THE PHARMACEUTICALS AND MEDICAL DEVICES AGENCY ANNUAL REPORT FY 2013 (April 2013 - March 2014)

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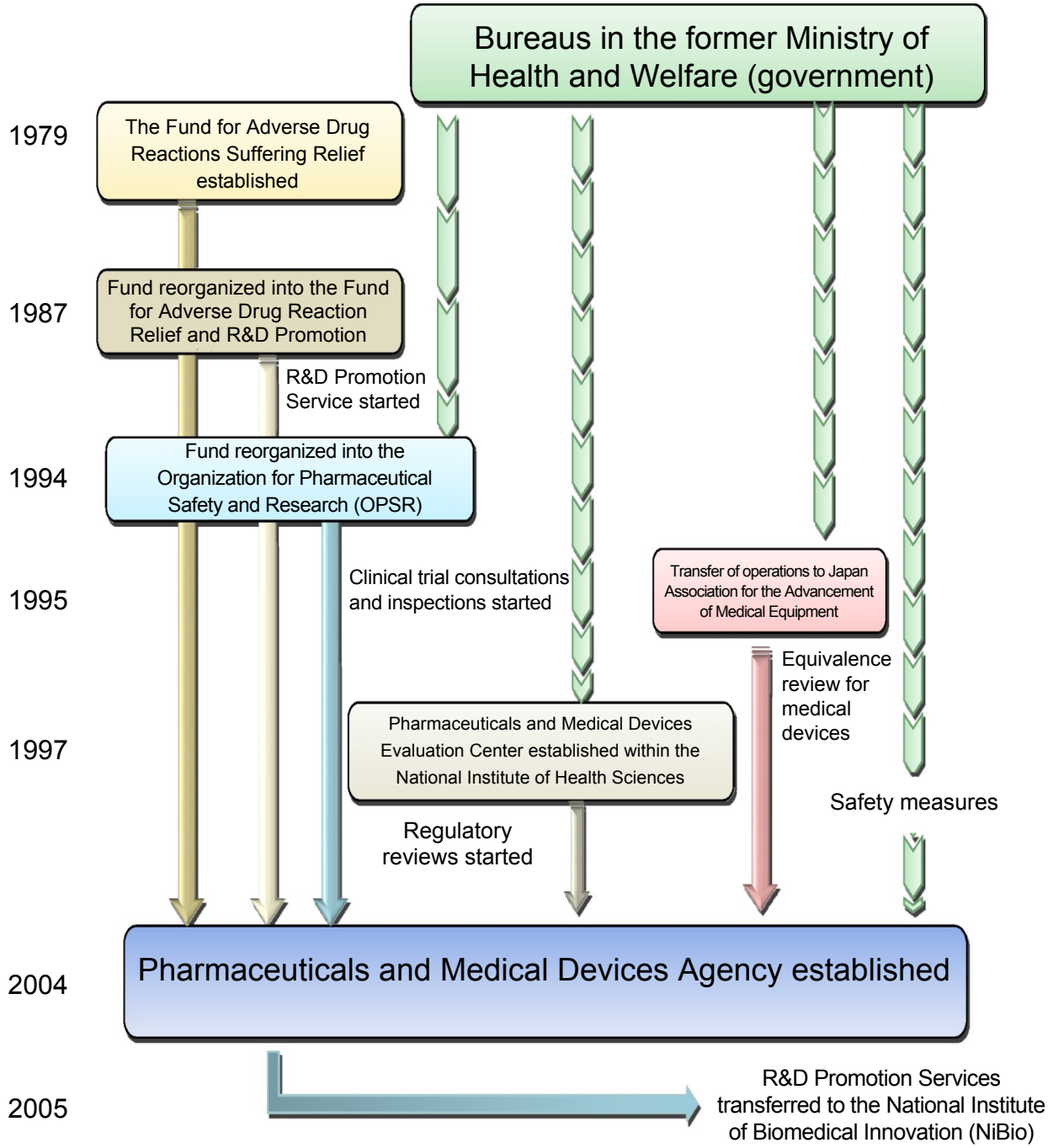
I. THE PHARMACEUTICALS AND MEDICAL DEVICES AGENCY

PART 1 History and Objective of PMDA

- As lessons learned from diseases caused by drugs such as thalidomide-induced fetal malformations and subacute myelo-optical neuropathy (SMON), the Fund for Adverse Drug Reactions Suffering Relief was established in October 1979 based on stipulations in the Adverse Drug Reaction Suffering Relief Fund Act (Act No. 55 of 1979), for the purpose of providing prompt relief to patients suffering from adverse drug reactions (ADRs). In 1987, the Fund started R&D-promoting operations under the name of the Fund for Adverse Drug Reaction Relief and R&D Promotion and was then reorganized into the Organization for Pharmaceutical Safety and Research (OPSR) in 1994 to play an additional role in equivalence reviews of generic drugs. Later, in 1997, the organization started to provide advice on clinical trials and conduct GCP/GLP inspections in relation to applications for approval of drugs.
- In 1997, the Pharmaceuticals and Medical Devices Evaluation Center (PMDEC) was established at the National Institute of Health Sciences (NIHS) in order to develop a full-scale regulatory review system and to make the contents of the review more advanced. It was decided that at the Center, reviews should be conducted by teams consisting of experts specializing in pharmaceutical science, medical science, biostatistics, etc. In addition, the Japan Association for the Advancement of Medical Equipment (JAAME) began operations in 1995 to conduct equivalence reviews of medical devices as a designated investigative body under the Pharmaceutical Affairs Act.
- From 1997 to 1999, there was a systematic and drastic increase in the number of the staff engaging in reviews and post-marketing safety measures at the former Ministry of Health and Welfare and the three organizations above (from 121 staff members in 1996 to 241 in 1999). However, there was a limit to further increasing the number of staff members and developing the structure as governmental organizations.

  In the midst of these situations, the Cabinet adopted the Special Service Agency Restructuring Plan in December 2001, in which it was decided that the OPSR should be dissolved and that the Pharmaceuticals and Medical Devices Agency (PMDA) should be newly founded by consolidating the operations allocated to PMDEC, OPSR, and JAAME in order to further enhance reviews and post-marketing safety measures. In 2002, a legislative bill for the Act on the Pharmaceuticals and Medical Devices Agency was discussed and passed at the 155th extraordinary session of the Diet, resulting in the establishment of PMDA on April 1, 2004 in accordance with the Act on the Pharmaceuticals and Medical Devices Agency (Act No.192 of 2002).
- PMDA's mission is to contribute to improvement in public health by providing prompt relief to people who have suffered health damage caused by adverse drug reactions or infections from biological products (Relief for Adverse Health Effects); providing guidance and reviews regarding the quality, efficacy, and safety of drugs and medical devices through a system that integrates the entire process from pre-clinical research to approval (Reviews); and collecting, analyzing, and providing on post-marketing safety information (Safety Measures).

  Previously, one of the objectives of PMDA was to promote basic research and development of drugs and medical devices that contribute to maintaining and improving the health of the nation (Promotion of R&D). However, the Regulatory Division and the Research Promotion Division were separated, and services for promotion of R&D were transferred to the National Institute of Biomedical Innovation (NiBio) in April 2005, in order to allow PMDA to focus specifically on reviews, safety measures, and relief services for adverse health effects.


Bureaus in the former Ministry of Health and Welfare (government)
1979
The Fund for Adverse Drug Reactions Suffering Relief established
1987
Fund reorganized into the Fund for Adverse Drug Reaction Relief and R&D Promotion
R&D Promotion Service started
1994
Fund reorganized into the Organization for Pharmaceutical Safety and Research (OPSR)
1995
Clinical trial consultations and inspections started
Transfer of operations to Japan Association for the Advancement of Medical Equipment
Equivalence review for medical devices
1997
Pharmaceuticals and Medical Devices Evaluation Center established within the National Institute of Health Sciences
Safety measures
Regulatory reviews started
2004
Pharmaceuticals and Medical Devices Agency established
2005
R&D Promotion Services transferred to the National Institute of Biomedical Innovation (NiBio)

PART 2 Outline of Operations

2.1. Relief Services for Adverse Health Effects

- As a service inherited from the OPSR, PMDA provides benefits for medical expenses, disability pensions, and bereaved family pensions to the sufferers of illnesses or disabilities caused by adverse drug reactions (Relief Service for Adverse Drug Reaction).
- Since April 2004, PMDA has provided benefits to sufferers of adverse health effects caused by infections from drugs and medical devices manufactured using ingredients and materials of biological origin (Relief Service for Infections Acquired through Biological Products).
- Since January 2008, PMDA has also provided benefits to patients with drug-induced hepatitis C, in accordance with the Act on Special Measures concerning the Payment of Benefits to Assist Individuals Affected by Hepatitis C through Specified Fibrinogen Products and Specified Blood Coagulation Factor IX Products Contaminated by Hepatitis C Virus (Act No. 2 of 2008) (Specified Relief Service).
- PMDA is also commissioned by the government and pharmaceutical companies to provide healthcare allowances and nursing care expenses to SMON patients (Service for Healthcare Allowances). In addition, PMDA works under the commission of the Yu-ai Welfare Foundation to make payments for healthcare expenses for HIV-positive and AIDS patients (Service for Healthcare Allowances).

2.2. Reviews

- In accordance with the Pharmaceutical Affairs Act, PMDA evaluates the efficacy, safety, and quality of drugs and medical devices for which applications have been submitted for regulatory approval, based on the current scientific and technological standards. In addition, PMDA conducts re-examinations/re-evaluations of drugs and medical devices, and reviews of applications for confirmation of clinical use of genetically modified biological entities pursuant to the Act on the Conservation and Sustainable Use of Biological Diversity through Regulations on the Use of Living Modified Organisms (Act No. 97 of 2003) (Reviews).
- In response to requests from clinical trial sponsors, PMDA provides guidance and advice through face-to-face consultations on clinical trials of new drugs and medical devices as well as on clinical trials for re-examinations/re-evaluations of approved products (Consultations).
- For products for which applications were made for reviews and re-examinations/re-evaluations, on-site and document-based inspections are conducted to determine whether documents attached to applications comply with Good Laboratory Practice (GLP), Good Clinical Practice (GCP), and the data integrity standards for product applications (GLP/GCP/GPSP Inspections).
- On-site and document-based inspections are conducted to determine whether manufacturing facilities and manufacturing control methods for new drugs and medical devices, etc., comply with the requirements of the Ministerial Ordinance on Good Manufacturing Practices/Quality Management System (GMP/QMS), whereby products of appropriate quality can be manufactured (GMP/QMS Inspections).
- PMDA conducts research for developing various standards, such as the Japanese Pharmacopoeia (JP), which is set forth in the Pharmaceutical Affairs Act (Research for Standards Development).

2.3. Safety Measures

- PMDA cooperates with the Ministry of Health, Labour and Welfare (MHLW) on the following services to improve the safety of marketed drugs and medical devices as well as to enable patients and healthcare professionals to use drugs and medical devices appropriately and with peace of mind.

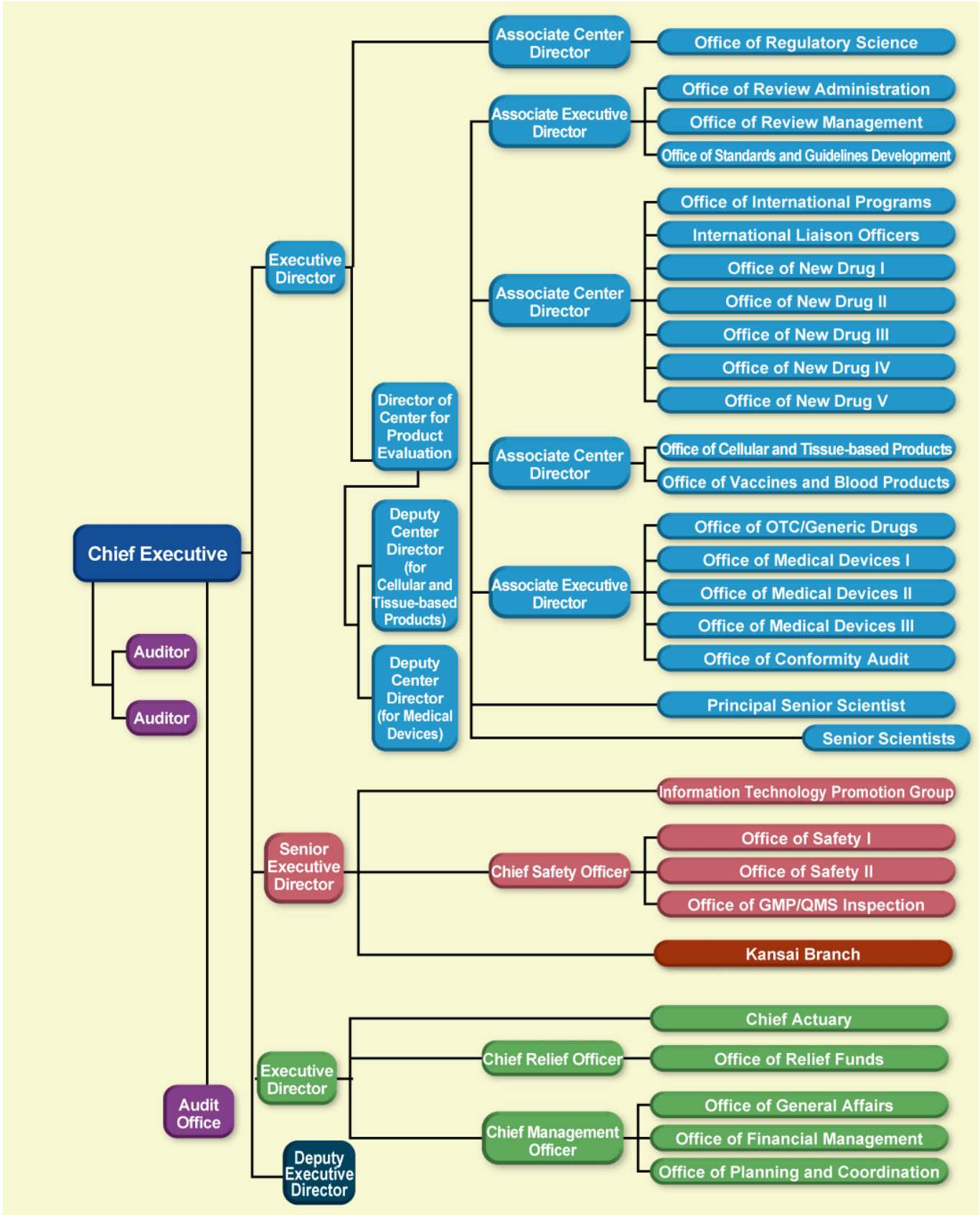
(i) Centrally collecting and organizing information on the post-marketing safety of drugs and medical devices from a broad range of sources, such as reports from companies, information from medical institutions, information from foreign regulatory agencies, and reports presented at academic conferences, relating to adverse drug reactions, device malfunctions, and infections (Collection and Organization of Information).

(ii) Conducting research and reviews relating to safety measures based on the information collected in (i) above (Research and Reviews).

(iii) Giving guidance and advice to marketing authorization holders (MAHs) as well as providing consultations to consumers upon request (Consultations).

(iv) Providing safety information on drugs and medical devices widely to healthcare professionals, patients, companies, etc., in a timely manner (Information Provision).

Structure of PMDA (as of March 31, 2014)



II. OPERATING PERFORMANCE FOR FY 2013

PART 1 Development of Fiscal Year 2013 Plan

1.1. Development and Implementation of Fiscal Year 2013 Plan

- PMDA is required to develop the Mid-term Plan in accordance with the Mid-term Targets designated by the Minister of Health, Labour and Welfare, and to obtain the Minister's approval for the plan (effective period of the Second Mid-term Targets: April 2009 to March 2014). In order to achieve the Mid-term Plan, PMDA is required to develop a plan on its management of operations for each fiscal year (fiscal year plan), submit these plans to the Minister, and announce these plans to the public.
- Also for FY 2013, the fiscal year plan was developed at the end of FY 2012 based on the Second Mid-term Targets and Mid-term Plan, the results of the evaluation on operating performance for FY 2012 provided by the Evaluation Committee for Incorporated Administrative Agencies of the Ministry of Health, Labour and Welfare (MHLW), and the opinions by the Commission on Policy Evaluation and Evaluation of Incorporated Administrative Agencies of the Ministry of Internal Affairs and Communications (MIC). The plan was submitted to the Minister of Health, Labour and Welfare and operations were performed in line with the plan.

1.2. Results of the Evaluation on Operating Performance for FY 2012

- It is stipulated that each ministry in charge of incorporated administrative agencies should establish an "Evaluation Committee for Incorporated Administrative Agencies" to conduct administrative processing relating to the agencies under its control. (Article 12 of the Act on General Rules for Incorporated Administrative Agencies [Act No. 103 of 1999])
- On August 13, 2013, PMDA received the "Results of the Evaluation on Operating Performance for FY 2012" from the Evaluation Committee for Incorporated Administrative Agencies of MHLW, which is responsible for evaluating the Agency's performance. The evaluation results showed that PMDA received "S" ratings for two evaluation items, "cost control efforts" and "expeditious operation and improvement of the system (drugs)," and "A" ratings for all other items.

  Note: S: Significantly exceeding the level prescribed in the Mid-term Plan
  A: Exceeding the level prescribed in the Mid-term Plan
  B: Somewhat exceeding the level prescribed in the Mid-term Plan
  C: Slightly below the level prescribed in the Mid-term Plan
  D: Below the level prescribed in the Mid-term Plan, therefore requiring drastic improvements
- PMDA posted the "Results of the Evaluation on Operating Performance for FY 2012" on its website, and reported it at its Advisory Council Meeting held on October 31, 2013.

Results of the Evaluation on Operating Performance of PMDA Provided by the Evaluation Committee for Incorporated Administrative Agencies of MHLW

Classification in the mid-term and fiscal year plan		Evaluation items		Results of evaluation	
				FY 2011 Performance	FY 2012 Performance
Part 1	Improvement in overall operations and quality in services of PMDA e.g., services to the public				
	(1) Efficient and flexible operations	1	Operation through target management and top management	A	A
		2	Ensuring of transparency by establishing deliberative bodies	A	A
	(2) Cost control by increased efficiency of operations	3	Cost control efforts	S	S
		4	Collection and management of contributions	A	A
	(3) Improvement of services to the public	5	Strengthening of the consultation system and disclosure of the work of the Agency	A	A
Part 2	Improvement in operations of each department and quality of other services e.g., services to the public				
1	Adverse health effect relief services				
	(1) Expansion and review of dissemination of information regarding the Relief System	6	Provision of information on the System and strengthening of the consultation system	A	A
	(2) Proactive public relations activity toward familiarity with the Relief System				
	(3) Securing of efficient management of the consultation office				
	(4) Promotion of improved efficiency of operations using databases	7	Expeditious processing of applications and improvement of the system	A	A
	(5) Promotion of expeditious processing of relief applications				
	(6) Promotion of collaboration with the review/safety offices	8	Conduct of cross-functional collaboration and health and welfare services	A	A
	(7) Appropriate conduct and expansion of health and welfare services				
	(8) Appropriate conduct of relief services for SMON patients and patients infected with HIV through blood preparations	9	Conduct of relief services for SMON patients and patients infected with HIV through blood preparations	A	A
	(9) Appropriate conduct of payment services for individuals affected by hepatitis C through specified fibrinogen products and specified blood coagulation factor IX products contaminated by hepatitis C				
2	Reviews and related services/post-marketing safety measures				
	(1) Faster access to the latest drugs and medical devices	10	Expeditious operation and improvement of the system (drugs)	S	S
		11	Expeditious operation and improvement of the system (medical devices)	A	A
		12	Expeditious operation and improvement of the system (inspections)	A	A
	(2) Improvement in reliability of reviews and related services/post-marketing safety measures	13	Improvement in reliability of review and related services/post-marketing safety measures	A	A
	(3) Reinforcement of post-marketing safety measures	14	Reinforcement of collecting, and systematization of organizing, assessing and analyzing information on adverse drug reactions/malfunctions	A	A
		15	Provision of safety information to companies/healthcare professionals and follow-up	A	A
		16	Provision of safety information to patients and consumers	A	A
Part 3	Budget, income and expenditure plan, and financial plan	17	Budget, income and expenditure plan, and financial plan	A	A
Part 4	Limit of short-term borrowing				
Part 5	Plan for transferring or mortgaging important asset if applicable				
Part 6	Use of surplus funds				
Part 7	Other operational matters specified by a ministerial ordinance of the competent ministry				
	(1) Personnel matters	18	Personnel matters and establishment of security	A	A
	(2) Ensuring security				

Evaluation scale on performance of Incorporated Administrative Agency of MHLW				
	S	Significantly exceeding the level prescribed in the Mid-term Plan	0	2
	A	Exceeding the level prescribed in the Mid-term Plan	18	16
	B	Somewhat exceeding the level prescribed in the Mid-term Plan	0	0
	C	Slightly below the level prescribed in the Mid-term Plan	0	0
	D	Below the level prescribed in the Mid-term Plan, therefore requiring drastic improvements	0	0

- The results of the evaluation conducted by the Evaluation Committee for Incorporated Administrative Agencies of MHLW were reviewed by the Commission on Policy Evaluation and Evaluation of Incorporated Administrative Agencies of MIC. The Commission submitted its conclusions as of December 16, 2013, with no particular findings on the evaluation results for PMDA.

1.3. Results of Tentative Evaluation on Operating Performance for Effective Period of Mid-term Targets

- On August 28, 2013, PMDA received the "Results of the Tentative Evaluation on Operating Performance for Effective Period of Mid-term Targets" from the Evaluation Committee for Incorporated Administrative Agencies of MHLW. The evaluation results were determined by averaging evaluation results for the past 4 years from FY 2009 to FY 2012, and the rating for “cost control efforts” was ”S” and the ratings for all other items were ”A” among 18 evaluation items.

  Note: S: Significantly exceeding the level prescribed in the Mid-term Plan
  A: Exceeding the level prescribed in the Mid-term Plan
  B: Somewhat exceeding the level prescribed in the Mid-term Plan
  C: Slightly below the level prescribed in the Mid-term Plan
  D: Below the level prescribed in the Mid-term Plan, therefore requiring drastic improvements

- PMDA posted the "Results of the Tentative Evaluation on Operating Performance for Effective Period of Mid-term Targets" on its website, and reported it at its Advisory Council Meeting held on October 31, 2013.

Results of PMDA's Tentative Evaluation on Operating Performance for Effective Period of Mid-term Targets

Classification in the mid-term and fiscal year plan		Evaluation items		Results of evaluation: Tentative Evaluation
Part 1	Improvement in overall operations and quality in services of PMDA e.g., services to the public			
	(1) Efficient and flexible operations	1	Operation through target management and top management	A
		2	Ensuring of transparency by establishing deliberative bodies	A
	(2) Cost control by increased efficiency of operations	3	Cost control efforts	S
		4	Collection and management of contributions	A
	(3) Improvement of services to the public	5	Strengthening of the consultation system and disclosure of the work of the Agency	A
Part 2	Improvement in operations of each department and quality of other services e.g., services to the public			
1	Adverse health effect relief services			
	(1) Expansion and review of dissemination of information regarding the Relief System	6	Provision of information on the System and strengthening of the consultation system	A
	(2) Proactive public relations activity toward familiarity with the Relief System			
	(3) Securing of efficient management of the consultation office			
	(4) Promotion of improved efficiency of operations using databases	7	Expeditious processing of applications and improvement of the system	A
	(5) Promotion of expeditious processing of relief applications			
	(6) Promotion of collaboration with the review/safety offices	8	Conduct of cross-functional collaboration and health and welfare services	A
	(7) Appropriate conduct and expansion of health and welfare services			
	(8) Appropriate conduct of relief services for SMON patients and patients infected with HIV through blood preparations	9	Conduct of relief services for SMON patients and patients infected with HIV through blood preparations	A
	(9) Appropriate conduct of payment services for individuals affected by hepatitis C through specified fibrinogen products and specified blood coagulation factor IX products contaminated by hepatitis C			
2	Reviews and related services/post-marketing safety measures			
	(1) Faster access to the latest drugs and medical devices	10	Expeditious operation and improvement of the system (drugs)	S
		11	Expeditious operation and improvement of the system (medical devices)	A
		12	Expeditious operation and improvement of the system (inspections)	A
	(2) Improvement in reliability of reviews and related services/post-marketing safety measures	13	Improvement in reliability of review and related services/post-marketing safety measures	A
	(3) Reinforcement of post-marketing safety measures	14	Reinforcement of collecting, and systematization of organizing, assessing and analyzing information on adverse drug reactions/malfunctions	A
		15	Provision of safety information to companies/healthcare professionals and follow-up	A
		16	Provision of safety information to patients and consumers	A
Part 3	Budget, income and expenditure plan, and financial plan	17	Budget, income and expenditure plan, and financial plan	A
Part 4	Limit of short-term borrowing			
Part 5	Plan for transferring or mortgaging important asset if applicable			
Part 6	Use of surplus funds			
Part 7	Other operational matters specified by a ministerial ordinance of the competent ministry			
	(1) Personnel matters	18	Personnel matters and establishment of security	A
	(2) Ensuring security			

Evaluation scale on performance of Incorporated Administrative Agency of MHLW			
	S	Significantly exceeding the level prescribed in the Mid-term Plan	1
	A	Exceeding the level prescribed in the Mid-term Plan	17
	B	Somewhat exceeding the level prescribed in the Mid-term Plan	0
	C	Slightly below the level prescribed in the Mid-term Plan	0
	D	Below the level prescribed in the Mid-term Plan, therefore requiring drastic improvements	0

1-4. Trends in Review of System/Organization of Incorporated Administrative Agencies

- Under the "Basic Policy for Reform etc. of Incorporated Administrative Agencies (adopted by the Cabinet on December 24, 2013)," it was decided that the government would make efforts as a whole so that this reform as the culmination of past efforts can be realized by promptly taking measures necessary for the reform, fully exerting the policy-implementing function of corporate bodies under the new system/organization, and ensuring that employees of each corporate body perform their duties with pride and contribute to the growth of the economy or the improvement of people's living as much as possible.

