

Wholesalers and retailers whose import values of target import promotion commodities were over 10% that of the standard fiscal year.

- Target commodities:

In principle, the commodities designated in Part 5 to Part 8 of the Standard Internal Trade Classification (SITC) and which are customs duties-exempted (refer to section 3).

- Contents: Limit amount stacked up-Up to 20% of increased import amount.

Redemption-Equal amounts over 5-year period.

(3) Target Commodities of Import Promotion Taxation System

1) The values of the target commodities are estimated at roughly 50% of the amount of products imported into Japan (about ¥5 trillion (US$40 billion) based on 1988 figures).

2) Target Commodities of the Taxation System

* Capital goods

About 1/2, including semiconductors, computers, motors, various kinds of machinery and their parts

* Intermediate goods

About 1/5, including synthetic rubber, tires

* Durable consumer goods

About 1/4, including home electrical appliances, automobiles, sporting goods (e.g. golf clubs)

c. Removal of Customs Duties

A decision was made to remove or lower commodity customs duties on December 20, 1989, which consisted of removing duties on 1,004 items and lowering duties on 4 items, with the amount concerned at roughly ¥1 ,700 billion ($13 billion). This measure removes customs duties on 56% of imported commodities (currently 42%).

This move by Japan to remove customs duties autonomously has brought success to the "Uruguay Round" customs duties negotiations and, at the same time, the government's move to exempt maximum customs duties autonomously has indicated the Japanese government's determination to promote further market liberalization to the world.

Also, from the perspective of improved the access the Japanese market by foreign products, the government has established a "System to Refund Taxes on Re-exported Commodities" in the event any imported commodity was re-exported from the country.

d. Biotechnology-related Equipment, Instruments and devices to Which Items 2 and 3 Apply

The items listed below have had the customs tariff schedules temporarily eliminated (0% customs tariff rate), effective April 1st, 1990

NO.	Description
84.18	Refrigerators, freezers and other refrigerating or freezing equipment, electric or other heat pumps other than air conditioning machines of heading No. 84.15:
84.19	Machinery, plant or laboratory equipment, whether or not electrically heated, for the treatment of materials by a process involving a change of temperature such as heating, cooking, roasting, distilling, rectifying, sterilizing, pasteurizing, steaming, drying, evaporating, vaporizing, condensing or cooling, other than machinery or plant of a kind used for domestic purposes; instantaneous or storage water heaters, non-electric: <Instantaneous or storage water heaters, non-electric:>
84.21	Centrifuges, including centrifugal dryers: filtering or purifying machinery and apparatus, for liquids or gases: Centrifuges, including centrifugal dryers:
90.18	Instruments and appliances used in medical, surgical, dental or veterinary sciences, including scintigraphic apparatus, other electro-medical apparatus and sight-testing instruments: Electrodiagnostic apparatus (including apparatus for functional exploratory examination or for checking physiological parameters):
90.22	Apparatus based on the use of X-rays or of alpha, beta of gamma radiation, whether or not for medical, surgical, dental or veterinary uses, including radiography or radiotherapy apparatus, X-ray tubes and other X-ray generators, high tension generators, control panels and desks, screens, examination or treatment tables, chairs and the like: Apparatus based on the use of X-rays. whether or not for medical, surgical, dental or veterinary uses, including radiography or radiotherapy apparatus:
90.23	
9023.00	Instruments, apparatus and models, designed for demonstrational purposes (for example, in education or exhibitions), unsuitable for other uses
90.24	Machines and appliances for testing the hardness, strength, compressibility, elasticity or other mechanical properties of materials(for example, metals, wood, textiles, paper, plastics):
90.25	Hydrometers and similar floating instruments, thermometers, pyrometers, barometers, hygrometers and psychrometers, recording or not, and any combination of these instruments: Thermometers, not combined with other instruments:
90.26	Instruments and apparatus for measuring or checking the flow level, pressure or other variables of liquids or gases(for example, flow meters, level gauges, manometers, heatmeters), excluding instruments and apparatus of heading No. 90.14, 90.15, 90.28 or 90.32:
90.27	Instruments and apparatus for physical or chemical analysis(for example, polarimeters, refractometers, spectrometers, gas or smoke analysis apparatus): instruments and apparatus for measuring or checking viscosity, porosity, expansion, surface tension or the like; instruments and apparatus for measuring or checking quantities of heat, sound or light(including exposure meters); microtomes:
90.28	Gas, liquid or electricity supply or production meters, including calibrating meters therefor:
90.30	Oscilloscopes, spectrum analyzers and other instruments and apparatus for measuring or checking electrical quantities, excluding meters of heading No. 90.28; instruments and apparatus for measuring or detecting alpha, beta, gamma, X-ray, cosmic or other ionizing radiation:

90.31	Measuring of checking instruments, appliances and machines, not specified or included elsewhere in this Chapter; profile projectors:
90 33	
9033.00	Parts and accessories(not specified or included elsewhere in this Chapter) for machines, appliances, instruments or apparatus of Chapter 90. Also, the two types of high-performance bioreactors are available another tax promotion measures of as same condition as above mentioned measures.

6. Japanese Industrial Standards (JIS)

As for the Industrial Standards on the biotechnology, bioindustry related products and machinery and equipment in Japan, the government now preparing JIS.

Now, an applicable one in existing JIS for biotechnology is the JIS K-7001 for industrial amylase The following are now preparing or discussing establishment of JIS.

a. Items under discussion by the council for JIS establishment

(1) Measuring instruments or devices for grape sugar(Glucose sensors)

(2) Plastic sterilization petri dishes

(3) Industrial isomerized (Glucose isomerized)

(4) Measuring methods of activity ratio for the lipase

(5) Micropipets

(6) Standard solution of glucose

b. Currently compilation of tentative standards

(1) Biotechnology dictionary (words, technical terms, etc.)

(2)Analysis methods for metals in high purity water

(3)Measuring methods for the number of active bacteria in highly pure water

(4)Measuring methods for electric conductivity ratio in highly pure water

(5) Measuring methods of TOC in highly pure water

(6) Technical terms or words for membranes

(7) Testing methods for desalination performances of reverse osmosis membranes with magnesium sulfate

(8) Testing methods for removing performances of reverse osmosis membranes with isopropyl alcohol

(9) Standardization methods for separation performances of reverseosmosis membranes

(10) Dimensions and structures of high precision filters for ultra-pure water production

(11) Testing methods for diffusion flow rates of high precision membranes

(12) Testing methods for bubble points of high precision membranes

(13) Testing methods for the initial flow rates of high precision membranes

(14) Testing methods for eluted materials (heavy metals) of high precision membranes

(15) Testing methods for eluted materials (recovery characteristics of resistivity) of high precision membranes

(16) Testing methods for eluted materials (organic materials) of high precision membranes

(17) Testing methods for microbe complementation performance of high precision ,membranes

(18) Testing methods for end toxin removal performance of ultra-filtermembranes

(19) Testing methods for microbe complementation performance of ultra-filtermembranes

(20) Correction methods for liquid volume meters for chemical analysis

(21) Testing methods for bacterial removal performance of HEPA

(22) Testing methods for bubble point of ultra-filtermembranes for air filtration

Table 10. Future Standardized Biotechnology-related Items

Items for Future Standardization	Priority	Existing JIS for References
a. Chemicals/reagents		
Glucose isomerized	A	
Protease	A	
Repase	B	
Cellulase	B	
Urease	B	
Glucose oxidase	B	
Papain	B	
Rennet	C	JIS K-7001 for industrial isomerized
Beta-amilase	C	
Hesperidinase	A	
Buffer solution	A	
Culture medium	C	
Restricted enzyme	C	
End metastasis enzyme	C	
Reverse transcriptase enzyme	C	
Cell wall solution enzyme	B	
b. Bio-equipment, devices and analyzers		
Basic general provisions	A	J15 K-0117 for general provision (Infra-red analysis methods) and others
Basic general provision for equipment and devices	A	The Drugs, Cosmetics and Medical Instruments Act (Sterilization, gerum free operation) FDA, ISO 2037/2851
Bacteria removal filters	A	ASTM-F838-83, J IS Z-4812 on high performance air filters for radioactivity aerosol