  * Basic Policy for Reform etc. of Incorporated Administrative Agencies (adopted by the Cabinet on December 24, 2013) [excerpt]

- Measures to be taken for each corporate body etc.

  [Pharmaceuticals and Medical Devices Agency (PMDA)]

  ○ It is a mid-term target management-type corporate body.(Note)

  ○ Based on the Japan Revitalization Strategy, PMDA should aim at prompt realization of “zero” review lag for pharmaceuticals and medical devices, and should strive to strengthen the structure of this corporate body with the use of its own financial resources from the viewpoint of acceleration and quality improvement of its reviews.

  ○ In this regard, PMDA intends to consider the possibility of introducing a fixed-term employment contract and an annual salary system considered so that expert human resources can be secured.

  (Note) A corporate body that conducts clerical and business operations while demonstrating great independence/autonomy by mid-term target management, with the objective of improving the quality of its operations such as services intended for the public.

PART 2 Improvement in Overall Management of Operations and Service Quality of PMDA

2.1. Efficient and Flexible Management of Operations

2.1.(1) Operation through target management

- In managing operations, PMDA clarifies the objectives and responsibilities of operations for each department, and strives to identify and resolve problems through managing its operational progress on a daily basis.
- In conjunction with the development of PMDA's annual plan for FY 2013, each office and division formulated their operating plans for segregation of duties. PMDA has operated through management of the targets set in the operating plans.

2.1.(2) Reinforcement of operational management system and top-down management

- PMDA intends to reinforce its function of strategy planning for overall operations, as well as a system for managing operations such as for risk management or check functions, and also plans to build an organizational system in which management decisions by the Chief Executive are promptly reflected in operations.
- To this end, as with the previous year, PMDA has been establishing opportunities for the Chief Executive to directly comprehend the operational progress and provide necessary instructions, and has also been reinforcing internal communication and coordination on its overall operations.

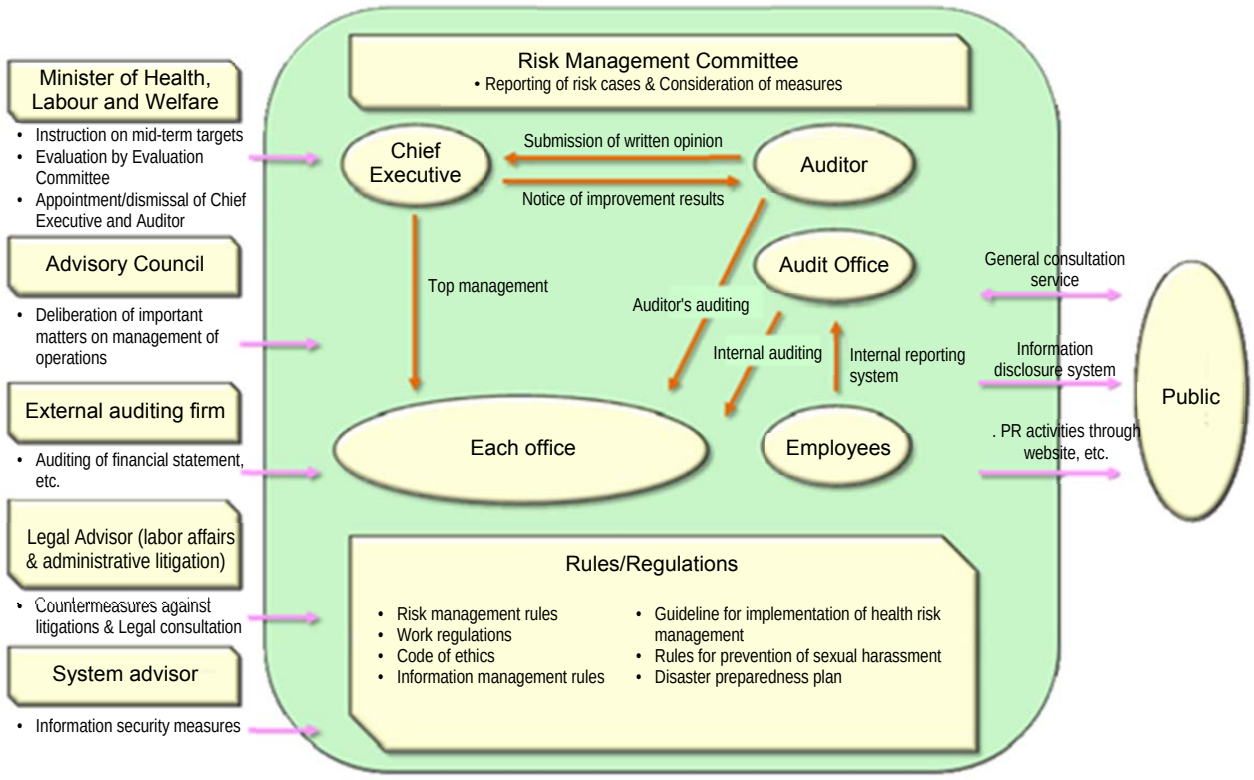
  Specifically, PMDA has regularly (once a week in principle) held "Board of Directors meetings," attended by the Chief Executive, executives and office directors. In addition, to reinforce communication and coordination with the Pharmaceutical and Food Safety Bureau (PFSB), MHLW, liaison meetings were held between the Chief Executive and the Head of the PFSB for discussion of the latest issues and topics.
- Meetings of the “Headquarters of Information Systems Management (headed by the Chief Executive)” established to further strengthen the structure of PMDA's information system management were held. At the meetings, the problems related to the completion of support for Windows XP etc., in the information infrastructure to comprehensively promote informatization were dealt with, and also several meetings of its sub-committee, “Committee on Investment in Information Systems” were held to assess the necessity, cost-effectiveness, technical difficulty, etc., of new development and upgrading of operation system from a comprehensive viewpoint, and then well-planned and efficient investment items were selected (Three meetings were held in FY 2013).
- In order to regularly understand the financial conditions to maintain sound financial performance and adequate operations, the "Financial Management Committee" headed by the Chief Executive has been holding meetings (12 meetings in FY 2013), during which reports were made on the monthly filing status and monthly cash flow analysis regarding review-related user fees by division, and the declared amount of contributions.
- In March 2014, a "Meeting to Hear from Employees" was held, and policies to deal with opinions, requests, etc., from employees were examined.
- Meetings of the health committee were held every month to deliberate measures etc., for maintaining and promoting the health of employees.

- PMDA convened opinion exchange sessions on new drugs twice (August and December 2013) and opinion exchange sessions on drug safety twice (August and December 2013) with the pharmaceutical industry.

  Also, regarding medical devices and *in vitro* diagnostics, PMDA helped the MHLW to hold regular opinion exchange forum on regulatory affairs for medical devices (July 2013) and to manage and hold the Action Program Review Committee's meetings (July and December 2013).

- The "Risk Management Committee" meetings were held once a month to allow the directors to discuss PMDA's risks. PMDA has continued its efforts to familiarize the executives and employees with risk management in accordance with the risk management manual.
- The Audit Office, which directly reports to the Chief Executive, has continued to conduct internal auditing and management of internal reporting systems.
- In order to respond to disaster risks resulting from fires and earthquakes, PMDA duly informed all executives and employees of the disaster preparedness plan.
- “Guidelines for return to work etc., for employees on administrative leave or leave of absence because of illness or injury” were formulated so that employees who recuperate for an extended period of time due to mental health problems etc., can smoothly return to work.

Risk Management System at PMDA



★ Risks PMDA may face:

A. Risks to the organization
   - Possibility of an event that damages or may damage the reputation of PMDA in society
   - Possibility of an event that significantly hinders or may hinder the execution of PMDA's operations
   - Possibility of an event that financially damages or may damage PMDA

B. Risks that PMDA should address as part of its tasks
   - Risks relating to PMDA's operations which might cause or expand serious adverse health effects due to drugs, medical devices, etc. (including drugs, medical devices, quasi-drugs, and cosmetics, as well as agents and equipment/devices, etc., subject to clinical trials)

- In order to systematically promote PR activities as a whole in consideration of the public needs and international perspectives, PMDA developed the "PMDA Public Relations Strategic Plan" (July 11, 2008) as a basic policy for its overall PR activities. The Agency is striving to proactively provide information in line with the strategic plan.
- Based on the "PMDA International Vision" developed in 2011, a vision which makes clear what PMDA aims for in its overall international activities, PMDA formulated its roadmap and is conducting proactive international activities such as reinforcing collaboration with Western and Asian countries, participating in and contributing to international regulatory harmonization, and providing information to foreign countries. In addition, the International Strategy Meeting established in the preceding year, in which board members are core members, was met six times in FY 2013. In the meeting, members discussed strategies toward the establishment of the PMDA's position in the international society by making reports and exchanging opinions on matters such as the progress status of the Road map for the PMDA International Vision and policies to deal with main international conferences. The contents were made widely known at the international liaison conference (held 11 times in FY 2013) intended for persons in charge in each division/department of their thorough dissemination.
- It is necessary to consider strengthening of the structure and improving the quality of operations toward the development of the Third Mid-term Plan (FY 2014 to FY 2018) and to promote the development work while comprehensively coordinating cross-sectional cooperation, and as such, the Deputy Executive Director was newly placed as the person who controls and coordinates PMDA’s operations as a whole.
- To respond to a request for promotion of the “Kansai Innovation Comprehensive Global Strategic Special Zone,” PMDA set up the Kansai Branch of Pharmaceuticals and Medical Devices Agency in Osaka City in October 2013 to conduct Pharmaceutical Affairs Consultation on R&D Strategy, and also GMP on-site inspections etc., from April 2014. Both operations are intended to target mainly users in the Kansai area. Aiming for the "enhancement of the PMDA function in the western Japan (Kansai region)," the request was submitted to the national government by the local governments of Kyoto Prefecture, Osaka Prefecture, Hyogo Prefecture, Kyoto City, Osaka City, and Kobe City.

2.1.(3) Advisory Council meetings

- In order to create opportunities for opinion exchange between knowledgeable persons of diverse fields, PMDA holds meetings of the "Advisory Council" (chaired by Atsushi Ichikawa, Dean of School of Pharmacy and Pharmaceutical Sciences, Mukogawa Women's University), which are open to the public. The Council consists of academic experts, healthcare professionals, and representatives from relevant industries, consumers, and the people who have suffered from adverse health effects caused by drugs, etc. By seeking opinions on operations and the

management system, the Council serves to secure fairness and transparency of PMDA's operations, in addition to contributing to streamlining the efficiency of its operations. Under the "Advisory Council," the "Committee on Relief Services" (chaired by Hideaki Mizoguchi, Professor Emeritus, Tokyo Women's Medical University) and the "Committee on Review and Safety Operations" (chaired by Atsushi Ichikawa, Dean of School of Pharmacy and Pharmaceutical Sciences, Mukogawa Women's University) were also formed to discuss specialized operational issues. The dates of the meetings and specific agenda for FY 2013 were as follows.

[Advisory Council] (FY 2013)

Agenda for the 1st Meeting (June 17, 2013)

(1) Annual Report FY 2012
(2) Financial Report FY 2012
(3) Recent main situations
(4) Next mid-term plan (opinion exchange)
(5) Employment status of personnel from the private sector
(6) Cash contributions etc., received by external experts commissioned for Expert Discussions etc.

Agenda for the 2nd Meeting (October 31, 2013)

(1) Results of the evaluation of operating performance for FY 2012 and results of tentative evaluation on operating performance for the effective period of mid-term targets (Evaluation Committee for Incorporated Administrative Agencies of MHLW)
(2) Situations of recent main efforts
(3) Issues to be discussed toward the Third Mid-term Plan
(4) Employment status of personnel from the private sector
(5) Cash contributions etc., received by external experts commissioned for Expert Discussions etc.
(6) Others

Agenda for the 3rd Meeting (February 4, 2014)

(1) Third Mid-term Plan (draft)
(2) Rate of contributions for infection relief fund (draft)
(3) Employment status of personnel from the private sector
(4) Cash contributions etc., received by external experts commissioned for Expert Discussions etc.
(5) Others

Agenda for the 4th Meeting (March 14, 2014)

(1) Third Mid-term Plan
(2) FY 2014 plan (draft)
(3) Budget for FY 2014 (draft)
(4) Extension of interim measures for restrictions on employment of personnel from the private sector
(5) Situations of recent main efforts
(6) Status of PMDA’s responses to opinions etc., given by members at the Advisory Council meetings for the past one year
(7) Employment status of personnel from the private sector

(8) Cash contributions etc., received by external experts commissioned for Expert Discussions etc.
(9) Others

[Committee on Relief Services] (FY 2013)

Agenda for the 1st Meeting (June 10, 2013)

(1) Annual Report FY 2012
(2) FY 2013 plan
(3) Results of an awareness survey on the Relief System for Sufferers from Adverse Drug Reactions
(4) Others

Agenda for the 2nd Meeting (December 11, 2013)

(1) Results of the evaluation of operating performance for FY 2012 and results of tentative evaluation on operating performance for the effective period of mid-term targets (Evaluation Committee for Incorporated Administrative Agencies of MHLW)
(2) Situations of recent main efforts and issues to be discussed toward the Third Mid-term Plan
(3) Rate of contributions for infection relief fund for FY 2014 and later
(4) Others

[Committee on Review and Safety Operations] (FY 2013)

Agenda for the 1st Meeting (June 14, 2013)

(1) Annual Report FY 2012
(2) FY 2013 plan
(3) Recent main situations
(4) Employment status of personnel from the private sector
(5) Cash contributions etc., received by external experts commissioned for Expert Discussions etc.
(6) Others

Agenda for the 2nd Meeting (December 26, 2013)

(1) Results of the evaluation of operating performance for FY 2012 and results of tentative evaluation on operating performance for the effective period of the Mid-term Targets (Evaluation Committee for Incorporated Administrative Agencies of MHLW)
(2) Operating performance by the end of October 2013 and issues to be addressed hereafter
(3) Issues to be discussed toward the Third Mid-term Plan
(4) Employment status of personnel from the private sector
(5) Cash contributions etc., received by external experts commissioned for Expert Discussions etc.

- The above meetings were open to the public, and the minutes from and materials for the meetings of the Advisory Council and its sub-committees were publicly released on the PMDA website.

http://www.pmda.go.jp/guide/hyogikaikankei.html

2.1.(4) Holding of Science Board meetings

- The Science Board was established in May 2012 as an external body to deliberate scientific aspects of drugs and medical devices reviews to ensure more appropriate responses to the

products using advanced science and technologies as well as to advance regulatory science, and reinforce collaborations and communications with academia and medical professionals in line with the future promotion of health care innovation. Members are external experts in areas including medicine, dentistry, pharmacy and engineering, and the board consisted of the Science Board (parent committee) and its subcommittees, the Pharmaceuticals Subcommittee, Medical Devices Subcommittee, Bio-products Subcommittee, and Cellular and Tissue-based Products Subcommittee in the first term (by March 2014). Materials relating to individual products may be used for discussion, and therefore meetings are closed to the public. The number of meetings and members in FY 2013 (as of March 31, 2014) were as follows:

1) The Science Board (parent committee), consisting of 16 members, had three meetings.
2) The Pharmaceuticals Subcommittee, consisting of 12 members, had six meetings (jointly with the Bio-products Subcommittee).
3) The Medical Devices Subcommittee, consisting of 17 members, had three meetings.
4) The Bio-products Subcommittee, consisting of 11 members, had six meetings (jointly with the Pharmaceuticals Subcommittee).
5) The Cellular and Tissue-based Products Subcommittee, consisting of 14 members, had five meetings.

- The minutes from and materials for the Science Board meetings were publicly released on the PMDA website.
  http://www.pmda.go.jp/guide/kagakuiinkaikankei.html

2.1.(5) Approaches for an efficient operation management system

- PMDA aims to establish an efficient operation system through flexible personnel allocation tailored to situations, as well as through effective use of external experts.
- In review divisions that particularly require flexible approaches, PMDA continued the group system where review teams are led by Review Directors who report to the Office Director.

  PMDA has continuously invited commissioned external experts to seek their professional opinions relating to scientifically significant matters at Expert Discussions on reviews and safety measures. (1,159 external experts are commissioned as of March 31, 2014.)
- PMDA also has commissioned external experts to seek their opinions on the relief service for health damage caused by adverse drug reactions and infections acquired through biological products. (124 external experts are commissioned as of March 31, 2014.)
- The list of the commissioned external experts is available on the PMDA website.
- Based on the need to secure impartiality and transparency of judgment given by external experts, PMDA developed the "Rules for Convening Expert Discussions etc., by the Pharmaceuticals and Medical Devices Agency" (December 25, 2008) as rules for conflict of interest. The establishment of these rules enables PMDA to ensure the transparency by releasing review reports and information on conflict of interest of commissioned external experts, and also allows outside parties to check the decision making process. Cash contributions and contract money received by external experts are reported to the Advisory Council and the Committee on Review and Safety Operations.
- In carrying out operations, PMDA has also commissioned lawyers and accountants as advisors to handle operations that require legal and tax expertise. In addition, the Agency has made use of

private companies for operational management of information systems and minimized the increase in the number of its regular staff.

- PMDA has continued to appoint a specialist who has advanced expertise regarding information systems and knowledge of pharmaceutical affairs as an information system advisor, to ensure consistency and coordination of operations relating to the Agency's information systems.

2.1.(6) Standardization of operating procedures

- In order to effectively utilize non-regular staff and limit the number of regular staff, PMDA has developed standard operating procedures (SOPs) for its major tasks. The contents of these SOPs have been examined and inspected, and revisions have been made as necessary. PMDA also used non-regular staff for routine operations.

2.1.(7) Development of databases

- In FY 2013, meetings of the Committee on Investment in Information Systems etc., were held to discuss the status of each information system, upgrading of the shared LAN system that serves as the common infrastructure system, and improvements in the security of the e-mail system, thereby taking effective measures.

  PMDA promoted the development of databases, including that of past final decision documents etc., for product approval by providing tags to the data, in order to systematically organize and store documents as well as to make it easy to collect and analyze information. PMDA also upgraded such databases to widely utilize such information to its operations of reviews etc.

- Among the notifications etc., issued by the MHLW and PMDA, those that are relevant to the Agency's operations or those that should be broadly disseminated to the public are posted on the following website:
  http://www.pmda.go.jp/operations/notice.html

2.1.(8) Promotion of the optimization of operations and systems

- Based on the "Plan for the Development of e-Government" (decided at the Liaison Meeting of the Chief Information Officers [CIO] of the Ministries and Agencies held on July 17, 2003) and the "Measures for the Realization of Optimal Operations/Systems at Incorporated Administrative Agencies" (decided at the Liaison Meeting of the CIOs of the Ministries and Agencies held on June 29, 2005), PMDA developed and publicized the Optimization Plan for Operations and Systems on March 28, 2008, and implemented works toward the creation of an optimum system for PMDA's operations in line with the revised version in June 2012 (A period from FY 2008 to FY 2014 is regarded as the implementation period).

  In FY 2013, PMDA promoted the design and development of an integrated review system, building of information systems and upgrading of existing systems for safety measure operations and the relief services, and in addition, proceeded with the design and development of the accounting system and personnel/salary system as systems for management division's operations. The Agency conducted research and reviews to reinforce the information management and IT control of PMDA as a whole. PMDA plans to implement system upgrading etc., to deal with the revised Pharmaceutical Affairs Act hereafter.

2.2. Cost Control through Increased Efficiency of Operations

2.2.(1) Retrenchment of general and administrative expense

- By making continuous efforts to improve operations and increase management efficiency, PMDA balanced the FY 2013 budget for general and administrative expenses (excluding expenses for office relocation and retirement allowance), in line with the cost-reduction measures specified in the Mid-term Plan. Basically, the FY 2013 budget reflected about a 15% reduction from the FY 2008 budget, and was added together with the expenses as listed below. However, the budget allocations for the listed expenses incurred starting in FY 2009, FY 2010, FY 2011, and FY 2012 were reduced by about 12%, 9%, 6%, and 3%, respectively, compared to those for the first year of each project.

  1) General and administrative expenses incurred starting in FY 2009 with efforts to speed up drug application reviews in accordance with the recommendations of the Council for Science and Technology Policy entitled "Revision of Structures Aimed at the Promotion of Science and Technology and the Return of Achievements to Society" (dated December 25, 2006)

  2) General and administrative expenses incurred starting in FY 2009, FY 2010, FY 2011, FY 2012, FY 2013 with efforts to speed up medical device application reviews based on the "Action Program to Accelerate Reviews of Medical Devices" (dated December 11, 2008)

  3) General and administrative expenses incurred starting in FY 2009 with efforts to strengthen and enhance safety measures in accordance with the Interim Report of the Committee for Investigation of Drug-induced Hepatitis Cases and Appropriate Regulatory Administration to Prevent Similar Sufferings, entitled "How the Regulatory Authority Should Function to Prevent Similar Drug-induced Diseases" (dated July 31, 2008)

  The budget shown above is based on the Mid-term Targets for cost control as directed by the Minister of Health, Labour and Welfare. PMDA aims to achieve the Mid-term Targets by appropriately operating within the allocated budget.

- In FY 2013, in order to pursue more efficient operations within the annual budget, PMDA promoted general competitive bidding based on the Plan for the Review of Optional Contracts etc., which was developed in April 2010. As with the previous year, PMDA conducted procurement activities through general competitive bidding for personal computers and office furniture resulting from the increase of employees, as well as purchase of expendables such as copy paper, thereby reducing procurement costs.

  Consequently, PMDA successfully reduced general and administrative expenses by 11.5% of its budget size which was subject to more efficient budget control, even excluding the unused budget amounts due to non-achievement of the target number of new employees.

2.2.(2) Cost control of operating expenses

- By increasing operational efficiency through promotion of digitization, PMDA balanced the FY 2013 budget for operating expenses (excluding expenses for office relocation, expenses related to payment of relief benefits, and single-year expenses due to new project launches etc.), in line with cost-reduction measures specified in the Mid-term Plan. Basically, the FY 2013 budget reflected about 5% reduction from the FY 2008 budget, and was added together with the expenses as listed below. However, the budget allocations for the listed expenses incurred starting in FY 2009, FY 2010, FY 2011, and FY 2012 were reduced by about 4%, 3%, 2%, and 1%, respectively, compared to those for the first year of each project.

1) Operating expenses incurred starting in FY 2009 with efforts to speed up drug application reviews in accordance with the recommendations from the Council for Science and Technology Policy

2) Operating expenses incurred starting in FY 2009, FY 2010, and FY 2011 with efforts to speed up medical device application reviews based on the "Action Program to Accelerate Reviews of Medical Devices"

3) Operating expenses incurred starting in FY 2009 with efforts to strengthen and enhance safety measures in accordance with the "Interim Report of the Committee for Investigation of Drug-induced Hepatitis Cases"

The budget shown above is based on the Mid-term Targets for cost control as directed by the Minister of Health, Labour and Welfare. PMDA aims to achieve the Mid-term Targets by appropriately operating within the allocated budget.

- In FY 2013, PMDA promoted general competitive bidding in relation to operating expenses, as with the case of general and administrative expenses, based on the "Plan for the Review of Optional Contracts etc." In the meantime, PMDA steadily managed the operations and strove to reduce costs while securing necessary operations, taking account of the trends for income as user fees and contributions, which are the financial sources of operations.

  Consequently, it was possible to reduce operating expenses by 4.7% as compared to the budget size subject to more efficient budget control, even excluding amounts that became unnecessary for reasons such as non-achievement of the target number of new employees and that cases of overseas GMP on-site inspections were fewer than expected.

2.2.(3) Competitive bidding

- Because PMDA promoted bidding for all contracts by measures such as shifting to general competitive bidding based on the "Plan for the Review of Optional Contracts etc.," the ratio of competitive contract schemes including competitive request for proposals and invitation to bids in all contracts increased by 1.3% in terms of the number of bids and by 13.9% in terms of the monetary amount compared to the preceding year.

		FY 2012	FY 2013	Change
General competitive bidding (including competitive request for proposals and invitation to bids)		123 bids (82.6%)	135 bids (83.9%)	12 bids (1.3%)
		2,748 million yen (62.9%)	5,838 million yen (76.8%)	3,090 million yen (13.9%)
Non-competitive optional contracts		26 bids (17.5%)	26 bids (16.2%)	±0 bids (-1.3%)
		1,622 million yen (37.1%)	1,769 million yen (23.3%)	147 million yen (-13.8%)
	Excluding contracts in relation to office lease, for which shift to competitive bidding is not appropriate	10 bids (6.7%)	5 bids (3.1%)	-5 bids (-3.6%)
		51 million yen (1.2%)	35 million yen (0.5%)	-16 million yen (-0.7%)
Total		149 bids 4,369 million yen	161 bids 7,606 million yen	12 bids 3,237 million yen

2.2.(4) Contract Review Committee meetings

- Based on "Inspection/Review of the Contract Status of Incorporated Administrative Agencies" (adopted by the Cabinet on November 17, 2009), PMDA established the "Contract Review Committee" in the Agency. The Committee consists of external knowledgeable experts as well as internal auditors. In the Committee meetings, PMDA underwent a pre-inspection of procurement cases etc., for which contracts were planned to be concluded in FY 2013, regarding the appropriateness of the contract schemes and of corrective measures for ensuring the competitiveness. The Committee held 4 meetings in FY 2013 and disclosed the summary of review on the website.

2.2.(5) Collection and management of contributions

- Contributions from marketing authorization holders (MAHs) of the industry enable PMDA to secure the major part of financial resources for relief services for adverse health effects such as adverse drug reactions and infections acquired through biological products and other operations to improve the quality, efficacy, and safety of drugs and medical devices. Specifically, contributions to the adverse drug reaction fund ("ADR contributions") are declared and made by MAHs of approved drugs, contributions to the relief fund for infections acquired through biological products ("infection contributions") are declared and made by MAHs of approved biological products, and contributions to post-marketing safety measures are declared and made by MAHs of drugs and medical devices.
- Basic data such as those concerning newly approved products (drugs and medical devices) and money transfer are automatically processed by the contribution collection management system, which is able to manage these contributions in an integrated fashion. Thus, PMDA efficiently conducted the operations of contribution collection and management, such as the calculation of products' transaction value which constitutes the basis of the contribution amount and the management of data concerning unpaid contributions. PMDA also ensured convenience for contributors through continuing consignment contracts with five major banks for receipt of contributions, resulting in a prompt transfer of funds.
- Regarding ADR contributions, infection contributions, and post-marketing safety measure contributions, PMDA set the collection rates to be no less than 99% in the Mid-term Plan. In FY 2013, the collection rates achieved for ADR contributions/infection contributions and safety measure contributions were 100% and 99.8%, respectively.

FY 2013 Contribution Collection Results

Category		Number of parties obligated to make contributions	Number of parties who made contributions	Collection Rate	Contribution amount (Million yen)
ADR contributions	MAHs of drugs	688	688	100%	3,590
	MAHs of pharmacy-compounded drugs	5,866	5,866	100%	6
	Total	6,554	6,554	100%	3,596
Infection contributions	MAHs of approved biological products	94	94	100%	869
Post-marketing Safety measures etc., contributions	MAHs of drugs	594	594	100%	978
	MAHs of medical devices	2,226	2,216	99.5%	244
	MAHs of drugs/ medical devices	213	213	100%	1,588
	MAHs of pharmacy-compounded drugs	5,866	5,866	100%	6
	Total	8,899	8,889	99.8%	2,816

Note: Since the figures for contribution amount are rounded off to the nearest thousand yen, the figures' sum does not always match the sum of the payment amounts.

- In order to efficiently improve contribution collection rates, the following efforts were made:

  1) PMDA continued to commission the Japan Pharmaceutical Association (JPA) to collect contributions from MAHs of pharmacy-compounded drugs.

  2) PMDA placed advertisements on websites and relevant trade journals, and tried to make the procedure known to all the parties obligated to make contributions by preparing and distributing a handbook on the procedure. Also, PMDA sent out written requests to all the contributors who have not yet made contributions, except the MAHs of pharmacy-compounded drugs.

(i) Collected ADR contributions and trends in the liability reserve

a. ADR contributions

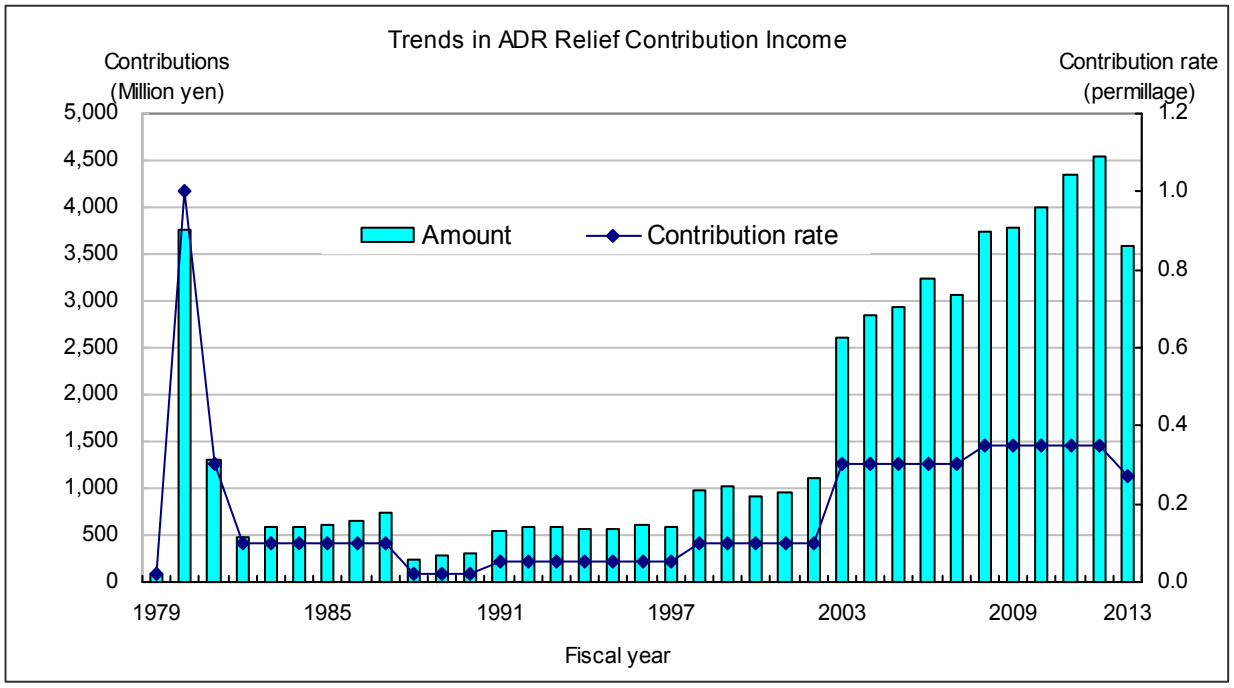
- In order to fund the relief service for adverse drug reactions, PMDA has collected ADR contributions from MAHs of approved drugs. In FY 2013, the contribution rate applied to such MAHs was set at 0.27/1000 and the collected amount was 3,596 million yen.

(Million yen)

Fiscal year	FY 2009	FY 2010	FY 2011	FY 2012	FY 2013
Contributions from MAHs of drugs	3,783 [742]	3,984 [716]	4,330 [713]	4,548 [688]	3,590 [688]
Contributions from MAHs of pharmacy-compounded drugs	8 [7,598]	7 [7,082]	7 [6,694]	6 [6,186]	6 [5,866]
Total amount	3,790	3,991	4,337	4,554	3,596
Contribution rate	0.35/1000	0.35/1000	0.35/1000	0.35/1000	0.27/1000

Note: Figures in [ ] represent the numbers of contributors.

- The ADR contribution income and the contribution rate since the establishment of this service are shown below.



b. Collected contributions for relief for infections acquired through biological products

- In order to fund the relief service for infections acquired through biological products, PMDA has collected infection contributions from MAHs of approved biological products. In FY 2013, the contribution rate applied to such MAHs was set at 1/1000 and the collected amount was 869 million yen.

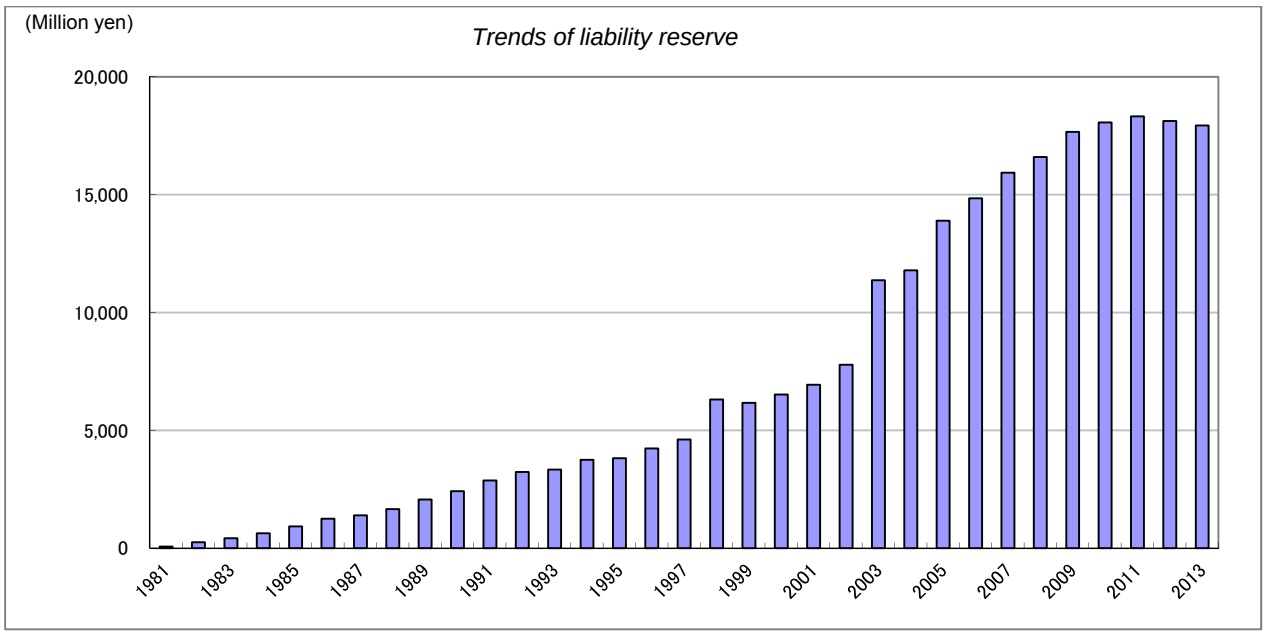
(Million yen)

Fiscal year	FY 2009	FY 2010	FY 2011	FY 2012	FY 2013
Contributions from MAHs of approved biological products	631 [97]	693 [93]	785 [92]	866 [92]	869 [94]
Contribution rate	1/1000	1/1000	1/1000	1/1000	1/1000

Note: Figures in [ ] represent the numbers of contributors.

c. Liability reserve

- In order to cover the estimated costs for relief benefits that eligible persons will receive in the future, PMDA calculates the amount that the Agency should possess at the end of every fiscal year and accumulates funds accordingly. The liability reserve at the end of FY 2013 was 17,934 million yen.



(ii) Collected contributions for post-marketing safety measures

- In order to fund services for improvements in the quality, efficacy, safety of drugs, etc., PMDA has collected contributions to post-marketing safety measures from MAHs of drugs and medical devices. In FY 2013, the contribution rate applied to such MAHs was set at 0.22/1000 for drugs excluding *in vitro* diagnostics and 0.11/1000 for *in vitro* diagnostics and medical devices, and the collected amount was 2,816 million yen.

(Million yen)

Fiscal year	FY 2009	FY 2010	FY 2011	FY 2012	FY 2013
MAHs of drugs/ medical devices	2,354 [3,019]	2,530 [2,922]	2,596 [2,974]	2,768 [2,970]	2,810 [3,023]
MAHs of pharmacy-compounded drugs	8 [7,594]	7 [7,082]	7 [6,694]	6 [6,186]	6 [5,866]
Total amount	2,362	2,537	2,603	2,774	2,816
Contribution rate	0.22/1000 (Drugs excluding *in vitro* diagnostics) 0.11/1000 (Medical devices and *in vitro* diagnostics)	0.22/1000 (Drugs excluding *in vitro* diagnostics) 0.11/1000 (Medical devices and *in vitro* diagnostics)	0.22/1000 (Drugs excluding *in vitro* diagnostics) 0.11/1000 (Medical devices and *in vitro* diagnostics)	0.22/1000 (Drugs excluding *in vitro* diagnostics) 0.11/1000 (Medical devices and *in vitro* diagnostics)	0.22/1000 (Drugs excluding *in vitro* diagnostics) 0.11/1000 (Medical devices and *in vitro* diagnostics)

Note: Figures in [ ] represent the numbers of contributors.

2.2.(6) Reduction in personnel expenses etc.

- The personnel expenses for FY 2013 were reduced by approximately 14.2% (in comparison with personnel expense per person for FY 2005), such as by steadily putting in place the remuneration system that was introduced in April 2007, taking into account the reform of the remuneration structure of national government employees.
- PMDA compared the remuneration system for its staff for FY 2012 with that of national government employees in order to facilitate the public's understanding of its remuneration levels, and released the results on its website.

(thousand yen)

Fiscal year	FY 2005 (Base year)	FY 2006	FY 2007	FY 2008	FY 2009	FY 2010	FY 2011	FY 2012	FY 2013
Unit personnel expense (Unit per person)	8,281	8,057	8,052	7,787	7,575	7,343	7,307	6,915	6,821
Rate of personnel expense reduction		-2.7%	-2.8%	-6.0%	-8.5%	-11.3%	-11.8%	-16.5%	-17.6%
Rate of personnel expense reduction (corrected)*		-2.7%	-3.3%	-6.6%	-7.0%	-8.1%	-8.4%	-13.1%	-14.2%

* *Corrected rates have been calculated by excluding amounts equivalent to that in the recommendations of the National Personnel Authority.*

2.2.(7) Promotion of measures for reduction of unnecessary expenditures

- In order to steadily implement measures for “Reinforcement of the efforts to reduce unnecessary expenditures” (March 31, 2011), which was first formulated in FY 2009 and revised in FY 2011 based on the efforts made in FY 2010, an e-mail message based on “Standard of practice for taking more efficient cost-cutting measures” was distributed every month to all employees to promote “efforts for cost-cutting.”

2.3. Improvement of Services to the Public

2.3.(1) General consultation service

- Based on the “General Consultation Guidelines” that specifies how to handle inquiries directed to PMDA and how to make use of comments and opinions to improve its operations, PMDA provides a general consultation service and makes questionnaires available at the reception desk, enabling the collection of comments and opinions of visitors regarding its overall operations. In addition, PMDA receives opinions etc., via telephone, facsimile, and the website.
- Since June 2010, PMDA has been disclosing the "Public Voice" sent to the Agency on its website on a weekly basis to make use of it to improve management of its operations.
- Among the 1,776 inquiries that PMDA received in FY 2013, 565 or approximately 30% of the total inquiries received were those relating to applications and consultations for drugs or medical devices.

	Inquiry/ consultation	Complaint	Opinion/ request	Others	Total
FY 2013	1,675 (532)	13 (3)	88 (30)	0 (0)	1,776 (565)

Note 1:Figures in parentheses represent the number of cases related to consultations and applications for approval of drugs or medical devices. They are included in the total numbers above.

Note 2:The Office of Review Administration also accepts inquiries on consultations and applications for approval of drugs or medical devices, separately from this general consultation service.

2.3.(2) Responses to consultations, complaints, and claims of dissatisfaction from companies regarding product reviews and product safety operations

- In addition to responding to consultations and complaints from general consumers, PMDA also handles complaints from relevant companies regarding product reviews and product safety operations.

- In FY 2004, PMDA established a system where, if an applicant files claims of dissatisfaction etc., regarding product reviews and product safety operations, the responsible office director (the Director of the Center for Product Evaluation or Chief Safety Officer, if the second claim of dissatisfaction has been filed in the same case) is to directly conduct an investigation and respond to the applicant within 15 working days. PMDA continued to operate the system in FY 2013.
- In addition, PMDA developed a consultation manual to handle complaints from relevant companies. From among the complaints received, PMDA selects and reviews those that would be helpful in improving its operations.

2.3.(3) Enrichment of the PMDA website

- PMDA has prepared and posted on its website the Annual Report for FY 2012, which discloses the Agency's operating performance for FY 2012.
- In addition, materials and minutes of the Advisory Council meetings and other meetings were also posted on the website in a timely manner to release the details of the meetings.
- "What's New" and "Topics" links on the top page and existing web content were updated promptly in accordance with requests made by relevant offices.

2.3.(4) Proactive PR activities

- In line with the PMDA Public Relations Strategic Plan (July 11, 2008) developed from the viewpoint of systematically promoting PR activities of the Agency as a whole, PMDA intends to improve services to the public by proactively providing information.

  In FY 2013, PMDA distributed leaflets, which is to introduce PMDA to the general public, at events in various locations. In addition, PMDA notified patient groups of the distribution of leaflets etc., and provided them to the groups that requested.

  For the occasion of "Drug and Health Week," PMDA conducted PR activities for the general public by distributing brochures/leaflets on PMDA's services, brochures on relief systems, give-away goods, etc., and giving lectures and running booths at events held in various regions, in cooperation with pharmaceutical associations in 12 prefectures.

  In addition, PMDA introduced its operations to researchers and healthcare professionals by making booth exhibitions at academic conferences.

  PMDA also issued monthly PMDA newsletters (e-mail magazines for prospective employees) and released them on its website. In addition, the Chief Executive delivered speeches etc., 32 times in Japan and 5 times overseas.

- For celebrating the 10th anniversary of PMDA’s establishment in April 1, 2004, PMDA forum was held in Tokyo on February 8, 2014 for the purposes of making PMDA's activities and efforts widely known to the public, enhancing the public's understanding and recognition of PMDA, increasing the public's awareness of the significance, roles, etc., of drugs and medical devices, and strengthening the collaboration with overseas regulatory authorities.

  With a total of about 800 participants, in Part 1 of the forum, Ms. Shinako Tsuchiya, Vice-Minister of Health, Labour and Welfare made a remark on the theme of “Toward Worldwide PMDA,” and then Dr. Tatsuya Kondo, Chief Executive of PMDA, gave a presentation titled “10-year Achievements of PMDA,” followed by a keynote speech by Dr. Fumimaro Takaku (President, Japanese Association of Medical Sciences) and guest presentations by Prof. Guido Rasi (Executive Director, European Medicines Agency [EMA]) and other guest speakers from overseas

regulatory authorities. In the Part 2, the future of drug products in Japan was discussed with the theme of “Got to know! Japanese Pharmaceuticals,” with Mr. Akira Ikegami, Journalist, as the chair, and Dr. Kondo, Chief Executive, Dr. Tomomitsu Hotta (President, National Cancer Center), Prof. Mayumi Mochizuki (Dean of Faculty of Pharmacy, Keio University), and Mr. Jugo Hanai (Chairman, Japan Federation of Drug-Induced Sufferers Organizations).

2.3.(5) Disclosure requests for agency documents

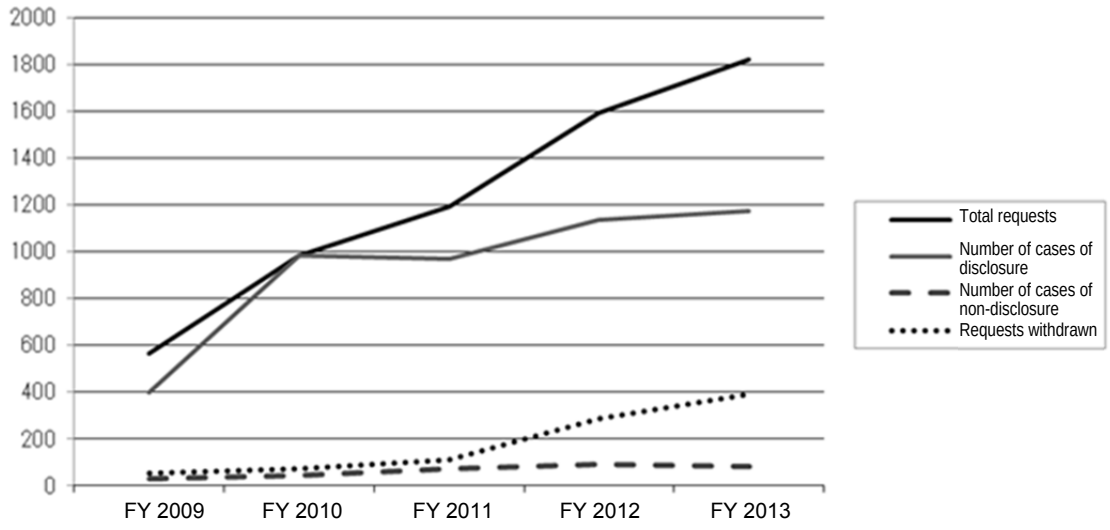
- The status of requests for disclosure of the documents based on the Act on Access to Information Held by Incorporated Administrative Agencies is shown below (for the past five years). In FY 2013, the number of requests increased by 14.4% compared to the previous fiscal year. PMDA appropriately processed them in accordance with the relevant laws and regulations.

Number of Requests for Disclosure of Agency Documents (Unit: Case)

	Total requests	Requests withdrawn	Decisions*					Objections made	Carry-over into FY 2014**
			Full disclosure	Partial disclosure	Non-disclosure	Non-existing documents	Refusal to answer whether the documents exist		
FY 2009	568	54	27	371	1	31	0	0	0
FY 2010	983	74	150	833	4	40	1	1	0
FY 2011	1,192	112	138	831	1	74	0	1	0
FY 2012	1,593	287	147	988	0	81	10	5	0
FY 2013	1,823	394	73	1,104	7	72	4	0	631

* *Regarding the number of requests in and after FY 2010, if a request is received as one case and multiple notifications on decision of disclosure etc., are separately issued for the request, the number of notifications for each decision on disclosure etc., are shown.*

** *"Carry-over into FY 2014" includes cases for which requests for disclosure were made at the end of the fiscal year and cases to which the prolongation of due dates for decision of disclosure etc., pursuant to laws and regulations were applied for reasons such as large amounts of documents.*



Note 1:The number of cases of disclosure includes full and partial disclosure.

Note 2: The number of cases of non-disclosure includes cases of non-existing documents and refusals to answer whether the documents exist.

Number of Requests for Disclosure of Agency Documents by Operational Category of Document

(Unit: Case)

Operational category/FY	FY 2009	FY 2010	FY 2011	FY 2012	FY 2013	Examples
Product application Review	479	902	1,046	1,410	1,675	Marketing notification for products not subject to approval, Notification of the results of GCP inspections
Post marketing Safety	89	78	139	176	131	ADR reports etc.,
Others	0	3	7	7	17	
Total	568	983	1,192	1,593	1,823	

Note: The numbers include requests that were withdrawn, those for the documents decided not to be disclosed, those for non-existing documents or those for the documents refused to answer whether the documents exist.

2.3.(6) Disclosure requests for personal information

- The status of requests for disclosure of personal information based on the Act on the Protection of Personal Information Held by Incorporated Administrative Agencies is shown below (for the past five years).

Number of Requests for Disclosure of Personal Information (Unit: Case)

	Total requests	Requests withdrawn	Decisions					Objections made	Carry-over into FY 2014
			Full disclosure	Partial disclosure	Non-disclosure	Non-existing documents	Refusal to answer whether the documents exist		
FY 2009	1	0	0	0	1	0	0	0	0
FY 2010	3	0	0	1	0	1	0	0	0
FY 2011	1	0	0	2	0	0	0	0	0
FY 2012	3	1	0	2	0	0	0	0	0
FY 2013	6	0	0	4	0	0	0	0	2

2.3.(7) Auditing

- PMDA undergoes audits conducted by an external auditing firm in accordance with the general rules for incorporated administrative agencies and by the Agency's Auditors. PMDA also conducts internal auditing systematically through the Audit Office for operations and accounts, from the perspective of internal control. The results of these audits are publicly reported to ensure transparency in the Agency's management and operations.
- In FY 2013, PMDA conducted internal audits on the management status of documents, cash and cash equivalents, PASMO (rechargeable pre-paid IC card for public transport etc.), competitive research funds, etc., and the status of compliance with rules restricting the work assignment of personnel from the private sector.

2.3.(8) Report on the financial standing

- From the perspective of ensuring the transparency of expenditures, PMDA disclosed its financial standing for FY 2012, including the use of user fees and contributions, in government gazettes and on its website. PMDA also released the budget for FY 2013 on its website.

2.3.(9) Release of "Plan for the Review of Optional Contracts etc."

- Following the inspection or review of optional contracts etc., PMDA released a report entitled "Follow-up on contract status of FY 2012" on the website in August 2013.

2.4. Personnel Matters

2.4.(1) Personnel evaluation system

- According to the Mid-term Targets, PMDA is required to evaluate personnel properly taking individual performance of employees into consideration. Moreover, in the Second Mid-term Plan (FY 2009 to FY 2013), PMDA intends to manage a personnel evaluation system in which the results of the evaluation and the attainment of individual goals are properly reflected in remuneration, pay raises, and promotions, to enhance the morale of employees.
- To this end, PMDA appropriately reflected the results of personnel evaluation during the period from April 2012 to March 2013 in pay raises etc., as of July 2013. In order to ensure the proper implementation of this personnel evaluation system, PMDA provided briefing sessions for all employees, and explained the "personnel evaluation system" to the new recruits as a subject of their training course.
- Starting in FY 2013, training programs for evaluators (managerial staff) were conducted by outsourcees in order to enhance the evaluation capability and enable the personnel evaluation to more effectively cultivate human resources and capability development.
- Interviews by secondary evaluators with evaluatees were started in FY 2013 for the purposes of knowing the working conditions of employees on a routine basis and of creating an opportunity of communication to establish a favorable relationship.