Gas sterilizers	A	The Japanese Pharmecopoeia
Thermal sterilizers	A	
Violet-ray sterilizers	A	JIS Z-8811 on measuring methods of sterilizing violet rays
Radioactive sterilizers	B	
Germ free mechanical seals	A	JIS B-2405 (General provision of mechanical seals)
Safety cabinets	A	JIS B-9922 (Clean benches)
Filtering plugs for culture test tubes	A	
Air filtering plugs for culture devices	A	
Pipets	A	
Micropipets		
Centrifuges (including ultra-centrifuges)	A	JIS T-1701 (Centrifuges for medical treatment)
Electrophoresis equipment	A	
DNA synthesizing devices	B	
Cell storage devices	A	
Clean benches	A	JIS B-9922 (Clean benches)
Filling chemicals and columns for liquid	A	JIS K-0124 (General provision of high speed chromatography liquid chromatography)
Microfilter membranes	A	
Dialysis membranes	A	
Ultrafiltermembranes	A	
Ion-exchange membranes	B	
Reverse osmosis membranes	B	
Glucose sensors	A	
Uric acid sensors	B	
Urea sensors	B	
Actic acid sensors	B	
General provision of biosensors	B	
c. Others		
Dictionary (Technical terms, words)	A	JIS Z-8 122 (Technical terms, words for contamination controls)
Bio-experiments rooms	A	Japan Air Cleaning Association (Guideline of operation management for clean rooms)

Table 11. Biotechnology Equipment and Devices Standardization

Equipment and devices	Priority	Main standardization items
Basic general provisions on analysis equipment	1	Type, performance, construction, calibration, and maintenance of equipment
Basic general provisions on equipment and devices	1	Construction, dimensions, etc. of piping and other connected portions

Bacteria filter	1	Outside diameter, dimensions, rated current, catching efficiency, initial pressure loss, pressure deformation, air- tightness, bacterial filtration efficiency, and filter mesh
Gas sterilizer	1	Type, sterilization system, service temperature and humidity, concentration and pressure of chemicals, and type of pressure- resistant oven
Heat sterilizer	1	Type, sterilization system, service temperature and pressure, and high pressure protective device
Ultra-violet ray sterilizer	1	Type, dimensions, purpose of use, construction, illumination time and distanced, luminance of ultra-violet ray, and effect of bacterial sterilization
Radiation sterilizer	2	Type, dimensions, purpose of use, construction, safety, dosage, radiation time, and sterilizing effect
Germ-free type mechanical	1	Sealing system, amount of leak, follow-up to movement, construction, and seal dimensions
Safety cabinet	1	Air-tight construction, exhaust system, dimensions, cleanliness, and filter type
Culturing test tube filter	1	Dimensions, material, permeability, durability, temperature, service life, and cock cleanliness
Incubator	1	Same as above
Petri dish	1	Dimensions, material, durability, and temperature
Micro-bivetter	1	Type, construction, amount and precision of bunchuu, reproducibility, and indication
Centrifugal separator (super-centrifugal separator)	1	Construction, dimensions, performance, and indication
Electrophoresis device	1	Power supply section (output stability, explosion-proof construction accessible to low temperature room), electrophoresis tank/bath (size, thickness, material and preparation method of ready-made gel)
DNA synthesizer	2	Yield in each step, amount of reagent consumed, stability of reagent, and purity of synthesized DNA
Cell preserver	1	Culture media for freezing, material of container, construction and freezing method
Clean bench	1	Wall surface material, air filter, and configuration of exhaust system
Filler column for liquid chromatography	1	Type, purpose of use, grain size, grain size distribution, dimensions of column, dimensions and performance of column, mounting method, and screw dimensions