2.4.(2) Systematic implementation of staff training

- In the operations for reviews, post-marketing safety measures, and relief service conducted by PMDA, highly specialized expertise is required. In addition, rapid strides are constantly being made in the advancement of technology for developing drugs and medical devices.
- Under such circumstances, it is necessary for PMDA to provide more effective capacity building activities to enhance the level of expertise of its staff. Therefore, in FY 2007, PMDA reorganized the existing training courses into two training courses: the General Training Course and the Specialized Training Course, so that employees can take each program in a structured way. In FY 2013, these structured training courses were continuously provided for employees.

  Furthermore, in order to provide efficient and effective training tailored to the qualities and capabilities of individual employees, PMDA actively deployed external institutions and experts, thereby enriching training programs. PMDA also facilitated the participation of employees in academic conferences etc., both in Japan and overseas to improve their knowledge and technical expertise.

Specifically, the Training Committee formulated plans for new recruit training, internal training, and external training based on the needs of each division. Various training programs, as listed below, were implemented.

1) General Training Course

(i) New recruit training was conducted between April and May 2013. The major subjects are as follows:
- Operations of each office, related systems/procedures
- Human skills (e.g., business manner, communications, motivation)
- Document management, reduction of unnecessary expenditures, etc.

(ii) Training programs one each for follow-up, mid-level employees and management-level employees, as part of training programs by job level l

(iii) Legal compliance training for all executives and employees to promote awareness of legal compliance and personal information protection

(iv) A TOEIC examination was conducted as part of efforts to improve the language skills of employees.

(v) In order to utilize electronic documents more efficiently, IT literacy training (Microsoft Office) was carried out for a total of 54 members through e-learning in which trainees learn at the personal computer on their own desk.

(vi) Three training program sessions were held, where invited lecturers from organizations of adverse drug reaction sufferers and organizations of patients etc., delivered their presentations.

(vii) PMDA conducted on-site training programs, such as visits to drug and medical device manufacturing facilities (9 facilities), IRBs of medical institutions, etc.

2) Specialized Training Course

(i) A total of 95 employees (68 in Japan, 27 overseas) were dispatched to universities in Japan and overseas as well as foreign regulatory authorities for trainings.

(ii) Special training programs mainly addressing technical issues which are provided by experts et al., invited as lecturers from regulatory authorities, corporations, and universities in Japan or overseas (34 sessions), training programs on laws and regulations including the Pharmaceutical Affairs Act to learn the regulatory system etc., (6 sessions), and training programs on clinical study design to learn biostatistics (12 sessions) were conducted. PMDA also conducted special training programs featuring introduction of product development programs and, design and supervision of medical devices at companies.

(iii) Case studies and medical writing training, etc., on product application reviews were conducted mainly for new recruits

(iv) A total of 14 employees were dispatched to technical training programs conducted by external institutions (e.g., Pharmaceuticals Promotion Association's Regular Course, National Institute of Public Health, and Union of Japanese Scientists and Engineers).

(v) Product hands-on training using medical devices in the areas of the cardiovascular system, orthopedics, etc., was also provided. For the acquisition of basic knowledge about medical devices, class I and II ME (Biomedical Engineering) technical trainings were also provided (19 employees).

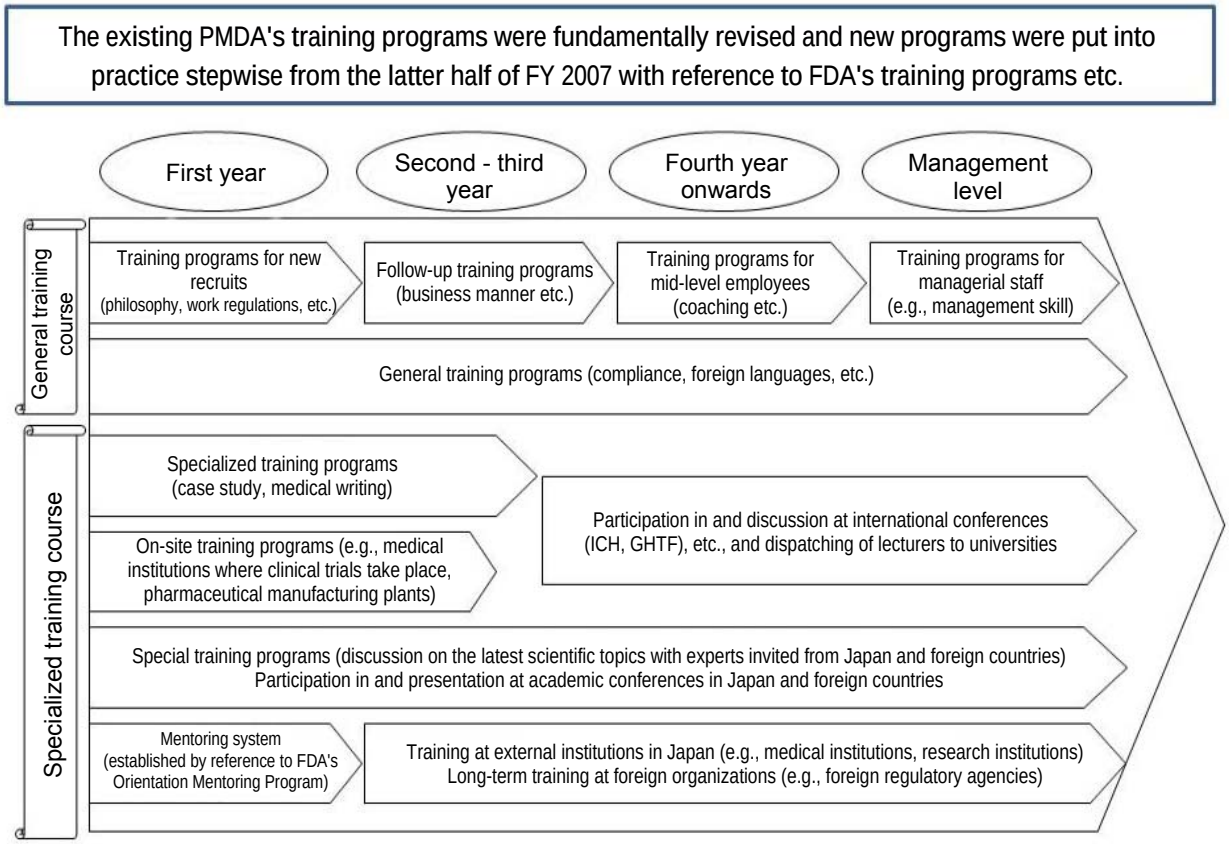
(vi) Five employees were dispatched to 2 medical institutions for practical training with pharmacists conducted at hospitals to learn clinical practice.

(vii) One employee was dispatched to an accounting training course provided by the Accounting Center, Ministry of Finance, to improve administrative processing skills. Also, 7 employees attended a grade 2 or 3 bookkeeping course. Also, 16 employees attended an external logical thinking course, a management course, a labor management course,

or a course for the Japan business law examination as a training for administrative staff members who are on main career tracks.

(viii) PMDA also conducted GMP on-site training programs at drug manufacturing facilities etc., and dispatched two employees to two facilities with the cooperation of relevant organizations.

Training and Human Resource Development



2.4.(3) Appropriate personnel allocation

- In order to secure the expertise of the staff members and operational continuity, PMDA aims to conduct appropriate personnel allocation.
  To achieve this target, PMDA conducted personnel allocation taking into consideration the knowledge and work experience of staff members. PMDA conducts mid- and long-term rotation of personnel except for the cases with health-related issues and special reasons related to operations.
- Also in FY 2013, personnel change and career progression were implemented in line with the basic policies for the PMDA Career Paths that were developed in March 2011.

2.4.(4) Securing of human resources through open recruitment

- It is an important task to recruit capable persons with professional expertise while paying due attention to the neutrality and impartiality of PMDA, in order to conduct its operation of reviews and post-marketing safety measures promptly and accurately.

- In the Second Mid-term Plan, in accordance with the recommendations of the Council for Science and Technology Policy, the Action Program to Accelerate Reviews of Medical Devices, and the proposals by the Committee for Investigation of Drug-induced Hepatitis Cases, the target number of regular employees at the end of the period (at the end of FY 2013) is set to be 751. PMDA is required to recruit capable persons in relevant areas, based on the recruitment plan for each job category. Therefore, PMDA held information sessions on career opportunities, and conducted open recruitment of regular technical employees twice in FY 2013 by making use of its website as well as job information websites.

Employment through Open Recruitment in FY 2013 *(as of April 1, 2014)*

1)	Technical (specialist) employees [open recruitment conducted twice]	
	Number of applicants	347
	Number of employments	44
2)	Administrative staff members who are on main career track [open recruitment conduced once]	
	Number of applicants	179
	Number of employments	10

FY 2013 Recruitment Activities

- Information sessions on career opportunities
  - February: Two sessions in Tokyo and one session in Osaka (total: 205 participants)
  - May: Two sessions in Tokyo and one session in Osaka (total: 133 participants)
- Activities performed in collaboration with directors/employees
  - Lectures on and explanation of the services at universities etc., by directors/ employees
  - Students visits by their alumni of young PMDA employees
- Tools for recruitment activities
  - Brochures for recruitment, posters for recruitment
  - The brochures and posters were sent out to approximately 500 institutions including medical schools of universities, medical institutions such as university hospitals, faculties of pharmaceutical science of universities, pharmacy departments of hospitals, faculties relevant to biostatistics and veterinary science, and research institutions. Also, the brochures were distributed at recruitment information sessions etc.
- Information to be posted on job information websites
  - Websites presenting job offers for new graduates in 2015 ("My Navi 2015" and "Rikunabi 2015")
  - Websites presenting job offers for mid-carrier recruitment “My Navi Career Change” and “Asahi Recruitment Web”

- Recruitment advertising in newspaper
  - Asahi Shimbun
    - As for continuous recruitment, 6 job categories—epidemiology, clinical pharmacology/pharmacokinetics, information science, GLP, GMP/QMS, and foreign language (English)— were newly added to the 4 conventional job categories (toxicity, IT system, clinical medicine, and biostatistics), resulting in a total of 10 job categories. As a consequence, 13 individuals were employed on an as-needed basis.

Numbers of Executives and Regular Employees

	FY 2009 April 1	FY 2010 April 1	FY 2011 April 1	FY 2012 April 1	FY 2013 April 1	FY 2014 April 1	At the end of the effective period of Third Mid-term Plan (end of FY 2018)
Total	521	605	648	678	708	753	1,065
Review Department	350	389	415	438	460	492	
Safety Department	82	123	133	136	140	152	
Relief Department	32	34	34	33	33	33	

Note 1: The "Total" includes 6 executives (including one part-time auditor). However, the number of executives is 5 as of April 1, 2014.

Note 2: The Review Department consists of the Director for Center for Product Evaluation, Associate Executive Directors, Associate Center Directors (excluding Associate Center Director responsible for Office of Regulatory Science), Advanced Review with Electronic Data Promotion Group, Office of International Programs, International Liaison Officers, Office of Review Administration, Office of Review Management, Office of Standards and Guidelines Development, Offices of New Drug I to V, Office of Cellular and Tissue-based Products, Office of Vaccines and Blood Products, Office of OTC/Generic Drugs, Offices of Medical Devices I to III, and Office of Conformity Audit, Chief of Kansai Branch, Consultation Division of Kansai Branch, and Senior Specialists.

Note 3: The Safety Department consists of the Chief Safety Officer, Offices of Safety I and II, Office of GMP/QMS Inspection, and Inspection Division of Kansai Branch.

2.4.(5) Appropriate personnel management based on work regulations

- PMDA is careful to conduct appropriate personnel management so that suspicion of inappropriate ties with pharmaceutical companies may not arise, by imposing certain restraints on recruitment and allocation of executives and employees as well as on employment with other organizations after resignation from PMDA.
- For this purpose, PMDA's work regulations prescribe the requirement of submission of a written oath for newly-employed staff members, rules for personnel allocation, restrictions regarding re-employment after resignation, and work restrictions for employees whose family members work in the pharmaceutical industry. PMDA conducts appropriate personnel management by making a handbook which provides outlines of related regulations, Q&A, and other information and distributing it to executives and employees and by keeping its staff members informed of these regulations through training sessions for new employees.
- Also, PMDA encouraged relevant employees to submit reports on donations etc., under the code of ethics, and also reviewed the details of the submitted reports.
- To secure capable human resources and prevent job separations, it is effective to create working environments for female employees to balance work with family, therefore, measures were taken such as revising working regulations to make it easier to use the system for maternal protection and setting up a system in which employees are allowed to take leave for accompanying an employee’s spouse who is transferred overseas.

- As countermeasures against power harassment in the work place, a structure for smooth prevention and resolution of power harassment was developed by taking measures such as revising working regulations for employees, newly formulating a manual to deal with problems related to power harassment, and placing a counseling staff member in each office, in addition to regulations related to prevention of sexual harassment which have already been implemented.
- For specially appointed experts accepted from universities, research institutes, etc., with the implementation of "Initiative to facilitate development of innovative drugs, medical devices, and cellular and tissue-based products," a handbook which briefly summarizes services and ethics in PMDA was made and distributed, and training sessions were provided to all specially appointed experts.

2.5. Ensuring Security

2.5.(1) Entry/exit access control

- To ensure security and protect confidential information, PMDA has installed a door access control system for each office to reinforce the internal security control.
- Specifically, the ID card based "access control system" installed at each office can log every entry through designated doors and prevent outsiders from freely entering

  In May 2010, in order to reinforce security, PMDA set up non-stop floors at which elevators do not stop unless the passengers (PMDA executives and employees, etc.) have appropriate ID cards.
- In order to ensure further strict access control, PMDA has also prescribed rules on its access control, and has made maximum efforts to thoroughly inform its staff members of these rules through the intranet and during new recruit training.

2.5.(2) Security measures for information systems

- Based on the FY 2013 plan, PMDA strove to maintain and improve the security of information in its information systems.
- In order to reinforce the data backup function, PMDA has been storing backup data in the information systems at remote locations since FY 2007.
- In order to reliably expand the use of secure e-mails in the audio transcription processes of records of consultations, PMDA improved the security.

Numbers of Users/Issued Certificates of the Secure e-mail System

	Number of registered companies	Cumulative total of issued certificates
Outside PMDA	53	725
Within PMDA		1,222

Note: The numbers of registered companies and issued certificates as of the end of March 2014

PART 3 Improvement in Management of Operations and Quality of Services in Each Division

3.1. Relief Services for Adverse Health Effects

To more widely inform the public of the Relief System for Sufferers from Adverse Drug Reactions and the Relief System for Infections Acquired through Biological Products (hereinafter collectively referred to as "Relief Systems"), PMDA, through relief fund services, takes the following measures to provide adequate and swift relief for those suffering from health damage caused by adverse drug reactions and infections acquired through biological products.

3.1.(1) Expansion and review of dissemination of information regarding the Relief System

(i) Release of payment cases etc., on the website

- PMDA has promptly published the decision on approval/rejection of claims for adverse reaction relief benefits with due consideration to protecting personal information. PMDA posts approved/rejected claims on its website every month, following the decision.
  In December 2012, PMDA started to distribute the information through its email service called "PMDA medi-navi" together with posting information on the website.
- Based on relevant information obtained from claims submitted for relief benefits, PMDA calls users' attention to the cases of health damage which have repeatedly occurred although precautions have already been provided in package inserts. The information was described in the "PMDA Request for Proper Use of Drugs" posted on the Medical Product Information web page and also distributed through "PMDA medi-navi" to further promote the proper use of drug products.
- To browse more easily between two websites for "Information on decision on approval/rejection of claims for adverse reaction relief benefits" and "Medical Product Information," which provides information on package inserts, adverse drug reactions/medical device malfunctions, recalls, application reviews, etc., banners link to the other web page have been placed on the top page of both websites.
- For the purpose of improving safety measures for drugs, such as understanding the trend in occurrence of adverse drug reactions, PMDA started the web page of the "Patient's Report for Adverse Drug Reactions" on March 26, 2012 on a trial basis to collect reports from patients via the Internet, and set up a link to enable access from the above web page to the "Relief System for Adverse Health Effects" web page.
- From the viewpoint of making the administration of the system more transparent, PMDA released the operating performance as of the end of September 2013 on its website.

(ii) Improvement of brochures etc.

- In order to raise public understanding of the Relief Systems and swiftly determine relief benefits, PMDA has made the following efforts:

  a) The catch phrase in the leaflet for the general public was modified by employing a conversation style instead of a one-way message. The setting used is as follows: First, a patient asks, "Should adverse drug reactions not occur to me if I use a drug product properly?" The question from the first-person perspective helps patients regard possible adverse reactions as "own concern." Next, a healthcare professional respond to the question, "No. Even if you use a drug

product properly, the drug product may cause a serious health damage in rare cases," so as to raise patients' awareness that anybody could be involved in adverse drug reactions.

In the brochure for healthcare professionals, "Please tell patients that a drug product may cause a serious health damage in rare cases even if they use it properly." is now included so that the healthcare professionals will become aware that "they are expected to properly tell patients about possible occurrence of adverse health damage and to work as a bridge to the use of the relief system."

In addition, electronic files (PDF format) of the same brochures were posted on the website for users' convenience.

b) PMDA has improved the instructions for doctors to fill in the drug administrations and diagnoses on medical certificates or certificates of prescription more easily. In FY 2013, PMDA newly developed instructions for completing medical and prescription certificates related to medical expenses/medical allowances; medical certificates of gastrointestinal tract disorders (barium preparations) and pulmonary disorders. PMDA also reviewed the instructions for completing medical certificates for disability pensions/pensions for raising handicapped children that is intended for the visually impaired.

These revised instructions were posted on the website.

c) PMDA made efforts to get more persons to know that claim forms can be downloaded from the following website for users' convenience.
http://search.pmda.go.jp/fukusayo_dl/

d) The guidance for claims to be enclosed with claim forms and the checklists for claimants were revised in accordance with the revision of amounts of payment on April 1, 2014, in order to reduce the claimants' burden by intelligibly indicating how to fill in the required information for the claiming and which documents should be enclosed with claim forms.

3.1.(2) Proactive PR activities of the Relief System

PMDA utilized an external consultant to implement efficient publicity including the following activities.

Newly conducted activities in FY 2013

(i) As a new PR tool of TV broadcasting, a 15-second infomercial was aired through six stations of TV Tokyo network to spread the relief system across the general public in accordance with the "Drugs and Health Week" from Thursday, October 17 to Wednesday, October 23, 2013.

(ii) In the medical science specialized zone in "Radio NIKKEI," a radio program from which healthcare professionals collect the latest information necessary for healthcare, the Relief System for Sufferers from Adverse Drug Reactions was featured as a special program for a total of three times, on Mondays from 20:40 to 21:00. The summary of the relief system was explained by a PMDA employee, and commentaries on the relief system were provided in conversations between the experts in healthcare and pharmaceutical areas, shown below, and an announcer of Radio NIKKEI.

Part 1 "Summary of Relief System for Sufferers from Adverse Drug Reactions"
October 28, 2013
Commentary: Mr. Haruo Okawara, Director, Office of Relief Funds, PMDA

Part 2 "Relief System from the Standpoint of Healthcare"
November 25, 2013
Commentary: Dr. Masayuki Amagai, Professor, Department of Dermatology, Graduate School of Medicine, Keio University

Part 3 “Relief System from the Standpoint of Pharmaceuticals”
December 23, 2013
Commentary: Dr. Masahiro Hayashi,
Director, Department of Pharmacy, Toranomon Hospital

(iii) To promote the understanding of the name and details of the Relief System for Sufferers from Adverse Drug Reactions, PMDA conducted the following activities:

- Tie-up publicity with specialized medical journals (Nikkei Medical, Nikkei Drug Information) and their web deployment
- Publicity by using large outdoor digital signage
  From Friday, January 10 to Thursday, January 23, 2014, PMDA run an infomercial on the relief system 30 times a day (420 times during the period) on the “WAKASA SEIKATSU Channel” (placed at the entrance to Shibuya Center-Gai).
- Producing animation-based Internet advertisement
- Placed a banner link to the special site for the relief system on the website of the Japan Medical Association
- Placed a banner link to the special site for the relief system on the website of the Nippon Pharmacy Association.

Activities conducted on-site

(i) Dispatching lecturers to training workshops held by medical institutions for their employees

In November 2013, the MHLW issued a notification* to prefectural governments and healthcare-related organizations, to request them to utilize PR materials on the Relief System in their training sessions for safety management of medical services and informed that PMDA is willing to send materials explaining the relief system and dispatch lecturers. After the issuance of the notification, PMDA staff members visited healthcare-related organizations to request for cooperation to implement training sessions for the Relief System.

In response to requests from medical institutions etc., based on the above approach, PMDA has dispatched its staff members as lecturers to 11 medical institutions for explaining the system, and sent the materials to 179 medical institutions etc., in FY 2013.

* Notification issued by Chief of the Office of Drug Induced Damages, General Affairs Division, Pharmaceutical and Food Safety Bureau, Ministry of Health, Labour and Welfare, dated November 29, 2013
“Ensuring of Familiarity with the Adverse Drug Reaction Relief System implemented by the Pharmaceuticals and Medical Devices Agency (request for cooperation)”

(ii) Academic conferences

PMDA conducted publicity activities at a total of 20 academic conferences including the 6 occasions below:

- Oral presentations
  - Kanto Block Meeting of Japanese Society of Hospital Pharmacists
  - 40th Western Branch Meeting of the Japan Society of Hepatology
  - Scientific Meeting of the Toshin Branch of Nagano Pharmaceutical Association
- Distribution of booklets and brochures
  - Annual Meeting of the Japanese Respiratory Society
  - Spring Meeting of Japanese Society of Allergology
  - Annual Meeting of the Japan Society of Transfusion Medicine and Cell Therapy

(iii) Workshops

PMDA staff explained the Relief System at a total of 27 workshops including the following occasions:

- Lifelong Learning Course at Faculty of Pharmaceutical Science, Toho University
- Faculty of Pharmaceutical Sciences, Josai University
- Workshop for preventive vaccination service workers (7 blocks nationwide)
- Hands-on workshop at medical safety support centers (2 sites: Tokyo and Osaka)

(iv) Requests for cooperation to government bodies, relevant organizations, etc.

PMDA informed the government bodies, relevant organizations, etc., of the current awareness of the Relief System, and requested cooperation in publicity activities.

- 5 government bodies, 1 public health center, 7 medical safety support centers
- 5 medical/dental associations, 7 pharmacists' associations, 2 nursing associations
- Nippon Pharmacy Association

(v) Others

At the 15th Forum on Eradication of Drug-induced Sufferings (sponsored by Japan Federation of Drug-induced Sufferers Organizations), PMDA opened a consultation desk for the Relief Systems and distributed leaflets.

Activities conducted continuously

(i) PMDA's original character "Doctor Q" has been continuously used since FY 2011. A period from October to December, covering the "Drug and Health Week (October 17 to 23)," was designated as an intensive publicity period also in FY 2013, during which a nationwide publicity campaign for the Relief Systems using the character was conducted.

- Newspaper advertisement (on all the major national dailies: Asahi, Mainichi, Yomiuri, Sankei, and Nikkei)
- On-screen advertisement at hospitals/pharmacies (A total of 652 sites: 173 hospitals and 479 pharmacies)
- Advertisement in professional magazines etc. (A total of 11 magazines etc., including medical journals and medical newspapers)
- Distribution and displaying of posters etc. (A total of 600 sites, including pharmacies and drug stores)
- Advertising on the website
- Creation of a special web page

(ii) PR utilizing the brochure for healthcare professionals "Know it better than anyone and pass along. Relief System for Sufferers from Adverse Drug Reactions" was conducted.
Also posted the brochures (PDF format) on PMDA's website.

(iii) PMDA updated the presentation slides entitled "What is the Relief System for Sufferers from Adverse Drug Reactions?" to accelerate the use of the slides in lectures, training sessions, etc., on the relief system at universities and hospitals.

(iv) PMDA posted, on its website, poster and medicine envelopes on which the advertisement of the Relief Systems is pre-designed for pharmacies to use.

(v) PMDA posted "Summary of the Relief System for Sufferers from Adverse Drug Reactions and the Cases of Non-payment of Relief Benefits Due to Improper Use of Drugs" in the "Pharmaceuticals and Medical Devices Safety Information No. 307 (November 2013)."

(vi) PMDA requested the Federation of Pharmaceutical Manufacturers' Associations of Japan to place the information on the Relief Systems in a journal, Drug Safety Updates (DSU) published by the Federation, and distributed the journal to medical institutions nationwide.

(vii) In collaboration with MHLW, PMDA enclosed the leaflet on the Relief System for Sufferers from Adverse Drug Reactions in the brochure "Pharmaceuticals and Medical Devices Safety Information Reporting System" to distribute it to relevant organizations etc.

(viii) PMDA placed the information on the Relief Systems in a brochure "Useful Information on Medicines" (published by MHLW and the Japan Pharmaceutical Association) in the "Drug and Health Week."

(ix) PMDA placed the advertisement using the same design as the leaflet on the Relief System for Sufferers from Adverse Drug Reactions in specialized journals (the Journal of the Japan Medical Association, the Journal of the Japan Pharmaceutical Association, the journal of the Japan Dental Association and the journal of the Japanese Society of Hospital Pharmacists).