Microfilter membrane film	1	Material, shape, thickness, and performance of film/membrane
Ultra-filtermembrane/film	1	Material, shape, dimensions, and performance of film/membrane
Reverse osmosis membrane	2	Material, shape, dimensions, and performance of membrane
Glucose sensor	1	Response characteristics and time, selectivity, service life, and service conditions
Uric acid sensor	2	Same as above
Urea sensor	2	Same as above
Lactic acid sensor	2	Same as above
General provisions on biosensors	2	Method and factors of configuration

International In Bioindustry

1. Japanese Bioindustry Contributing to the World

Although the bioindustry of Japan has a poor record in basic research, it has accumulated the required technology from a long experience in the fermentation industry, and the commercialization of this knowledge is advancing in diverse industries.

Thus, the bioindustry in Japan is expected to contribute to the progress of the world' s economy through increased basic research, and increased utilization of the country's traditional biotechnology such as fermentation technology and this will further the buildup of application technologies. This will also take the form of technological cooperation with neighboring Asian countries where biomass resources are abundant.

a. Cooperation in Basic Research

Although Japan's bioindustry has a traditional background, such as with the fermentation industry, it is lagging behind the United States in the aspect of basic research as represented by the fact that the recombinant DNA technology, a key technology in the field, was first developed in the United States. However, by utilizing the results of basic research obtained in foreign countries and by applying the knowledge to commercial uses, Japan has become a forerunner in the international arena, along with the Unites States. In the future, Japan will be required to end its dependence on the results of basic research developed in other countries and opt to do as much basic research in biotechnology as possible for itself. This will allow Japan to present the rest the rest of the world with new scientific discoveries and technologies, and to lead progress in the global economy, operation making contributions to expanding the technological frontier of the world and making the results the property as shared by the people of the world.

To realize this goal, in addition to the beefing up of basic research in Japan, it will be necessary for Japan to promote basic research under the scheme of international cooperation such as through the promotion of an exchange of researchers and joint R&D projects with foreign countries.

In particular, the Human Frontier Science Program which Japan proposed at the summit meeting in Venice has the intention of promoting basic research, including the elucidation of in vivo priority functions through international collaboration. This thereby contributes to the science and technology frontier of mankind, and so it is desired to promote the program with the united effort of the world in promoting the program.

b. Cooperation among Bioindustry Support Industries

In Japan, the application of biotechnology is promoted in many industrial areas such as chemical, agriculture, forestry, fisheries, food, electrical/electronic, resource and energy, and pharmaceuticals. This generates diverse needs for equipment and reagents to promote the development of biotechnology. To respond to these diverse needs, the bioindustry support industries provide equipment and reagents related with the bioindustry, these items are forming a growing market in Japan, too.

In the meantime, in the West recently, there is a tendency in nearly all areas to utilize biotechnology. In view of this trend, it is expected that a variety of needs will be generated in the future regarding the bioindustry-related equipment and reagents So Japan is expected to answer the needs of the West by Using its growing support industries.

c. Cooperation through Technological Accumulation of the Fermentation Industry, etc.

The fermentation industry in Japan has a long tradition and its technological level is assessed very favorably when compared with the world standard. The industry has a technological development potential to overcome the problems that will be incurred as a-result of the process of commercialization in the bioindustry, and to mass-produce microorganisms and cells. Also, its bioreactor technology level is also high as is observed in its success in the bio-industrial production of amino acid through immobilized enzymes (leading the world in this area) and in the application of general-purpose industrial chemicals, and acrylamide (used against fungi). For this reason, Japan is expected to assist foreign countries in their R&D for application and production, by utilizing the technological accumulation of the fermentation industry, etc.

d. Technological Cooperation

Because of their tropical rain forest climate, Southeast Asian countries, which are geographically close to Japan, have an abundant resource of biomass. These countries desire to have biotechnology transferred smoothly from the developed countries because the technology will help them to achieve economic growth by the production of useful substances from the biomass resources abundantly available in their own countries and also because the technology will help them to address food problems resulting from the population explosion. For this reason, Japan is expected to actively carry out the transfer of technology in the field of biotechnology to these countries.