(x) PMDA moved the banner link to the special web page for the relief system to the top page of the website of the Japan Pharmaceutical Association to raise the visibility of the banner.

(xi) For the purpose of making the relief system familiar to general public, PMDA placed an in-train advertisement of the relief system for one month from December 27, 2013 to January 26, 2014.

(xii) PMDA put the website address of the relief system on the educational material titled “Learn Yakugai (Drug-Induced Sufferings),” which had been prepared by MHLW, and enclosed a poster when distributing the material to junior high schools, boards of education, etc., nationwide.

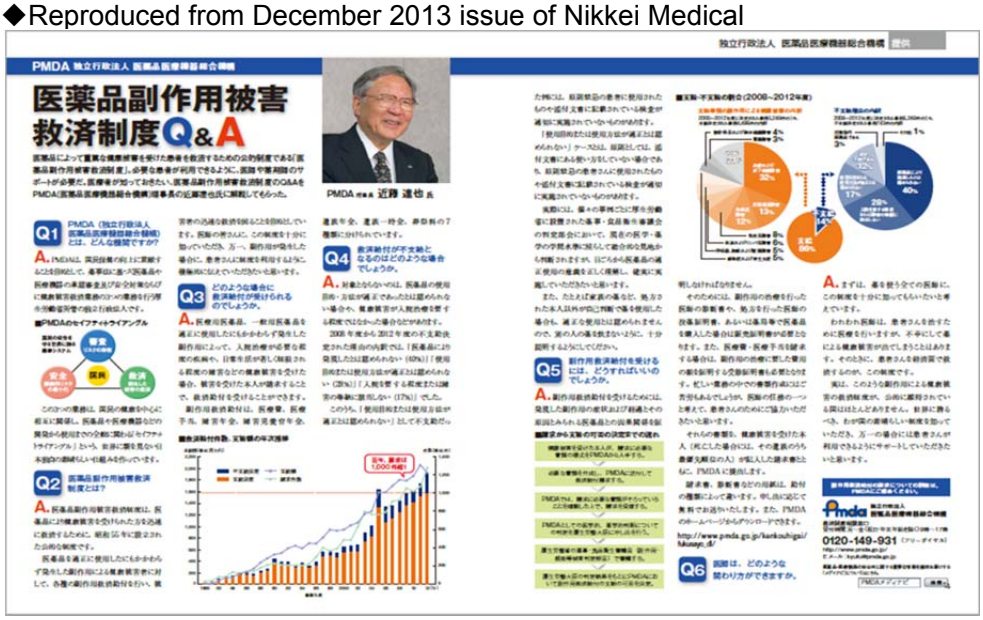
(xiii) In order to understand the level of people's awareness of the Relief System for Sufferers from Adverse Drug Reactions and conduct more effective PR activities, PMDA conducted the awareness survey on the Relief System among the general public and healthcare professionals.
Survey period: January 27 to February 13, 2014

[Newspaper advertisement using the original character "Doctor Q"]

[Brochure for healthcare professionals]

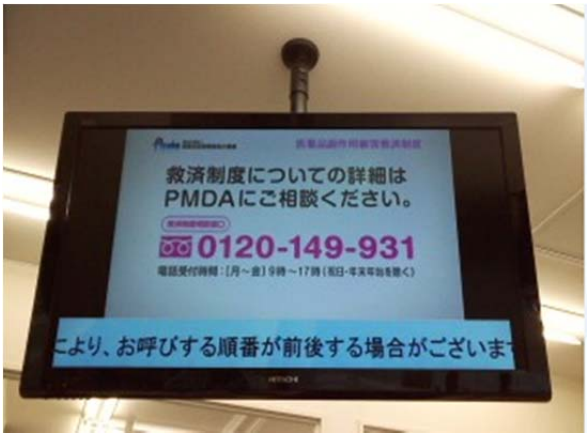
[Tie-up publicity with healthcare journals]

◆Reproduced from December 2013 issue of Nikkei Medical



医薬品副作用被害
救済制度Q&A

[Pharmacy vision; In-hospital vision]



(Pharmacy vision)

(In-hospital vision)

[In-train Advertisement]

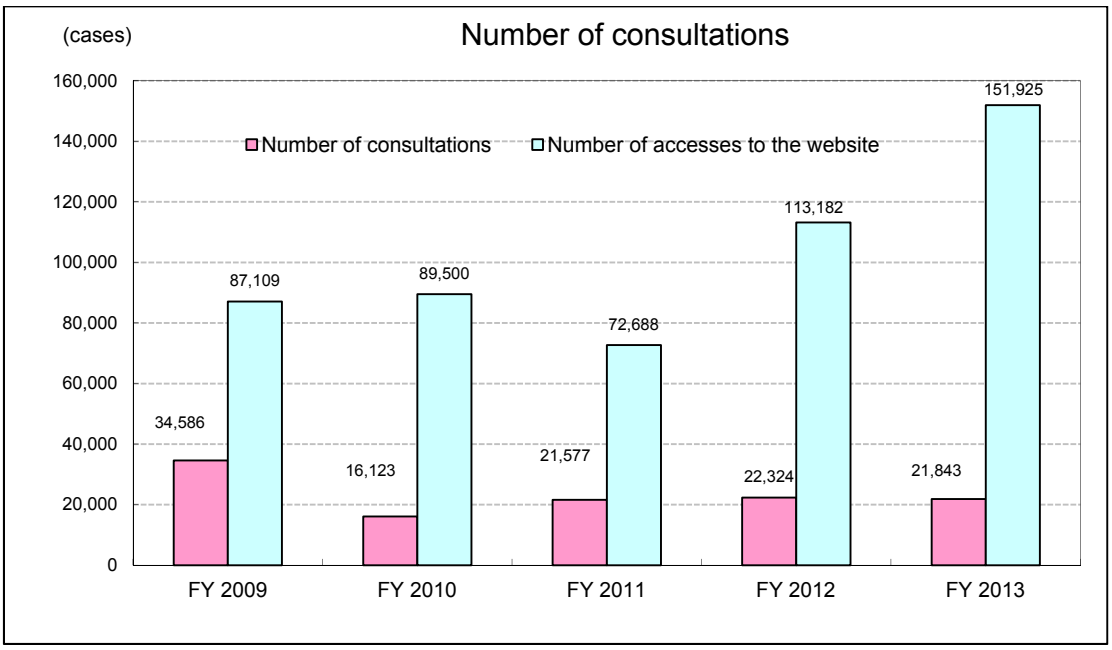
[Outdoor digital signage]

3.1.(3) Securing of efficient management of the consultation service

- In FY 2013, the number of consultations at the Relief System Consultation Service was 21,843, with a ratio of 97.8% compared with the previous fiscal year (22,324 consultations).
- In FY 2013, the number of accesses to the website was 151,925, with a ratio of 134.2% compared with the previous fiscal year (113,182 accesses).
- The number of accesses to the web page of the relief system was 69,616, with a ratio of 237% compared with the previous fiscal year (29,375 accesses).
- PMDA tried to keep the people who seek consultation informed of the fact that the request form etc., can be downloaded from its website.

Fiscal Year	FY 2009	FY 2010	FY 2011	FY 2012	FY 2013	Compared with FY2012
Number of consultations	34,586	16,123	21,577	22,324	21,843	97.8%
Number of accesses to the website	87,109	89,500	72,688	113,182	151,925	134.2%

* *Taking into account opinions from the users, PMDA introduced the pre-recorded voice guidance on September 25, 2009 to inform callers that telephone consultation is provided for inquiries on the Relief System for Sufferers from Adverse Drug Reactions and then to direct the callers to the consultation service. Only the number of consultations that was actually handled by PMDA was counted (before that, significant numbers of inquiries or complaints on products from persons who saw the contact information on the outer boxes of over-the-counter (OTC) drugs were included).*



<Relief system consultation service>

- ♦ Toll-free number: 0120-149-931
  (Office hours: Monday - Friday [except public holidays and New Year's holidays] 9:00 -17:00)
- ♦ Relief System Consultation Service e-mail address: kyufu@pmda.go.jp

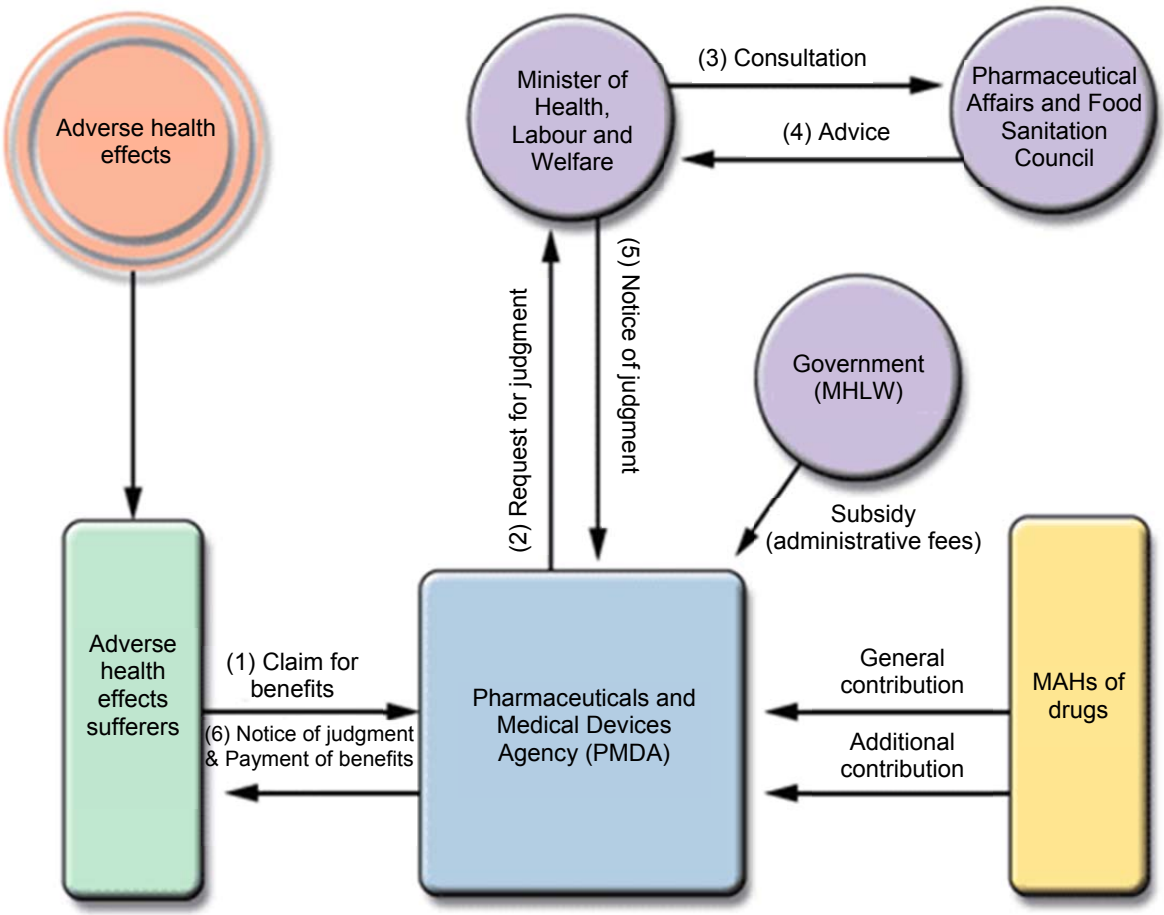
3.1.(4) Promotion of improved efficiency of operations using databases

- In efforts toward “optimization of the systems for Relief Services for Adverse Health Effects based on the Optimization Plan for Operations and Systems,” unification of versions of OS and upgrading of the consultation card system were done as preparative procedures for measures such as strengthening of the function of the relief benefits service system and integrating of management of information related to relief benefits through databases (unification of databases).

3.1.(5) Promotion of expeditious processing of relief benefit claims

- In order to conduct prompt administrative processing of relief benefit services, PMDA, upon receiving a claim for relief benefit, investigates and organizes the facts given in such a claim, and requests the Minister of Health, Labour and Welfare to make a medical and pharmaceutical judgment on the claim. For this purpose, the following operations are conducted: Fact-finding investigations of the claimed event; Preparation of a summary chart showing case narratives over time; and Preparation of investigation reports etc.

[Flow of Adverse Health Effect Relief Services]



* Applicants who are not satisfied with the judgment on approval/rejection of claims for relief benefits may file a request for a review of the decision to the Minister of the MHLW.

- In accordance with the Second Mid-term Plan, PMDA plans to exercise judgment on approval/rejection of claims within 6 months for 60% or more of the total number of judged cases in each fiscal year. In FY 2013, PMDA planned to have the number of claims judged within 6 months at 60% or more, while ensuring that 70% or more of claims are judged within 8 months of the standard administrative processing time and then made an effort to expedite the operations.

  In FY 2013, the number of claims was markedly increased from 1,280 in FY 2012 to 1,371, and the number of claims judged was also increased from 1,216 in FY 2012 to 1,240. Also, the number of claims judged within 8 months was 1,063, which was much higher than 923 in FY 2012 and accounts for 85.7% of the total judged cases. And the number of claims judged within 6 months was 754, much higher than 553 in FY2012 and the achievement rate of claims judged within 6 months was 60.8% of the total judged cases, showing that respective rates were higher than the annual targets.

(i) Relief Service for Adverse Drug Reactions

PMDA provides payment of benefits consisting of medical expenses, medical allowances, disability pensions, pensions for raising handicapped children, bereaved family pensions, lump-sum benefits for bereaved families, and funeral expenses for diseases, disabilities, and deaths that occurred on or after May 1, 1980, caused by ADRs even though drugs were used properly.

a. Performance of Relief Service for Adverse Drug Reactions

The performance for FY 2013 is shown below.

Fiscal Year			FY 2009	FY 2010	FY 2011	FY 2012	FY 2013
Number of claims			1,052	1,018	1,075	1,280	1,371
Number of judged cases			990	1,021	1,103	1,216	1,240
	Approved		861	897	959	997	1,007
	Rejected		127	122	143	215	232
	Withdrawal		2	2	1	4	1
	Within 8 months	Number of cases	733	765	809	923	1,063
		Achievement rate*1	74.0%	74.9%	73.3%	75.9%	85.7%
	Within 6 months	Number of cases	360	434	534	553	754
		Achievement rate*2	36.4%	42.5%	48.4%	45.5%	60.8%
Cases in progress*3			746	743	715	779	910
Median processing time [months]			6.8	6.4	6.1	6.2	5.8

**1 The percentages of the cases judged within 8 months out of the total number of cases judged during the fiscal year.*

**2 The percentages of the cases judged within 6 months out of the total number of cases judged during the fiscal year.*

**3 The numbers of cases in progress at the end of each fiscal year.*

b. Number of claims by type of benefit

The numbers of claims filed in FY 2013 by type of benefit are shown below.

Fiscal Year		FY 2009	FY 2010	FY 2011	FY 2012	FY 2013
Number of claims		1,052	1,018	1,075	1,280	1,371
Types of benefit	Medical expenses	902	854	909	1,101	1,200
	Medical allowances	943	911	964	1,168	1,252
	Disability pensions	71	74	77	83	88
	Pensions for raising handicapped children	11	4	4	1	7
	Bereaved family pensions	36	46	47	46	49
	Lump-sum benefits for bereaved families	50	54	63	53	54
	Funeral expenses	83	100	107	98	105

Note: A single claim could be classified into more than one type of benefit.

c. Judgment status by type of benefit

The number of approved cases and amounts of benefits in FY 2013 by type of benefit are shown below.

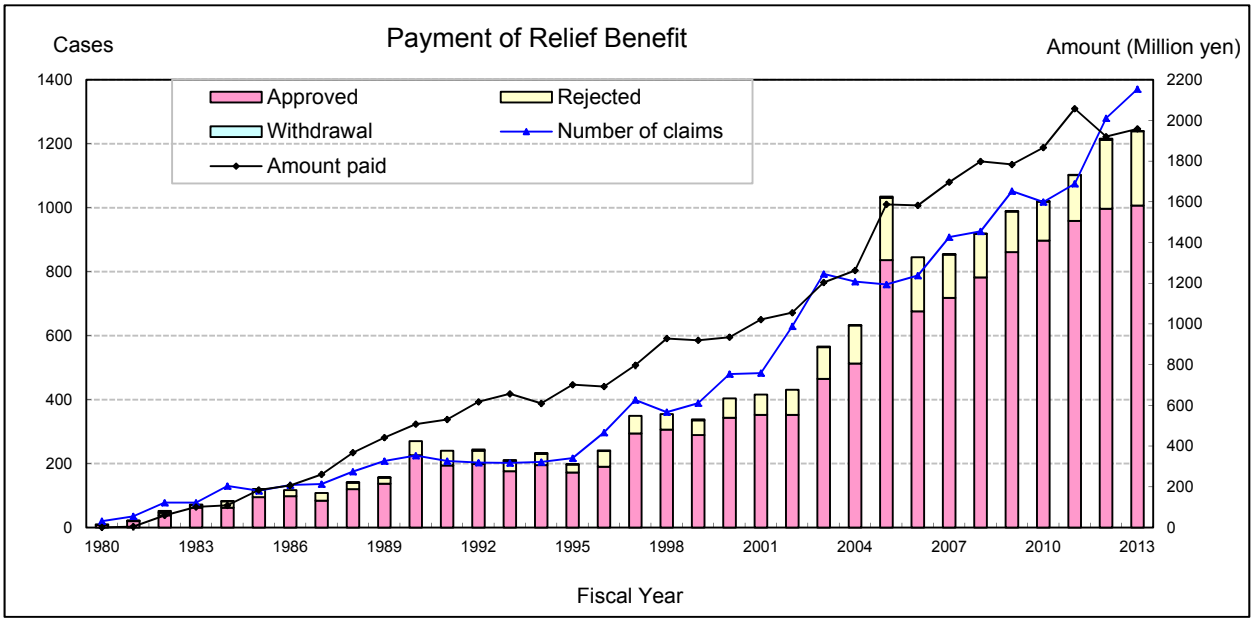
(Unit: Thousand yen)

Type	FY 2009		FY 2010		FY 2011	
	Number of cases	Amount paid	Number of cases	Amount paid	Number of cases	Amount paid
Medical expenses	763	86,666	803	87,475	836	93,284
Medical allowances	813	70,963	837	71,142	895	75,198
Disability pensions	26	804,251	38	853,854	28	881,885
Pensions for raising handicapped children	7	50,804	5	44,210	6	49,606
Bereaved family pensions	18	545,843	31	583,501	35	614,318
Lump-sum benefits for bereaved families	30	215,342	29	214,081	47	328,093
Funeral expenses	46	9,914	63	12,927	80	16,006
Total	1,703	1,783,783	1,806	1,867,190	1,927	2,058,389

Type	FY 2012		FY 2013	
	Number of cases	Amount paid	Number of cases	Amount paid
Medical expenses	892	97,905	886	95,025
Medical allowances	947	75,326	945	82,730
Disability pensions	28	861,595	39	905,233
Pensions for raising handicapped children	0	43,744	3	40,785
Bereaved family pensions	32	602,068	31	603,130
Lump-sum benefits for bereaved families	32	227,696	32	220,032
Funeral expenses	62	12,438	59	12,249
Total	1,993	1,920,771	1,995	1,959,184

Note 1:"Number of cases" is the number of approved cases. "Amount paid" is the amounts of the benefits paid for both new and existing cases.

Note 2:Since the amounts are rounded off to the nearest thousand yen, the sum of the figures in each column does not always match the total.



(ii) Relief Service for Infections Acquired through Biological Products

PMDA provides payment of benefits consisting of medical expenses, medical allowances, disability pensions, pensions for raising handicapped children, bereaved family pensions, lump-sum benefits for bereaved families, or funeral expenses for diseases, disabilities, or deaths that occurred on or after April 1, 2004, caused by infections even though biological products (*) were used properly.

* Biological products refer to drugs, quasi-drugs, cosmetics, or medical devices that are manufactured using materials or ingredients derived from humans or other living matter (excluding plants), which are designated as special products requiring special caution from the perspective of health care by the Minister of Health, Labour and Welfare upon hearing opinions from the Pharmaceutical Affairs and Food Sanitation Council.

a. Performance of relief for infections

The performance for FY 2013 is shown below

Fiscal Year	FY 2009	FY 2010	FY 2011	FY 2012	FY 2013
Number of claims	6	6	9	4	7
Number of judged cases	10	7	7	6	4
Approved	8	6	3	4	4
Rejected	2	1	4	2	0
Withdrawal	0	0	0	0	0
Cases in progress*1	3	2	4	2	5
Achievement rate*2	100.0%	85.7%	100.0%	100.0%	100.0%
Median processing time [months]	5.4	6.9	4.4	4.7	4.3

*1 *Cases not concluded at the end of each fiscal year.*

*2 *The percentages of the cases judged within 8 months out of the total number of cases judged during the fiscal year.*

b. Number of claims by type of benefit

The numbers of claims filed in FY 2013 by type of benefit are shown below.

Fiscal Year		FY 2009	FY 2010	FY 2011	FY 2012	FY 2013
Number of claims		6	6	9	4	7
Types of benefit	Medical expenses	5	5	6	2	6
	Medical allowances	6	5	8	4	7
	Disability pensions	0	1	0	0	0
	Pensions for raising handicapped children	0	0	1	0	0
	Bereaved family pensions	0	0	0	0	0
	Lump-sum benefits for bereaved families	0	1	0	0	1
	Funeral expenses	0	1	0	0	1

Note: A single claim could be classified into more than one type of benefit.

c. Judgment status by type of benefit

The number of approved cases and amounts of benefits in FY 2013 by type of benefit are shown below.

(Unit: Thousand yen)

Type	FY 2009		FY 2010		FY 2011		FY 2012		FY 2013	
	Number of cases	Amount paid	Number of cases	Amount paid	Number of cases	Amount paid	Number of cases	Amount paid	Number of cases	Amount paid
Medical expenses	6	375	5	425	3	213	2	83	3	258
Medical allowances	8	567	5	384	3	282	4	282	4	356
Disability pensions	–	–	–	–	–	–	–	–	–	–
Pensions for raising handicapped children	–	–	–	–	–	–	–	–	–	–
Bereaved family pensions	–	2,378	–	2,378	–	2,370	–	2,362	–	2,353
Lump-sum benefits for bereaved families	–	–	1	7,160	–	–	–	–	–	–
Funeral expenses	–	–	1	193	–	–	–	–	–	–
Total	14	3,320	12	10,540	6	2,865	6	2,726	7	2,967

Note: Since the amounts are rounded off to the nearest thousand yen, the sum of the figures in each column does not always match the total.

3.1.(6) Promotion of collaboration with the review and safety departments

- To enhance collaboration with the other divisions at PMDA, information on claims and decisions on approval/rejection of claims for adverse reaction relief benefits were provided to the Offices of Safety etc., with due consideration to protecting personal information. In addition, Office of Relief Funds and Offices of Safety conducted joint meetings about once a month to promote information sharing.
- Based on relevant information obtained through claims submitted for relief benefits, PMDA calls users' attention to cases which have repeatedly occurred though precautions have been already provided in package inserts. The information was described in the "PMDA Request for Proper Use of Drugs" posted on the Medical Product Information web page, explaining points for safe use of drugs etc., in an easy-to-understand way that allows healthcare professionals to readily use the information, in order to further promote the proper use of drug products.

  Reference: The "PMDA Request for Proper Use of Drugs" is distributed via e-mail in "PMDA medi-navi" to healthcare professionals etc.

- The Office of Relief Funds and the Offices of Safety promoted the collaboration by clarifying their roles and responsibilities regarding the "Relief System Consultation Service" and the "Drugs and Medical Devices Consultation Service."

3.1.(7) Appropriate conduct of health and welfare services

- In cases where it is necessary to offer any assistance other than benefit payment in order to provide swift relief for adverse health effects stemming from adverse drug reactions, PMDA conducts health and welfare services for sufferers from adverse health effects as below in accordance with the Act on the Pharmaceuticals and Medical Devices Agency:

(i) Investigative Research for Improvements in Quality of Life of Sufferers of Serious and Rare Adverse Health Effects Caused by Drug Products

As part of health and welfare services, PMDA established an Investigative Research Team for Improvements in the Quality of Life (QOL) of Sufferers from Serious and Rare Adverse Health Effects Caused by Drug Products in April 2006, and the team initiated investigative research to obtain information for examining the ideal way to provide necessary services and measures for improving the QOL of sufferers from serious and rare adverse health effects, who have not necessarily been supported sufficiently by general measures for disabled people. This research project was carried out, taking into account the results (March 2006) of a survey on the actual state of adverse health effects stemming from adverse drug reactions.

In FY 2013, PMDA summarized the operating performance for FY 2012, prepared an investigative research report, and conducted an investigative research in 87 subjects with serious adverse health effects, including Stevens Johnson syndrome, Reye's syndrome, and those similar to Reye's syndrome.

[Contents of the Research]

PMDA collects, analyzes, and evaluates reports, such as survey forms etc., from sufferers from adverse health effects regarding the condition of various efforts in their daily life (87 volunteers in FY 2013).

[Research Team]

Team Leader: Atsushi Ozawa, Professor, Graduate School of Comprehensive Human Sciences, University of Tsukuba (Master's Program in Lifespan Developmental Science)
Takao Takahashi, Professor, School of Medicine, Keio University (Department of Pediatrics)
Kazuo Tsubota, Professor, School of Medicine, Keio University (Department of Ophthalmology)
Chieko Matsunaga, Associate Professor, School of Health and Welfare, International University of Health and Welfare

(ii) Consultation Services to Address Mental Issues etc.

The survey on the actual state of adverse health effects stemming from adverse drug reactions showed the necessity of care for persons with deep mental trauma due to adverse health effects such as diseases, disabilities, etc. caused by adverse drug reactions, as well as the importance of consultation support for persons with remarkable restrictions in daily living due to such adverse health effects. Therefore, PMDA held many discussions with organizations of adverse drug reaction sufferers etc., regarding the conduct of support services for persons who have received benefits under the Relief Systems, and consequently, Consultation Services to Address Mental Issues etc., were initiated in January 2010.

Consultation services by experts who are qualified for welfare were conducted, for the purpose of providing advice etc., on mental care and on the use of welfare services to persons suffering from adverse health effects caused by adverse drug reactions or infections acquired through biological products, and their families. In FY 2013, 46 consultations were performed.

(iii) Distribution of the Benefit Recipient Card

For beneficiaries of adverse reaction relief benefits, in January 2010, PMDA started a service in which a handy, credit-card size certificate is issued upon request. The card shows specific information such as the name of the drug(s) that is considered or suspected to have caused the adverse reaction to the card holder. In FY 2013, the card was issued to 508 persons.

(iv) Investigative Research for Improvements in QOL of Patients with Hepatitis C Caused by Treatment for Congenital Diseases

As part of health and welfare services, PMDA established an Investigative Research Group for Improvements in QOL of Patients with Hepatitis C Caused by Treatment for Congenital Diseases in August 2010, and the group initiated research to study the actual living conditions of sufferers from infections acquired through biological products and thereby obtain information for examining the ideal way to provide necessary services and measures for improving the QOL of sufferers.

In FY 2013, PMDA summarized the operating performance for FY 2012, prepared an investigative research report, and conducted research in 164 subjects.

[Contents of the Project]

PMDA collects, analyzes, and evaluates reports, such as survey forms etc., to clarify the various conditions in daily life of sufferers from serious infections among individuals affected by hepatitis C caused by treatment for congenital diseases (164 volunteers in FY 2013).

[Research Team]

Team Leader: Kugahisa Teshima, Professor, Faculty of Social Welfare, Japan College of Social Work
Namiki Izumi, Deputy Director, Musashino Hospital, Japanese Red Cross Society
Midori Shima, Professor, Department of Pediatrics, Nara Medical University
Akira Terashima, Professor, Faculty of General Welfare, Urawa University

3.1.(8) Appropriate provision of healthcare allowances for SMON patients and HIV-positive patients affected through blood products

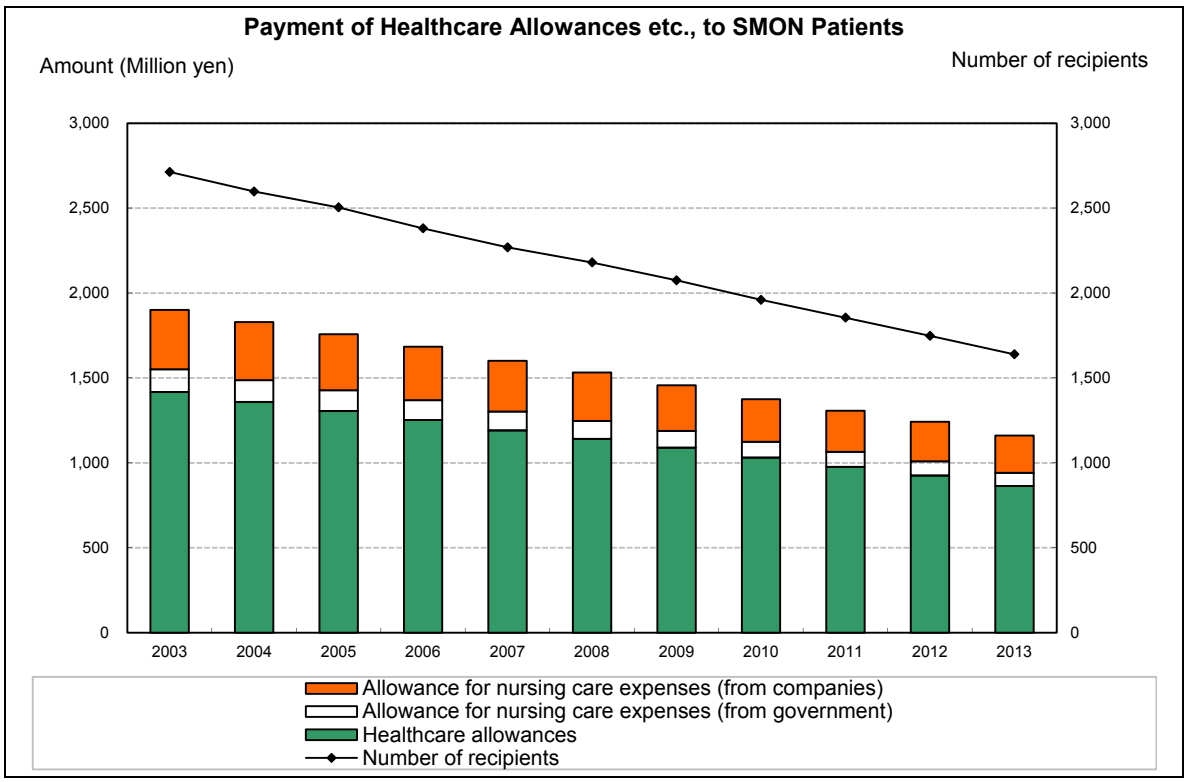
- PMDA appropriately provided healthcare allowances etc., to SMON patients and HIV-positive patients affected through blood products under commission of relevant organizations, giving due consideration to the confidentiality of personal information.

(i) Services for SMON patients (commissioned payment of healthcare allowances)

- PMDA provides healthcare allowances and nursing care expenses to SMON patients for whom a settlement has been reached in court. At the end of FY 2013, the number of patients receiving such allowances was 1,639, and the total amount paid in FY 2013 was 1,161 million yen.

Fiscal Year		FY 2009	FY 2010	FY 2011	FY 2012	FY 2013
Number of recipients		2,075	1,960	1,855	1,748	1,639
Amount paid (thousand yen)		1,457,724	1,375,622	1,306,329	1,241,368	1,160,994
Break down	Healthcare allowances	1,089,491	1,031,376	975,567	924,669	864,462
	Allowance for nursing care expenses (from companies)	268,749	250,946	241,890	233,050	219,630
	Allowance for nursing care expenses (from government)	99,485	93,300	88,872	83,650	76,902

(Note) Since the amounts of the benefits are rounded off to the nearest thousand yen, the amount paid does not always match the sum of the breakdown categories.



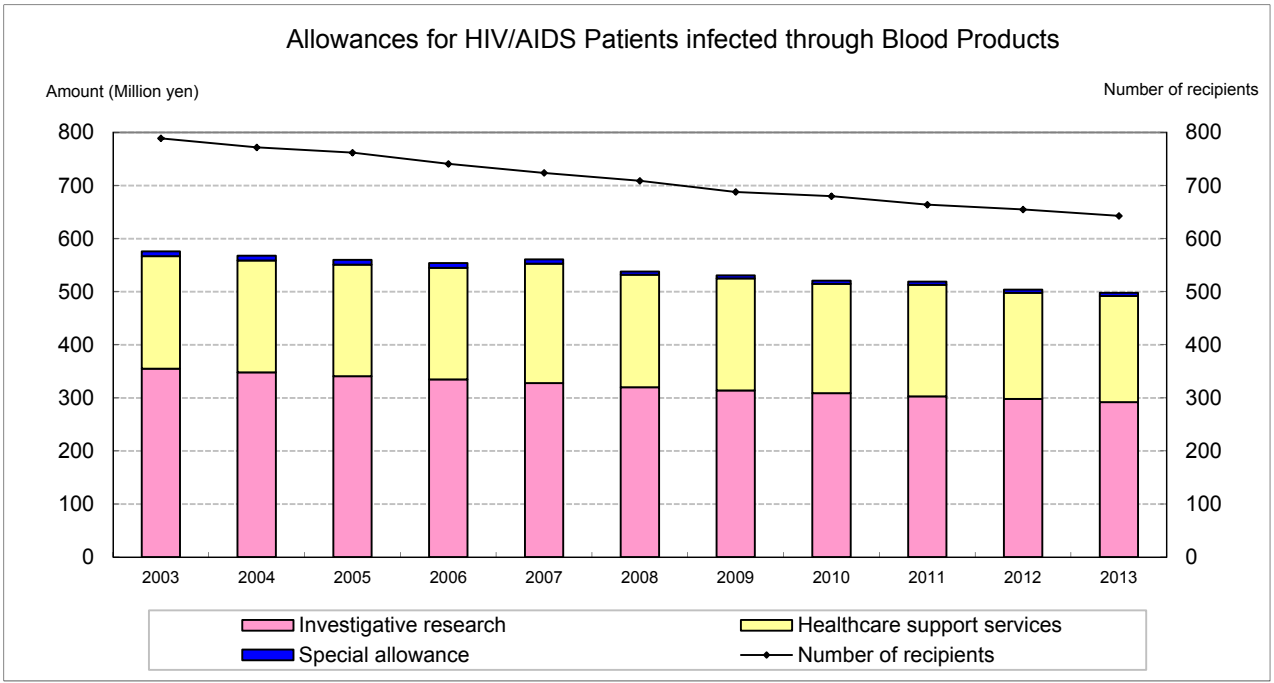
(ii) HIV-related services (commissioned payment of healthcare allowances)

- PMDA provides allowances relating to the following 3 services for HIV-positive patients affected through blood products under commission of the relevant organization. In FY 2013, 529 HIV-positive patients received allowances relating to the investigative research, 112 AIDS patients received allowances relating to the healthcare support service and 2 AIDS patients received special allowances. The total number of patients receiving allowances relating to the 3 services was 643, and the total amount paid in FY 2013 was 498 million yen.

  a. Payment of healthcare allowances for HIV-positive patients (who have not developed AIDS), as part of the investigative research
  b. Payment of healthcare allowances for AIDS patients for whom a settlement has been reached in court, as the healthcare support service
  c. Payment of special allowances etc., for AIDS patients for whom a settlement has not been reached in court

Fiscal Year	FY 2009		FY 2010		FY 2011	
	Number of recipients	Amount paid (thousand yen)	Number of recipients	Amount paid (thousand yen)	Number of recipients	Amount paid (thousand yen)
Investigative research	566	313,676	562	309,355	547	302,763
Healthcare support services	120	210,600	116	206,100	115	210,000
Special allowance	2	6,300	2	6,300	2	6,276
Grand Total	688	530,576	680	521,755	664	519,039

Fiscal Year	FY 2012		FY 2013	
	Number of recipients	Amount paid (thousand yen)	Number of recipients	Amount paid (thousand yen)
Investigative research	540	297,790	529	292,349
Healthcare support services	112	199,500	112	199,650
Special allowance	3	6,362	2	6,232
Grand Total	655	503,652	643	498,230



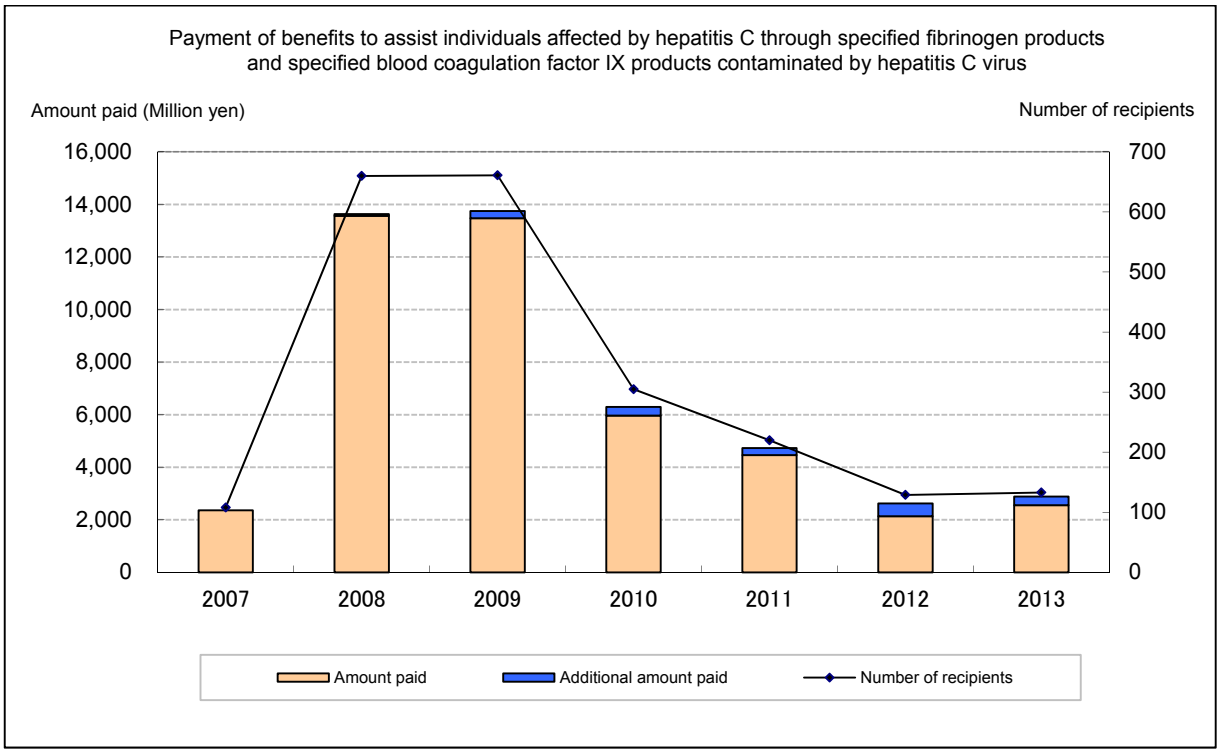
3.1.(9) Appropriate provision of the payment of benefits to assist individuals affected by hepatitis C through specified fibrinogen products and specified blood coagulation factor IX products contaminated by hepatitis C virus

- PMDA started the service of providing benefits to individuals affected by hepatitis C according to the Act on Special Measures concerning the Payment of Benefits to Assist Individuals Affected by Hepatitis C through Specified Fibrinogen Products and Specified Blood Coagulation Factor IX Products Contaminated by Hepatitis C Virus* on January 16, 2008. The number of benefit recipients was 133, with 2,888 million yen as the total amount paid in FY 2013.

* The revised Act went into effect on September 14, 2012, and thereby the time frame for claiming benefits was extended by 5 years (until January 30, 2018).

	FY 2007	FY 2008	FY 2009	FY 2010
Number of recipients	108	660	661	305
(Of which: number of recipients of additional payment)	(0)	(4)	(22)	(20)
Amount paid (thousand yen)	2,360,000	13,632,000	13,748,000	6,293,000
(Of which: amount of additional payment)	(0)	(68,000)	(272,000)	(324,000)
Number of consultations	16,814	3,607	894	1,286

	FY 2011	FY 2012	FY 2013
Number of recipients	220	129	133
(Of which: number of recipients of additional payment)	(20)	(28)	(18)
Amount paid (thousand yen)	4,732,000	2,624,000	2,888,000
(Of which: amount of additional payment)	(268,000)	(488,000)	(332,000)
Number of consultations	674	982	473



3.2. Reviews and Related Services and Safety Measures Services

In order to enable the public to safely use drugs and medical devices that meet international standards, through reviews and related services and post-marketing safety measures, PMDA is required to provide more effective drugs and medical devices to clinical practice faster and with greater safety, while ensuring that drugs and medical devices are used properly, preventing health hazards, and responding appropriately and promptly if any hazard occurs. To this end, PMDA has taken the following operations to reinforce the systems for consultations/reviews and post-marketing safety measures, and to organically link the operations, thereby achieving the Mid-term Targets and FY 2013 plan.

To deal with products using advanced science and technologies in a more focused manner, the Science Board consisting of external experts in the areas of medicine, dentistry, pharmaceutical sciences,

engineering, etc., and its secretariat, the Office of Review Innovation, were established in FY 2012. In FY 2013, PMDA focused on these efforts to continuously improve the quality of its operations ranging from reviews/consultations to post-marketing safety measures.

3.2.(1) Accelerated access to the latest drugs and medical devices

New drugs

- Various measures were implemented or reviewed with the aim of increasing the number of reviewers and improving the quality of reviews, based on the 5-year Strategy for Medical Innovation (Medical Innovation Conference on June 6, 2012), the successor to the 5-year Strategy for Creation of Innovative Pharmaceuticals and Medical Devices (dated April 26, 2007), and with an eye on “Japan Revitalization Strategy - JAPAN is BACK-” and “Healthcare and Medical Strategy” formulated on June 14, 2013.

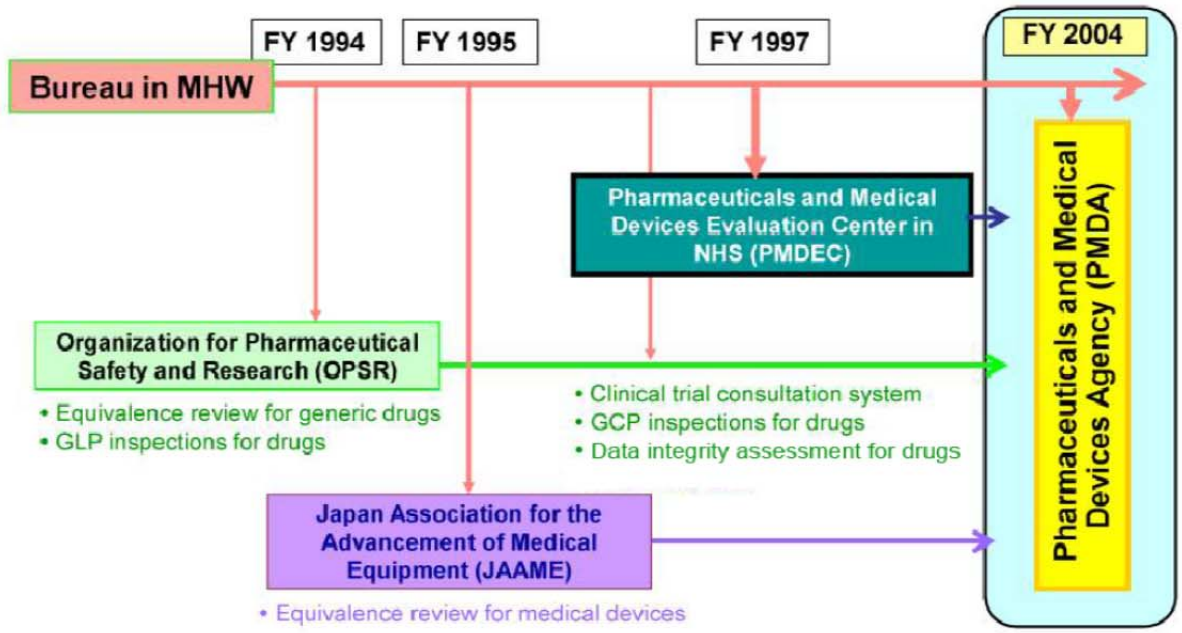
(i) Appropriate and prompt reviews

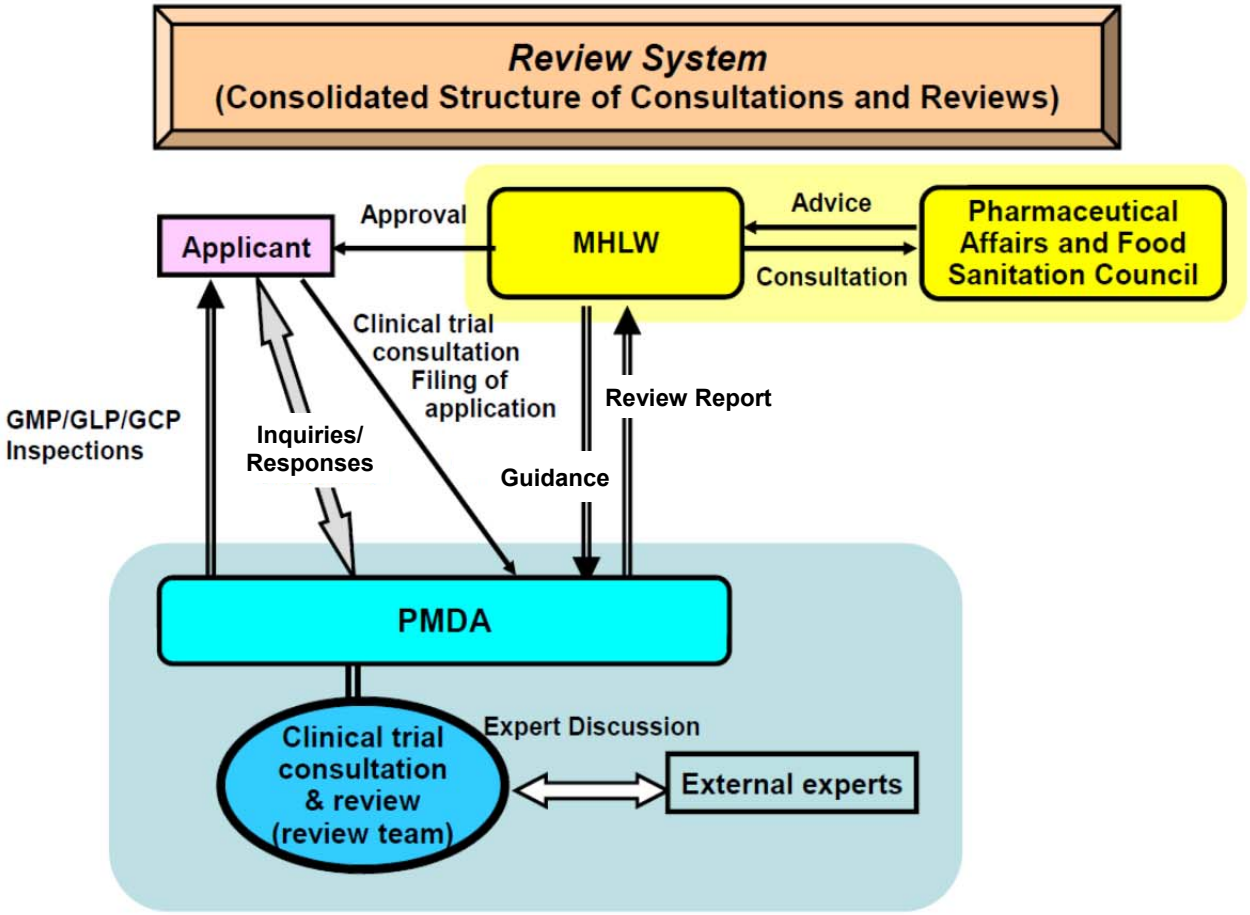
a. Structure for clinical trial consultations and reviews

- The review system for drugs and medical devices has been significantly improved since 1997. In FY 2004, PMDA was founded to consolidate review functions while the final authority for approval of drugs and medical devices was left to the Ministry of Health, Labour and Welfare (MHLW).Further improvements in the review system were made by taking the following measures:

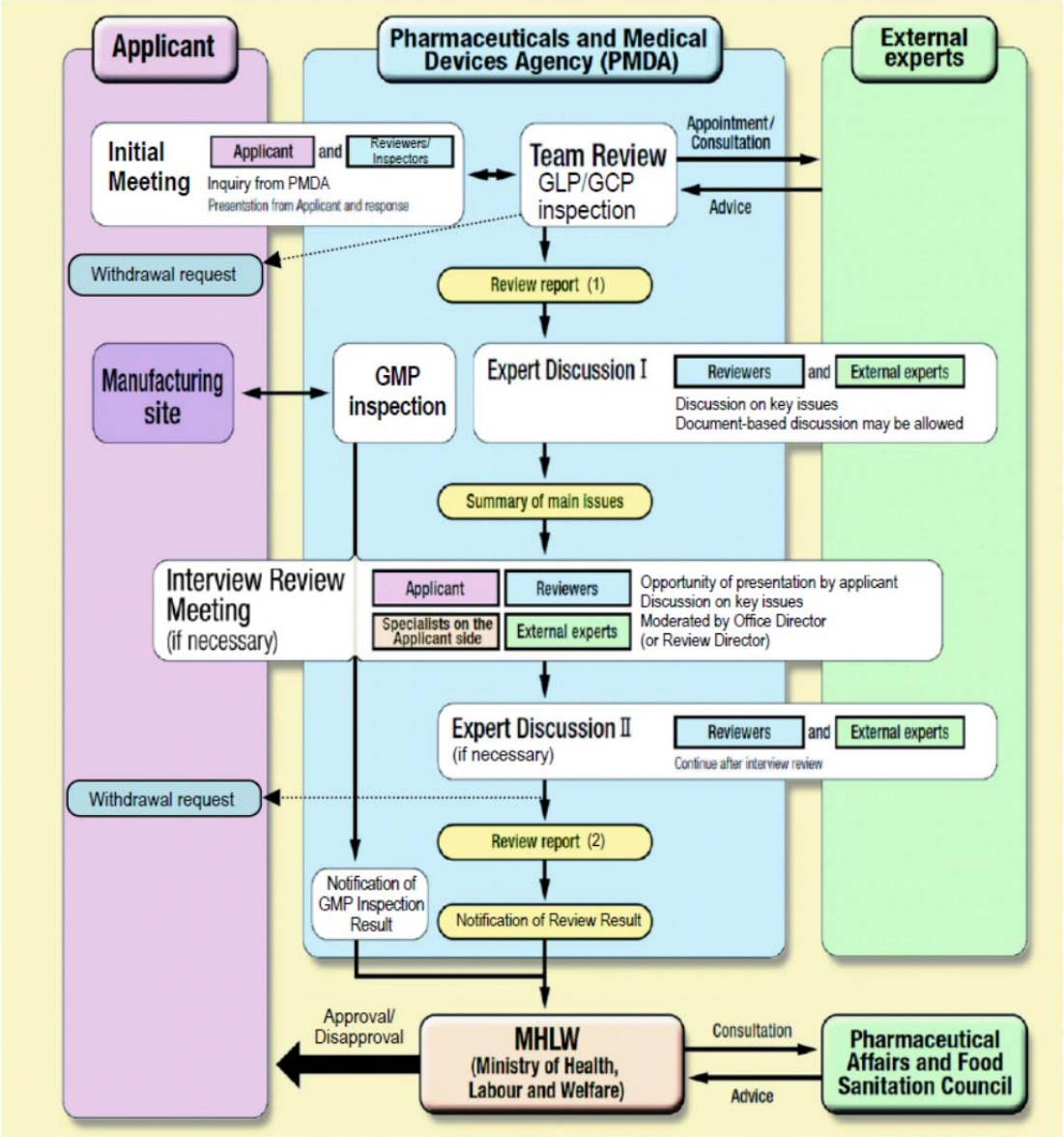
  1) In order to ensure the consistency and efficiency, the roles of three review-related agencies were re-examined thoroughly, and integrated into one agency as "incorporated administrative agency, the Pharmaceuticals and Medical Devices Agency."
  2) Substantial increase in the number of staff including reviewers.
  3) Introduction of a coherent system in which the process from clinical trial consultations until reviews is conducted by the same team with the same staff members.
  4) Enhancement of reviews of biological and biotechnology-derived products.
  5) Reinforcement of functions for reviewing medical devices.