2. Bioindustry Contributing to the Revitalization of Local Economies

Biotechnology is characterized by a diversity in the use of various species of life forms, if I vivo constituents, and in the areas of their application.

So, it would not be an exaggeration to say that the progress of biotechnology is achieved through the utilization of variations in technologies as applied to varieties of biomass resources. A system of conducting diverse R&D efforts will be effective.

In the meantime, since in Japan traditional microorganism utilization industries exist throughout the country, the biotechnological potential is very likewise high throughout the country. Also, for concerns such as agricultural waste from agricultural areas and forest waste from forestry areas, there exist biomass resources peculiar to the individual districts.

When many businessmen, including those from small and middle-sized companies, promote the development of biotechnology in their respective arena, the result will be support for a variety of technologies. This will develop as the variety of biomass resources increase; this, in turn, can be explained by the industry's potential, due to causes both modern and rooted in the community. Also, when a variety of companies in the field come to grips with the development of biotechnology by using their own special art, it will greatly contribute to the revitalization of local economies.

In this sense, the bioindustry is expected to contribute to the formation of revitalized local economy, which will be one of the problems for Japan to overcome in the immediate future.

3. Promotion of International Cooperation and Exchange

The Japanese bioindustry must contribute to the world and to the promotion of international cooperation in order to reduce the risk involved in technological developments and raise the efficiency of R&D. For these purposes, the following measures will have to be taken.

a. Promotion of Personnel Exchange

> The exchange of personnel is the most fundamental and efficient means of international cooperation and interaction. The past cases of personnel exchange were mostly done by dispatch of Japanese delegations to other countries. But in the future, universities, public research institutes, and private companies alike should strive to accept talents from abroad.

b. Promotion of Information Exchange through International Biotechnology Symposia, etc.

> In the future, it is hoped that this will give the information exchange the necessary momentum by promoting the information exchange (at the governmental level) through utilization of multilateral negotiations. Such forums occur with summit meetings, the OECD, and bilateral negotiations for industrial cooperation; likewise, the possibility exists (at a private sector level) by holding international biotechnology fairs consisting of international biotechnology symposiums formed by the leading experts in and outside of Japan, and through international exhibitions by the bioindustry related companies.

c. Promotion of International Joint Projects

> In the Venice Summit of 1987, Japan proposed the Human Frontier Science Program. It was created with the objectives of laying clear the superior functions that a life form possesses, encouraging the development of new science and technology which are more friendly with nature and humans. The goal was to contribute to the solution of various problems facing mankind. It will be necessary to promote this kind of programs energetically in the future.

d. Promotion of Technological Cooperation

Recently, the newly industrialized countries and other developing countries alike, have begun to come to grips with biotechnology, and their expectations for Japanese assistance in this field is becoming higher. Biotechnology not only contributes to the solution of medicare, food, and other problems facing these nations, but also is a very suitable technology to utilize biomass which abundantly exist in these nations. Therefore, it is necessary to actively promote training for the technical skills that are needed in the developing countries, and to assist technological cooperation for technological transfer to these nations.