Transition of approval review system on drugs and medical devices





Flowchart of review process

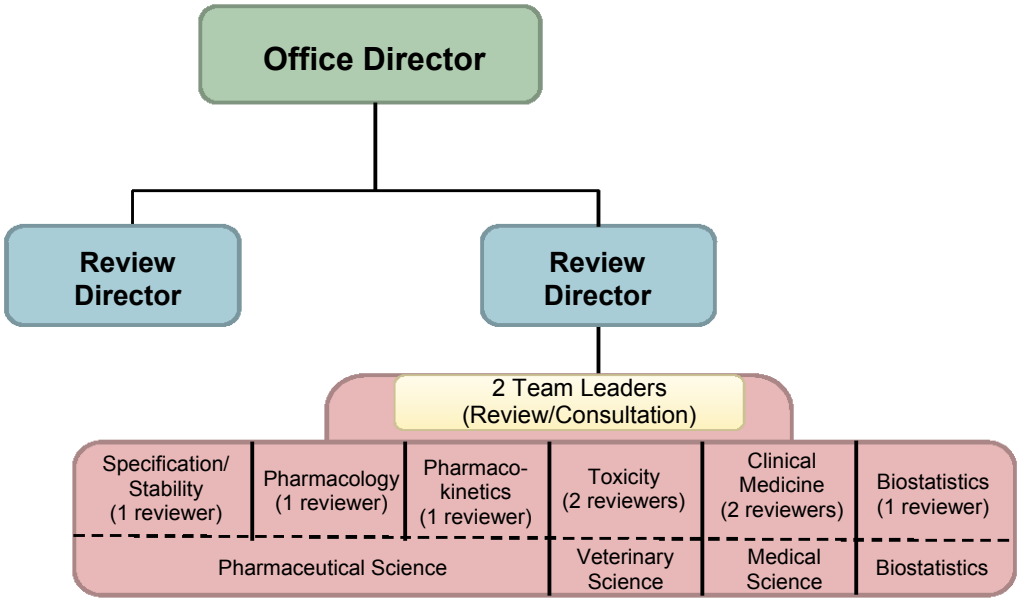


Review Performance for FY 2013 (drugs)

(1) Number of Expert Discussions conducted: 244 (187 document-based discussions, 57 meetings)
(2) Applications deliberated at the Drug Committees (under Pharmaceutical Affairs and Food Sanitation Council [PAFSC]): 89
Applications reported to the Drug Committees (under PAFSC): 39

- Reviews of new drugs were conducted by review teams under the guidance of an office director and a review director. As a general rule, each review team consists of experts who have academic degrees in pharmaceutical science, veterinary medicine, medicine, biostatistics, and other specialized courses. Each review team is typically comprised of team leader(s), deputy team leader(s), and reviewers specializing in quality, toxicology, pharmacology, pharmacokinetics, clinical medicine, or biostatistics.

Organization Chart for Reviews of New Drugs



- In order to strengthen the review system, PMDA increased the number of reviewers allocated to the categories where many new drug applications were being filed and the review process for them was likely to be prolonged.
- Reviews of new drug applications are shared among the responsible offices and teams according to the review categories by therapeutic area. The review categories are as follows:

Review Categories Covered by the Offices of New Drugs

Office	Review Categories	
Office of New Drug I	Category 1	Gastrointestinal drugs, dermatologic drugs, immunosuppressive drugs, and others (not classified as other categories)
	Category 6-2	Hormone drugs, drugs for metabolic disorders (including diabetes mellitus, osteoporosis, gout, and inborn errors of metabolism)
Office of New Drug II	Category 2	Cardiovascular drugs, antiparkinsonian drugs, anti-Alzheimer's drugs
	Category 5	Reproductive system drugs, drugs for urogenital system, combination drugs
	Radiopharmaceuticals	Radiopharmaceuticals
	In vivo diagnostics	Contrast agents, reagents for function tests (excluding *in-vitro* diagnostics)
Office of New Drug III	Category 3-1	Central/peripheral nervous system drugs (excluding anesthetic drugs)
	Category 3-2	Anesthetic drugs, sensory organ drugs (excluding drugs for inflammatory diseases), narcotics
Office of New Drug IV	Category 4	Antibacterial drugs, antiviral drugs (excluding AIDS drugs), antifungal drugs, antiprotozoal drugs, anthelmintic drugs
	Category 6-1	Respiratory tract drugs, anti-allergy drugs (excluding dermatologic drugs), sensory organ drugs (drugs for inflammatory diseases)
	AIDS drugs	Anti-HIV drugs
Office of New Drug V	Oncology drugs	Antineoplastic drugs
Office of Cellular and Tissue-based Products	Cellular and tissue-based products	Regenerative medicine products (cellular and tissue-based products)
	Gene therapy products	Gene therapy products, Cartagena
	Bio-CMC	Quality of biologics, biosimilars
	Biological devices (quality)	Biological devices (quality)
Office of Vaccines and Blood Products	Vaccines	Vaccines, antitoxic serum, etc.
	Blood products	Blood products

- PMDA conducted clinical trial consultations for new drugs based on the team-reviewed guidance plan drafted by three persons, the Review Director as well as the consultation leader and the deputy consultation leader, who were appointed from among the review team members.

b. Reinforcement and improvement in the transparency of the progress management of reviews

- As an effort to further accelerate reviews and related services, the project management system was introduced in FY 2008 for progress management and coordination of reviews of new drugs. In FY 2013, based on the experience accumulated so far, this scheme was further integrated into the review system.
- In order to conduct reviews and related services promptly and appropriately to achieve the target review times as specified in the Mid-term Plan, PMDA held meetings of the Progress Management Committee for Reviews and Related Services once every 3 months to ensure that the Chief Executive and other executives of PMDA can accurately grasp the progress of reviews and related services and support improvement, as needed. In this way, operational progress was monitored,

while particularly relevant information for new drugs was dealt with comprehensively and approaches for solving operational challenges were considered.

- The Review Segment Committee for Progress Management with the Director of the Center for Product Evaluation as its head, to control the progress of reviews, was continuously convened throughout FY 2013. In the meetings, opinions for the advancement of the system were exchanged, information on the overall review status for new drugs and associated issues, including GCP and GMP inspections, were shared, measures addressing challenges and future approaches were examined, and the detailed review status of new drugs and other products under review were reported. (11 meetings were held in FY 2013.)

  At the Review Segment Committee for Progress Management, taking into account reports from office directors of review divisions, necessary guidance was continuously provided by the Director of the Center for Product Evaluation and the Associate Center Director, and the results of discussion of issues and improvement measures for products with a difficulty that required a prolonged review time were notified within review segments.

- In accordance with the "Way of Explaining the Progress of Review of New Drug Applications" (PMDA Notification No. 1227001 dated December 27, 2010), the progress of the PMDA review is to be communicated to applicants in each review stage. The relevant office director appropriately held meetings with applicants upon their request to explain the progress and outlook of the review to them.

c. Standardization of review

- From the perspective of clarification of review standards, reviewers were informed of the "Points to be Considered by the Review Staff Involved in the Evaluation Process of New Drug" released in FY 2008 that provide basic considerations for review. The document is posted on the PMDA website.

d. Consultations and reviews based on medical care needs

- PMDA actively exchanged opinions with healthcare professionals by participating in academic conferences etc.,, in and out of Japan, to comprehend their needs. The Agency conducted consultations and reviews, taking into account the information obtained in this manner.

- In order to encourage pharmaceutical companies to develop drugs and indications that have been approved in Europe and the U.S. but not approved in Japan, the Investigational Committee on Medically Necessary Unapproved Drugs and Off-Label Use Drugs (chaired by Dr. Tomomitsu Hotta, President of National Cancer Center) was established in the MHLW in February 2010, and has been active. PMDA continuously supports this Committee, and deals with clinical trial consultations and reviews based on the results of the investigations by the Committee.

- In order to resolve the drug lag of unapproved drugs and off-label use drugs with high medical needs, PMDA promptly and timely grasped information on approval status etc., at FDA and EMA, and collected/organized evidence information etc., and then developed a database of unapproved drugs to compare the information to the approval status etc., in Japan. Specifically, PMDA has registered 308 products including drugs with a new active ingredient approved between April 2009 and February 2014, and released them on the PMDA’s website with considerations of undisclosed information for some of contents of the database.

e. Consistency between clinical trial consultations and reviews

- In order to ensure the consistency between clinical trial consultations and reviews, review team members are involved in all the clinical trial consultations for products falling under the category to which they are assigned. Coherence from consultations to reviews is maintained and teams are flexibly organized as necessary.

  Also, in FY 2013, to further secure the consistency of clinical trial consultations etc., efforts to provide feedback information on previous clinical trial consultations were started.

f. Appropriate conduct of re-examination and re-evaluation

- When a certain period has passed since approval of new drugs, re-examinations are conducted to confirm the efficacy and safety, based on data of use-results surveys that have been conducted by marketing authorization holders (MAHs) etc.

  Already-approved drugs that have been specified by the Minister of Health, Labour and Welfare are re-evaluated for their efficacy and safety, in the light of the current standards of medical/ pharmaceutical sciences, based on the data submitted by MAHs. In addition, re-evaluations for quality are conducted to ensure that the dissolution of drugs in solid oral dosage forms meets the quality requirements. Once the quality has been assured, an appropriate dissolution specification is established to ensure that the quality of the drug in solid oral dosage forms is maintained at a certain level.

- In FY 2013, 121 products underwent re-examination, while no product underwent re-evaluation for drug efficacy, and no product underwent re-evaluation for quality. As re-evaluation for quality, scientific evaluation had practically been terminated for traditional Chinese medicines, non-steroidal anti-inflammatory agents, and antimetabolites by the end of FY 2013.

Number of Re-examinations/Re-evaluations Conducted

		FY 2009	FY 2010	FY 2011	FY 2012	FY 2013
Products that underwent re-examination		164	115	81	50	121
Re-evaluations	Products that underwent re-evaluation for drug efficacy	0	0	0	0	0
	Products that underwent re-evaluation for quality	12	53	0	0	0

Note: Number of products for which a notice of re-examination/re-evaluation results was issued in respective fiscal year.

g. Promotion of digitization in reviews

- In addition to a new electronic submission and review system used by PMDA, Pharmaceutical and Food Safety Bureau (PFSB) in MHLW, Regional Bureaus of Health and Welfare, and prefectural governments, the system for reviews and related services is comprised of the following individual systems necessary for executing reviews, inspections, and management of user fees: (i) review support system for drugs etc., (ii) new drug database system, (iii) DEVICE System, (iv) conformity audit support system, (v) medical device review support system, (vi) clinical trial database system, (vii) eCTD viewer system, (viii) medical device malfunction reporting system, and (ix) management system for information on adverse drug reactions (*[viii] is only used to reference data) etc.

- This new electronic submission and review system enables the PMDA staff to manage progress through the entire process from acceptance of applications for marketing approval and manufacturer's license and notifications, etc., on drugs, quasi-drugs, cosmetics and medical devices, until those approvals or licenses come into effect. In addition, PMDA uses this system for

operations related to registration and licensing, such as entry of the information included in product application forms (product application management software), acceptance of the product applications, data exchange among review/inspection authorities, recording of review memorandums, preparation of Marketing Approval Documents and management of the registration list.

- The status of development, upgrading, etc., of review systems in FY 2013 is shown below.

1) Optimization Plan for Operations and Systems (next review system)

- Toward the realization of the Optimization Plan for Operations and Systems, requirements, etc., for the existing review system were handled, the systems were integrated, and linkage test and comprehensive test were completed for the next review system intended for uniform management of information. In addition, operational tests were carried out to confirm that operations can be performed without delay in line with a scenario created under the actual operational conditions.

2) Upgrading the eCTD viewer system

- The eCTD viewer system was upgraded to improve the related hardware and software to pursue integration with the next review system in the new LAN environment.

3) Development of the reporting system for medical device malfunctions during clinical trials

- The reporting system for medical device malfunctions etc., during clinical trials had been developed to receive reports etc., from sponsors etc., on device malfunctions during clinical trials under the Pharmaceutical Affairs Act and to enhance the efficiency of management of the information.

4) Development of functions of the brand name similarity verification system

- For brand names of drugs for which application is submitted, the brand name similarity verification system was developed mainly for the purpose of improving the work efficiency for verification of similarities in names to other products.

5) Conversion to electronic data of final decision documents for regulatory approval for drugs etc., and clinical trial notifications

- Final decision documents for regulatory approval for drugs, etc., clinical trial notifications for agents and devices, etc., were converted into digital image data which can reduce storage space and be stored for a long time. PMDA promoted the efficiency and acceleration of reviews by using the search function to view these image data.

- For the purpose of more widely utilizing information and enhancing the efficiency of reviews/consultations, the data were converted to PDF data with transparent text so that documents/materials on designation of orphan drugs, simple consultations, consultations, post-marketing surveillance plans, etc., can be searched for text information in them.

h. Improvement of environment for eCTD

- The eCTD verification tool and eCTD off-line viewer that are distributed free of charge to applicants were upgraded so that the tools can work with Windows 8, Internet Explorer 10, Acrobat XI, etc., to improve applicants' convenience.

i. Development of the Japanese Pharmacopoeia

- In FY 2013, the Japanese Pharmacopoeia Draft Committee held a total of 95 meetings, and posted information on the PMDA website to seek public comments regarding 232 official monographs (60 new articles, 172 amendments, 1 deletion), 8 general tests (1 new test, 7 amendments), 13 ultraviolet-visible reference spectra, 17 infrared reference spectra, amendments to other General Notices, and partial revision of the General Rules for Preparations as a draft of Supplement 2 to the 16th edition of the Japanese Pharmacopoeia (JP) (published as a Ministerial Announcement in February 28, 2014).

  The number of official monographs reported to MHLW thus far was as follows:

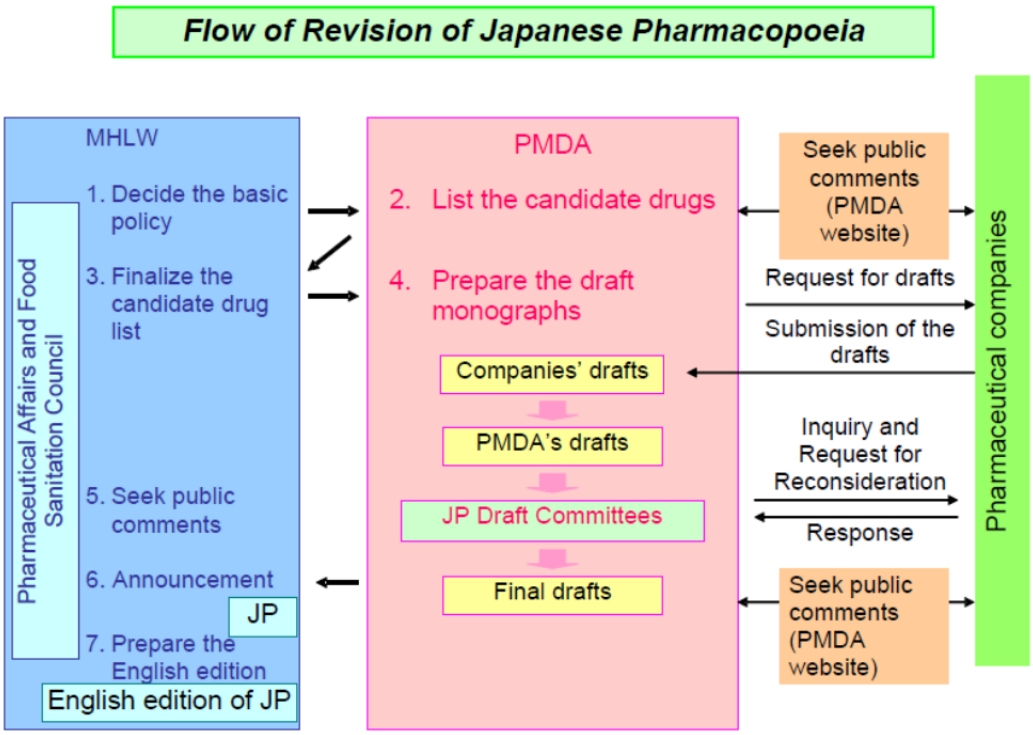
Month and year reported	Mar. FY 2007	Nov. FY 2008	Mar. FY 2009	Aug. FY 2009	Aug. FY 2010	Mar. FY 2012	Jan. FY 2013	Sep. FY 2013
New monographs	90	1	106	-	106	77	0	60
Amendments	171	1	122	2	330	176	1	172

Note: The JP drafts prepared include drafts for the official monographs shown in this table as well as drafts for General Notices, General Rules for Preparations, General Rules for Crude Drugs, General Tests, Processes and Apparatus, and General Information. PMDA usually provides those drafts to MHLW 6 months before the publication. In FY 2013, the draft of Supplement 2 to the 16th edition of the Japanese Pharmacopoeia (JP) (published as a Ministerial Announcement in February 28, 2014) was reported in September 2013.

Ministerial Announcement on the Japanese Pharmacopoeia (JP) by MHLW

	15th edition	15th edition Supplement 1	Partial revision	15th edition Supplement 2	Partial revision	16th edition	16th edition Supplement 1	Partial revision	16th edition Supplement 2
Month and year announced	Mar. FY 2006	Sep. FY 2007	Mar. FY 2009	Sep. FY 2009	Jul. FY 2010	Mar. FY 2011	Sep. FY 2012	May FY 2014	Feb. FY 2014
New monographs	102	90	1	106	0	106	77	0	60
Amendments	272	171	1	122	2	330	176	1	173
Deleted monographs	8	6	0	1	0	15	4	0	1
Total number of monographs	1,483	1,567	1,568	1,673	1,673	1,764	1,837	1,837	1,896

- PMDA provides information such as the status of the JP draft review or international harmonization of pharmacopoeial standards, in addition to calling for public comments on drafts on the Japanese Pharmacopoeia page of PMDA's Japanese website. In addition, the Agency gives information on international harmonization of pharmacopoeial standards to overseas users on the Japanese Pharmacopoeia page of the PMDA English website.
  (URL: http://www.pmda.go.jp/kyokuhou.html)



j. Implementation of Master File workshop

- Workshops were held twice for drug substance manufacturers, in-country representatives, MAHs, etc., to explain how to fill out the applications for registration of Master File and to present examples of PMDA's responses to inquiries after the registration.

(ii) Introduction of new review systems

a. Implementation of prior assessment consultations

- To preliminarily evaluate the quality, efficacy and safety of drugs from the pre-application stage, PMDA had offered prior assessment consultations as a pilot scheme since FY 2009. The scheme has been formally implemented since FY 2011. In FY 2013, the request forms were separately received for consultations to be conducted in the first half of the fiscal year and for those in the second half. Consultations provided are broken down by review category, as follows.

  Review Category 1, 1 product (number of consultation categories, 6; the same applies hereinafter); Review Category 6-2, 1 product (6); Review Category 2, 1 product (1); Review Category 3, 1 product (6); Review Category 6-1, 1 product (4); Oncology drugs, 2 products (6); Blood products, 2 products (3)

  (* When consultations were provided for an identical product in the first and second halves of the fiscal year for different consultation categories, it was included as 1 product).

b. Efforts toward introduction of the system of risk managers and risk management plans for drugs

- To consistently manage the safety of drugs from the clinical trial stage to post-marketing stage 13 risk managers were placed in 12 review teams. In each new drug review team, the safety assessment and reports on cancellation of conditions for approval in relation to post-marketing surveillance (PMS) were prepared.
- Information regarding all the submitted risk management plans (RMPs) for drugs was shared among risk managers, and key issues in the review were discussed. In addition, case examples of

post-marketing modification of RMPs were shared to ensure the consistency. In FY 2013, RMPs for 4 products were made public.

c. Consideration toward the construction of the Advanced Review and Consultation with Electronic Data

- Task Force for Advanced Review and Consultation with Electronic Data (decided by the Chief Executive) was set up in September to consider issues for the establishment of the advanced review and consultation with electronic data for the purpose of reducing the burden on applicants and improving the quality of reviews and consultations by electronically accumulating application data, performing analyses by advanced methods, and utilizing the information.

  Toward the establishment of the advanced review and consultation with electronic data, PMDA exchanged opinions continuously with the pharmaceutical industry regarding various issues, and held a briefing session for pharmaceutical companies etc. Also, after the introduction of the basic system, electronic clinical data were provided on a trial basis, analyses of those data using the introduced software were performed, and a pilot program to confirm its feasibility was conducted.

(iii) Approaches to solve the drug lag

- The targets for total review time (from application date to approval date; the same applies hereinafter) for drug applications submitted on or after April 1, 2004, the regulatory review time (including the review time at the MHLW; the same applies hereinafter), and the applicant's time were set up. Both the regulatory authorities and applicants have been making efforts toward the achievement of the targets.
- New drug applications (for drugs that are clearly different from approved drugs in terms of active ingredients, contents, administration, dosage, indications, efficacy, etc.; the same applies hereinafter) submitted to MHLW were reviewed by PMDA review teams consisting of experts in pharmaceutical science, veterinary medicine, medicine, biostatistics, etc.
- In order to ensure consistency among the review teams and carry out review work promptly and appropriately with regard to new drugs, PMDA provided the services in accordance with the "Procedures for Reviews of New Drugs" regarding reviews and related procedures, and the SOPs for various related operations.
- The status of reviews of new drugs (excluding applications of drug products* that are reviewed by PMDA and approved only through the administrative process at MHLW) in FY 2013 is shown below:

  * Drugs that are identical to approved drugs in terms of active ingredients, administration, dosage and indications or are within the scope of approved drugs in terms of administration, dosage and indications.

a. Review times for new drugs (priority review products designated by the Minister of Health, Labour and Welfare; hereinafter referred to as "priority review products")

Median Review Time for New Drugs (Priority Review Products)

Targets

Fiscal Year	FY 2009	FY 2010	FY 2011	FY 2012	FY 2013
Total review time [months]	11	10	9	9	9
Regulatory review time [months]	6	6	6	6	6
Applicant's time [months]	5	4	3	3	3

* *PMDA is aiming to achieve the review times shown in the table for 50% (median) of products.*

Results

Fiscal Year	FY 2009	FY 2010	FY 2011	FY 2012	FY 2013
Total review time [months]	11.9 (24.5)	9.2 (12.6)	6.5 (9.2)	6.1 (9.0)	7.2 (9.1)
Regulatory review time [months]	3.6 (6.7)	4.9 (6.8)	4.2 (5.5)	3.8 (4.7)	3.6 (5.1)
Applicant's time [months]	6.4 (15.9)	3.4 (7.6)	2.0 (4.7)	1.5 (5.7)	3.8 (5.2)
Number of approved applications	15	20	50	53	42

Note 1: Products covered were those for which applications were filed in or after FY 2004. The number of cases is based on ingredients. For details, refer to the list of approved products included in the supplementary information

Note 2: Values in parentheses are reference values (80th percentile).

Note 3: In or after FY 2010, public knowledge-based application products related to the "Study Group on Unapproved and Off-label Drugs of High Medical Need" are included in priority review products.