Related Organizations

1. Agencies

Basic Industries Bureau, MITI Biochemical-Industry Division	
3-1, Kasumigaseki l-chome, Chiyoda-ku, Tokyo l00	Phone: 03-591-8513
Agency of Industrial Science and Technology (AIST) Director for Development of Basic Technology for Future Industries	
3-1, Kasumigaseki l-chome, Chiyoda-ku, Tokyo I 00	Phone: 03-591-7869
National Chemical Laboratory for Industry, AIST,	
Higashi I -chome, Tsukuba City, Ibaraki Pref. 305	Phone: 0298-54-4457
Research Institute for Polymers and Textiles, AIST	
1-4, Higashi l-chome, Tsukub a City, Ibaraki Pref. 305	Phone: 0298-54-6216
Fermentation Research Institute, AIST	
1-3, Higashi l-chome, Tsukuba City, Ibuaki Pref. 305	Phone: 0298-54-6000
Ministry of Agriculture, Forestry and Fisheries	
2-1, Kasumigaskei l-chome, Chiyoda-ku, Tokyo	Phone: 03-502-8111
Science and Technology Agency	
2-2, Kasumigaseki 2-chome, Chiyoda-ku, Tokyo l00	Phone: 03-501-5271
Ministry of Health and Welfare	
2-2, Kasumigaseki l-chome, Chiyoda-ku, Tokyo I 00	Phone: 03-503-171 1
Ministry of Education	
2-2, Kasumigaseki 3-chome, Chiyoda-ku, Tokyo 100	Phone: 03-581-4211

2. Organizations

Research Association for Utilization of Light Oil	
Shiba YS Bldg., 16-9, Shiba 2-chome, Minato-ku, Tokyo 105	Phone: 03-455-6011
Research Association for Petroleum Alternatives Development (RAPID)	
4-2, Uchikanda l-chome, Chiyoda-ku, Tokyo 101	Phone: 03-233-353 1
Fuel Alcohol Research Association (FARA)	
Dowa Bldg., 10-5, Shinbashi 5-chome, Minato-ku, Tokyo 105	Phone: 03-459-6387
Research Association for Biotechnology	
Saruta Bldg., 4-10, Akasaka l-chome, Minato-ku, Tokyo 107	Phone: 03-583-8291

Bioindustry Development Center (BIDEC)	
Dowa Bldg., 10-5, Shinbashi 5-chome, Minato-ku, Tokyo 105	Phone: 03-433-3545
Research Association for Biotechnology of Agricultural Chemicals	
5-X, Nihonbashi-Muromatchi l-chome, Chuo-ku, Tokyo 103	Phone: 03-243-0677

Exhibition

1. Agritex (Lifescience Japan)

Organizer:	Nihon Kogyo Shinbun Ltd. Promotion Division 28-5, Kanda-Jimbocho l-chome, Chiyoda-ku Tokyo 101
Phone:	03-292-3561
Fax:	03-292-6137
Exhibits:	Seeding, seeding producing equipment and systems, plant (vegetable) factory models, water culture systems, environmental control equipment, sensors, etc.
Frequency:	Bi-annual (1991)
Site:	Tokyo International Fair Ground (Harumi)

2. Annual Meeting of Japan Pharmaceutical Association-Machinery Exhibition

Organizer:	Japan Pharmaceutical Equipment & Machinery Association Secretariat 12-15, Shibuya 2-chome, Shibuya-ku, Tokyo 150
Phone:	03-407-8831
Fax:	03-407-9557
Exhibits:	Pharmaceutical, biological and information service equipment.
Frequency:	Annual (July, 1990)
Site:	Nagoya Trade & Industry Center.

3. Bio-Industry Exhibition (High-Technology Tokyo)

Organizer:	Nikkan Kogyo Shinbun Ltd. Business Division 8-10, Kanda-kita l-chome, Chiyoda-ku, Tokyo 102
Phone:	03-222-7232
Fax:	03-221-7 137
Exhibits:	Information equipment and systems relating to technology of separating and refining products in large quantities, biotechnology, laboratory technology and production technology.
Frequency:	Annual (May, 1990)
Site:	Tokyo International Fair Ground (Harumi)

4. Biotex (Lifescience Japan)

Organizer:	Nihon Kogyo Shinbun Ltd. Promotion Division 2X-5, Kanda-Jimbocho l-chome, Chiyoda-ku Tokyo 10 1
Phone:	03-292-3561
Fax:	03-292-6137
Exhibits:	R&D equipment, systems and facilities relating to gene recombination, mass cultivation of bacteria(microorganisms), fusion of bacteria, bioreactors, biomass, etc.
Frequency:	Bi-annual (1991)
Site:	Tokyo International Fair Ground (Harumi)