Reference: When excluding public knowledge-based applications for unapproved drugs (FY 2010 and after)

Fiscal Year	FY 2010	FY 2011	FY 2012	FY 2013
Total review time [months]	12.0 (13.2)	9.2 (10.7)	9.0 (10.0)	8.0 (9.9)
Regulatory review time [months]	5.3 (7.9)	4.1 (5.5)	3.4 (4.9)	3.4 (5.0)
Applicant's time [months]	6.0 (7.9)	5.0 (7.0)	4.6 (6.8)	4.1 (6.2)
Number of approved applications	13	18	25	31

- Priority reviews are conducted for applications for orphan drugs and other drugs that are regarded as having particularly high medical need (drugs for serious diseases and with distinctly superior efficacy or safety as compared to existing drugs or therapies). In FY 2013, 42 priority review products (including 11 public knowledge-based applications for the "Study Group on Unapproved and Off-label Drugs of High Medical Need") were approved.

- In FY 2013, there were 10 applications intended for priority review for drugs with particularly high medical needs, 8 applications were judged as “applicable” and 1 application was judged as “not applicable.” As of the end of FY 2013, there was 1 product under investigation.
- For priority review products approved in FY 2013, the median total review time was 7.2 months and the median regulatory review time was 3.6 months, achieving the target review times. The median applicant's time was 3.8 months, not achieving the target time, but toward its improvement, PMDA has been asking companies of new drugs to provide cooperation and to proactively utilize clinical trial consultations before filing applications, through periodic exchanges of opinions between the industry and PMDA.

  The priority review products accounted for 30% of products approved in FY 2013, showing a reduction from 40% in FY 2012.

b. Review times for new drugs (standard review products)

Median Review Time for New Drugs (Standard Review Products)

Targets

Fiscal Year	FY 2009	FY 2010	FY 2011	FY 2012	FY 2013
Total review time [months]	19	16	12	12	12
Regulatory review time [months]	12	11	9	9	9
Applicant's time [months]	7	5	3	3	3

* *PMDA is aiming to achieve the review times shown in the table for 50% (median) of product.*

Results

Fiscal Year	FY 2009	FY 2010	FY 2011	FY 2012	FY 2013
Total review time [months]	19.2 (24.8)	14.7 (22.7)	11.5 (15.7)	10.3 (11.9)	11.3 (12.3)
Regulatory review time [months]	10.5 (15.3)	7.6 (10.9)	6.3 (8.2)	5.7 (7.1)	6.7 (8.0)
Applicant's time [months]	6.7 (10.7)	6.4 (12.2)	5.1 (9.6)	4.2 (6.0)	4.6 (6.5)
Number of approved applications	92	92	80	81	96

Note 1: Products covered were those for which applications were filed in or after FY 2004. The number of cases is based on ingredients. For details, refer to the list of approved products included in the supplementary information

Note 2: Values in parentheses are reference values (80th percentile).

- For standard review products approved in FY 2013, the median total review time was 11.3 months and the median regulatory review time was 6.7 months, achieving the target times. The median applicant's time was 4.6 months, not achieving the target review time, but toward its improvement, PMDA has been asking companies of new drugs to provide cooperation and to proactively utilize clinical trial consultations before filing applications, through periodic exchanges of opinions between the industry and PMDA.
- The number of applications under review at the end of FY 2013 was 96 (including 19 applications for orphan drugs; 4 public knowledge-based applications for unapproved drugs; 6 applications for

priority review products excluding orphan drugs and public knowledge-based applications for unapproved drugs).

Review Status of New Drugs by Fiscal Year of Application

New drugs (FY of submission)	Applications	Approved	Not approved	Withdrawn	Under review
In or before FY 2003 ending Mar. 31, 2004	140	108	0	29	3
FY 2004	87	78	0	9	0
FY 2005	57	50	0	7	0
FY 2006	102	93	0	9	0
FY 2007	92	78	0	14	0
FY 2008	81	76	0	4	1
FY 2009	106	87	1	18	0
FY 2010	116	105 (1)	0	11	0 [-1]
FY 2011	130	128 (3)	0	2	0 [-3]
FY 2012	139	130 (98)	0	4 (2)	5 [-100]
FY 2013	123	36 (36)	0	0	87 [87]
Total	1,173	969 (138)	1	107 (2)	96 [-17]

Note 1: Values in parentheses indicate those processed in FY 2013 (included in values on their left).
Note 2: Values in brackets indicate difference from the status reported in FY 2012.

Number of Applications Processed and Time Spent by Review Process

	Review process	1. From receipt of applications to initial meeting	2. From initial meeting to Expert Discussion	3. From Expert Discussion to notification of review result	4. From notification of review result to approval
FY 2013	Number of applications processed	46 applications	42 applications	111 applications	138 applications
	Median total review time [days]	70.5 days	181.5 days	28.0 days	44.0 days

Note 1: The median total review times are the sum of the regulatory review time and applicants' time.
Note 2: Values are calculated based on the applications filed in or after April 2004.

(iv) Efficient conduct of clinical trial consultations

a. Conduct of priority consultations

- In FY 2013, there were no requests for designation for priority consultations of drugs that are considered to have particularly high medical need. PMDA conducted 2 consultations for a designated ingredient.

b. Acceleration of the procedure for clinical trial consultations

- As for the acceleration of clinical trial consultations, PMDA streamlined the procedures for applicants to request consultations as well as for PMDA to receive requests. The revised procedures were implemented for requests for consultations to be provided in or after October 2010. The target duration from consultation request to consultation, about 2 months, has been firmly maintained.

c. Implementation of clinical trial consultations and improvement of the system

Number of Consultations Conducted

	FY 2009	FY 2010	FY 2011	FY 2012	FY 2013
Conducted consultations	370	390	447	387	354
Withdrawals	23	44	30	20	30
Total (conducted and withdrawn consultations)	393	434	477	407	384

Number of Prior Assessment Consultations for Drugs Conducted

	FY 2009	FY 2010	FY 2011	FY 2012	FY 2013
Conducted consultations	33	30	33	19	32
Withdrawals	0	0	0	0	0
Total (conducted and withdrawn consultations)	33	30	33	19	32

Number of Consultations on Pharmacogenomics/Biomarkers Conducted

	FY 2009	FY 2010	FY 2011	FY 2012	FY 2013
Conducted consultations	1	1	1	0	0
Withdrawals	0	0	0	0	0
Total (conducted and withdrawn consultations)	1	1	1	0	0

Number of Consultations on Drug Product Eligibility for Priority Review Conducted

	FY 2009	FY 2010	FY 2011	FY 2012	FY 2013
Conducted consultations	–	–	2	7	10
Withdrawals	–	–	0	0	0
Total (conducted and withdrawn consultations)	–	–	2	7	10

Note 1: Prior assessment consultations for drugs and consultations on pharmacogenomics/biomarkers have been conducted since FY 2009, and consultations on drug product eligibility for priority review for drugs have been conducted since FY 2011. The numbers of both types of consultations were counted on the basis of delivery dates of consultation documents to PMDA.

Note 2: Prior assessment consultations for drugs were counted on the basis of number of consultation categories (quality; non-clinical, toxicity; non-clinical, pharmacology; non-clinical, pharmacokinetics; phase I study; phase II study; and phase II/III study).

- In FY 2013, PMDA conducted a total of 354 consultations (including 30 withdrawals).
- To cope with all the requests for clinical trial consultations (excluding prior assessment consultations, consultations on pharmacogenomics/biomarkers, and consultations on drug product eligibility for priority review) as a general rule, consultations are scheduled according to scheduling requests received, and when the consultation schedule cannot be fixed for a desired month, the consultation is scheduled within one month before or after that month. In FY 2013, PMDA provided a total of 312 consultations (including 30 withdrawals), responding to all of the clinical trial consultations requested (The target was achieved).
- PMDA aimed to complete the process from conduct of clinical trial consultation to finalizing consultation records within 30 business days for 80% of products subjected to consultation. In FY 2013, the target was achieved in 310 (96.6%) of 321 consultations.
- In order to improve the quality of consultations, in January 2007, PMDA introduced a system for all clinical trial consultations in which PMDA's opinions for content to be addressed in the consultations are presented to the applicants beforehand (preliminary opinion disclosure system).

Number of Consultations for Drugs by Review Category in FY 2013

Review category	Results												Total
	Apr.	May	Jun.	Jul.	Aug.	Sep.	Oct.	Nov.	Dec.	Jan.	Feb.	Mar.	
Category 1 (Gastrointestinal drugs etc.)	0	4	3	1	2	3	4	4	2	1	1	8	33
Category 6-2 (Hormone drugs)	2	2	8	4	1	2	4	1	2	1	2	1	30
Category 2 (Cardiovascular drugs)	4	2	2	4	2	1	1	4	5	2	5	4	36
Category 5 (Drugs for the urogenital system etc.)	0	0	3	3	1	2	2	0	3	1	0	1	16
Radiopharmaceuticals	0	0	0	0	0	0	0	0	0	0	0	1	1
In vivo diagnostics	0	1	1	0	1	1	0	0	0	0	1	0	5
Category 3-1 (Central nervous system drugs etc.)	1	2	7	2	6	1	5	2	5	2	0	1	34
Category 3-2 (Anesthetic drugs etc.)	1	0	3	2	1	1	0	0	1	0	1	1	11
Category 4 (Antibacterial agents etc.)	0	2	3	4	3	1	3	3	3	2	0	1	25
Category 6-1 (Respiratory tract drugs etc.)	2	6	3	1	0	3	5	4	6	5	4	6	45
AIDS drugs	1	0	0	0	1	0	0	0	0	0	0	0	2
Oncology drugs	4	7	5	3	4	6	6	5	6	3	5	7	61
Cellular and tissue-based products	0	0	0	0	0	0	1	0	0	0	0	1	2
Gene therapy products	0	0	0	0	0	-	-	-	-	-	-	-	0
Bio-CMC	3	1	4	0	4	3	1	2	1	2	1	0	22
Vaccines	1	0	2	4	1	1	0	2	4	2	1	1	19
Blood products	3	0	1	0	1	1	2	3	1	0	0	0	12
[Re-listed] Prior assessment	1	1	7	0	5	0	0	2	4	0	2	10	32
[Re-listed] Drug product eligibility for priority review	1	1	3	0	1	0	1	1	0	0	0	2	10
Pharmacogenomics/biomarkers	0	0	0	0	0	0	0	0	0	0	0	0	0
GLP/GCP compliance	0	0	0	0	0	0	0	0	0	0	0	0	0
Total	22	27	45	28	28	26	34	30	39	21	21	33	354
Withdrawal	4	0	4	2	2	5	0	1	5	3	2	2	30
Grand Total	26	27	49	30	30	31	34	31	44	24	23	35	384

Note 1: A consultation covering several categories was counted in terms of its main category.

Note 2: Prior assessment consultations are conducted for the following categories: quality; non-clinical, toxicity; non-clinical, pharmacology; non-clinical, pharmacokinetics; phase I study; phase II study; and phase II/III study.

Note 3: The numbers of prior assessment consultations, consultations on pharmacogenomics/biomarkers, and consultations on drug product eligibility for priority review were counted on the basis of delivery dates of consultation documents to PMDA.

Note 4: Consultations on pharmacogenomics/biomarkers were conducted by the Omics Project Team.

Note 5: Consultations on GLP/GCP compliance were all conducted by the Office of Conformity Audit, regardless of category.

d. Reclassification of consultation categories and their uses

- Regarding clinical trial consultations for drugs, PMDA has considered reclassification of consultation categories in order to more meticulously deal with various needs in each stage of development, taking into account demands from the industry and previous experiences.

(v) Promotion of evaluation of new technologies

a. Utilization of external experts

- As PMDA is required to raise the expertise of its guidance and review, particularly in the fields of the latest technologies such as biotechnology and genomics, PMDA has continued to commission external experts who have a high-level knowledge to play a role of expert advisors for PMDA, in order to seek professional opinions on scientifically important matters at Expert Discussions for reviews and post-marketing safety measures.

  (As of March 31, 2014, the number of commissioned experts is 1,159 including external experts commissioned for issues relating to safety measures)

- The number of Expert Discussions conducted in FY 2013 was 244 (187 through document-based discussions; 57 through meetings).

- PMDA utilized external experts in Expert Discussions for application reviews and clinical trial consultations for biological pharmaceuticals and cellular and tissue-based products. Also in this field, PMDA promoted exchanging information with FDA and EMA through telephone conferences etc.

b. Support for the development of national guidelines

- PMDA assisted the development of guidelines by study groups for evaluation of regenerative medicine and vaccines, and the following guidelines etc., were issued.

  PMDA provided cooperation for the creation and release of the Guidance for Evaluation of Autologous Induced Pluripotent Stem Cells-derived from Retinal Pigment Epithelial Cells included in “Publication of the Guidance for the Evaluation of Emerging Technology Medical Devices” (PFSB/ELD/OMDE Notification No. 0529-1 dated May 29, 2013.)

- PMDA provided cooperation for the investigation for the research report on “Investigation on Quality, etc., of Biosimilars/Follow-on Biologics” supported by drug review administration expense in review promotion funds, and supported research etc., on materials necessary for applications for follow-on biologics, etc.

- PMDA worked with MHLW to develop shared research reports “Research on detection/risk evaluation of abnormal prion in cellular and tissue-based products and biological drugs,” “Research on Bacterial Endotoxin Test Methods,” and “Research on standards for bovine-derived materials” in the Project for Comprehensive Research of Regulatory Science for Drugs, Medical Devices, etc., “Evaluation of the Safety of Innovative Drugs against Viruses and Infectious Agents” (General/Shared Research Report for FY 2013) supported by Health and Labour Sciences Research Grants.

- PMDA supported the preparation of the administrative notice dated April 15, 2013 “Q&A about the guidance for preparation of registration application forms for Master File for Drug Substances etc., related to manufacturing of cellular and tissue-based products and materials to be attached to application forms” and made efforts to thoroughly publicize the contents by posting on its website and giving speeches at academic conferences etc.

- PMDA participated in the examination in a research project supported by Health and Labour Sciences Research Grants (Global Health Issues Promotion Research Project), which is titled "Research on Methods for Evaluating Quality, Efficacy, etc., of Vaccines for Travelers etc," and led

by Dr. Kazunobu Ouchi, the principal researcher. PMDA provided cooperation for studies of methods for developing vaccines for travelers.

- PMDA participated in the examination in a research project supported by Health and Labour Sciences Research Grants (Global Health Issues Promotion Research Project), which is titled "Research on Standards for Investigation and Quality Control toward Practical Use of Next-Generation Vaccines" and led by Dr. Ken Ishii, the principal researcher. PMDA provided cooperation for studies on developing next-generation vaccines.
- Regarding the Minimum Requirements for Biological Products, PMDA provided cooperation for amendment work taking into account changes in environments surrounding drugs such as discovery of new knowledge, scientific advances including development of new measuring techniques, and the situations of standards adopted overseas (PFSB/ELD Notification No. 0912-9, September 12, 2013 "Handling of Marketing Approval Applications etc., for Drugs in Association with Partial Amendment to the Minimum Requirements for Biological Products").
- The team of the nanomedicine initiative project, which is one of the Projects across Multi-offices in PMDA for development of standards, provided cooperation for drafting the notification jointly issued by EMA "Reflection Paper on the Development of Block Copolymer Micelle Medicinal Products (PFSB/ELD Notification No. 0110-1, dated January 10, 2014)" and Q&A about the notification (PFSB/ELD Administrative Notice, dated the same day).
- The teams of the microdose clinical trial project and the nanomedicine initiative project examined the handling procedures of clinical trial notifications for development of relevant drugs, and submitted a proposal to the Evaluation and Licensing Division, PFSB, MHLW. As a result, PFSB/ELD Notifications No. 0531-4 and -8 dated May 31, 2013 and Q&A about the notifications (PFSB/ELD Administrative Notice, dated August 30, 2013) which include the proposed procedures were issued. Also, the team of the nanomedicine initiative project examined the handling of attached materials at the time of making approval application and submitted a proposal to the Evaluation and Licensing Division. As a result, a description of the handling was included in PFSB/ELD Notifications No. 0110-1 dated January 10, 2014.
- The team of the post-approval manufacturing changes project examined matters related to drug quality reviews, descriptions in approval documents etc. and provided cooperation for issuing "Questions & Answers (Q&A) about Master File for Drug Substances etc. (No. 4) (PFSB/ELD Administrative Notice, dated October 29, 2013)." Also, the team examined matters related to descriptions of manufacturing methods in approval documents for drugs/quasi-drugs containing three or more active ingredients, and is preparing a related notification.
- Centering on PMDA's companion diagnostics project team, PMDA organized basic principles on companion diagnostics and related drugs, and cooperated for drafting the notification of "Points to Consider on Application for Approval of Companion Diagnostics and Related Drugs (PFSB/ELD Notifications No. 0701-10 dated July 1, 2013 and Q&A about its notification [PFSB/ELD Administrative Notice, dated the same day]). Also, taking into account the notification, PMDA prepared "Technical Guidance on Development of Companion Diagnostics and Related Drugs" showing the concept of development and Q&A about the notification (PFSB/ELD Administrative Notice, dated December 26, 2013). Also, PMDA provided cooperation for drafting PFSB/ELD/OMDE Notification No. 0219-4 dated February 19, 2014 and PFSB/ELD/OMDE Notification No. 0328-7 dated March 28, 2014 showing points to consider on descriptions in approval documents for companion diagnostics.
- In addition to the above, about 10 notifications etc., were issued in FY 2013 with the cooperation of relevant review categories or offices in PMDA.

- From the viewpoint of proactively promoting regulatory science research and making use of its achievements in PMDA's operations, taking into account the results of examinations at the Regulatory Science Research Evaluation Committee etc., PMDA examined research projects for FY 2013 (7 designated projects: 3 new projects and 4 continued projects). Results of one of these research projects were published in an academic journal.

c. Preliminary reviews on gene therapy products, Cartagena Act, etc.

- PMDA had conducted preliminary review of gene therapy products prior to the initiation of clinical trials as to whether or not the quality and safety conformed to the guidelines, but in July 2013, the preliminary review system was abolished (interim measures were taken until the end of August) and replaced with Pharmaceutical Affairs Consultations on R&D Strategy.

Number of Applications for Preliminary Reviews and Number of Completed Reviews

	FY 2009		FY 2010		FY 2011		FY 2012		FY 2013	
	No. of applications	No. of completed cases	No. of applications	No. of completed cases	No. of applications	No. of completed cases	No. of applications	No. of completed cases	No. of applications	No. of completed cases
Cellular and tissue-based products	2	2	0	1	1	1	–	–	–	–
Gene therapy products	0	2	1	1	1	0	2	2	0	1

Note: The preliminary reviews of cellular and tissue-based drugs and medical devices were abolished in July 2011. The preliminary reviews of gene therapy drugs were abolished in July 2013. One product for which application had been filed was withdrawn.

- With regard to the use of genetically modified living organisms, preliminary reviews are conducted about approval of Type 1 Use and confirmation of Type 2 Use under the "Act on the Conservation and Sustainable Use of Biological Diversity through Regulations on the Use of Living Modified Organisms (Cartagena Act)." PMDA set the target regulatory review time to be 6 months for approval of Type 1 Use and 3 months for confirmation of Type 2 Use, with the goal of achieving 50% (median) of applications for each type.

Review under the Cartagena Act (Median Regulatory Review Time)

	FY 2009	FY 2010	FY 2011	FY 2012	FY 2013
No. of preliminary reviews for Type 1 Use	0	0	0	0	0
Median review time [months]	–	–	–	–	–
No. of preliminary reviews for Type 2 Use	11	13	15	21	24
Median review time [months]	2.5	2.5	2.0	1.2	0.9

Note: "Type 1 Use" refers to cases where measures are not taken to prevent the release to the environment and "Type 2 Use" refers to cases where such measures are taken.

d. Implementation of Pharmaceutical Affairs Consultations on R&D Strategy

- PMDA has been offering Pharmaceutical Affairs Consultations on R&D Strategy since July 2011 mainly for universities, research institutions and venture companies that have promising seeds to provide guidance and advice concerning studies and clinical trials that are necessary at the initial

stage of product development in order to allow innovative pharmaceuticals and medical devices to be developed in Japan. The number of consultations was as follows.

- In FY 2013, a total of 121 on-site individual orientations were offered in Osaka, Kyoto, Kobe, Fukushima, Nagoya, Hiroshima, Fukuoka, etc., (included in the values on their left in the table below)
- In response to the "Regulatory Reform Implementation Plan" adopted by the Cabinet on June 14, 2013, the conventional system for confirmation applications for gene therapy drugs has been handled in Pharmaceutical Affairs Consultations on R&D Strategy (interim measures were taken until the end of August) since July 1, 2013, continuously from cellular and tissue-based products.
- Introductory consultations and pre-consultation meetings were also conducted in the Kansai branch of PMDA which was established in October 2013.

Number of Pharmaceutical Affairs Consultations on R&D Strategy Conducted

Introductory consultations	FY 2011 (Note 1)	FY 2012	FY 2013	Total
Drugs (excluding CTP)	45	83	78 [6]	206 [6]
Medical devices (excluding CTP)	70	200	134 [12]	404 [12]
CTP	3	19	25 [2]	47 [2]
Total	118	302	237 [20]	657 [20]

Pre-consultation meetings	FY 2011 (Note 1)	FY 2012	FY 2013	Total
Drugs (excluding CTP)	71	89	147 [12]	307 [12]
Medical devices (excluding CTP)	39	93	91 [7]	223 [7]
CTP	43	72	108 [7]	223 [7]
Total	153	254	346 [26]	753 [26]

(Face-to-face) Consultations	FY 2011 (Note 1)	FY 2012	FY 2013	Total
Drugs (excluding CTP)	19	26	58	103
Medical devices (excluding CTP)	3	5	33	41
CTP (Note 3)	9 (11)	9 (15)	32 (45)	50 (71)
Total (Note 3)	31 (33)	40 (46)	123 (136)	194 (215)

Note 1: Pharmaceutical Affairs Consultations on R&D Strategy were started in July 2013.

Note 2: Values in brackets are the number of consultations conducted at the Kansai branch and included in the figures on their left (implemented from October 2013).

Note 3: Values in parentheses are the total number of consultations counted individually if those were conducted over several days. Such consultations were conducted within a necessary range for sufficient assurance of the quality and safety of those cellular and tissue-based products or gene therapy drugs prior to submissions of the clinical trial notification.

e. Support for the Super Special Consortia for development of advanced medicine

- The period of making efforts for the Super Special Consortia for development of advanced medicine already ended. Therefore, PMDA did not hold consultation meetings on pharmaceutical regulatory affairs in FY 2013. However, PMDA maintained its cooperative relationship for related issues.

  Clinical trial consultations etc., concerning topics addressed by the Super Special Consortia were conducted as follows: 4 pharmaceutical affairs consultations on R&D strategy (2 consultations on

drug strategy and 2 consultations on medical device strategy). PMDA promptly dealt with all of the consultations. There were no cases for clinical trial consultations for drugs and medical devices.

Over-the-counter drugs and generic drugs

- To promote self-medication and wide use of generic drugs, PMDA gave presentations in international conferences, and various briefing sessions on filing of applications. PMDA posted the materials used for those sessions on its website.

(i) Appropriate and prompt reviews

a. Consultations and reviews based on medical care needs

- PMDA staff members have participated in academic conferences etc., in and out of Japan, and actively exchanged opinions with healthcare professionals to comprehend their needs. The Agency has conducted consultations and reviews, taking into account the information obtained in this manner.

b. Efforts toward Introduction of risk management plans for generic drugs

- Toward smooth introduction of risk management plans for generic drugs, PMDA conducted trial operations to ask for submissions of draft risk management plans for generic drugs containing zoledronic acid (hydrate) and sildenafil citrate as an active ingredient, in order to examine issues such as the scope, timing of submission, and contents to be described, etc.

c. Promotion of digitization in reviews

- See [New drugs] (i)-g.

d. Development of the Japanese Pharmacopoeia

- See [New drugs] (i)-i.

e. Development of draft revision of Japanese Standards of Quasi-drug Ingredients

- PMDA supported the MHLW's process of the revision of Japanese Standards of Quasi-drug Ingredients, by helping MHLW to hold a total of 2 meetings of the "Review Committee on Japanese Standards of Quasi-drug Ingredients" in FY 2013. Based on the meetings, Administrative Notices regarding “Japanese Standards of Quasi-drug Ingredients 2006” (April 10, 2013 and November 6, 2013) were issued. In addition to that, PMDA outsourced clerical works and prepared “Standards of Quasi - Drug Cosmetic Excipients” to publicize the standards in the appendix that are used for approved quasi-drug cosmetics for the purpose of accelerating reviews and reducing the time and effort for application.

f. Enhancement of the review system for traditional Chinese medicines and crude drug products

- PMDA made efforts to improve qualities of reviewers through exchanging of opinions with experts in traditional Chinese medicines/ crude drugs by having reviewers participate in the Japanese Pharmacopoeia Crude Drug Committee and also in the research group supported by Health and

Labour Sciences Research Grants which involves the division of crude drugs at the National Institute of Health Sciences (NIHS) as collaborative researchers.

(ii) Approaches to shorten review times

- PMDA set up the target regulatory review times for applications of generic drugs etc., submitted on or after April 1, 2004, and has since conducted reviews toward achievement of these targets.
- In order to carry out reviews of generic drugs etc., promptly and accurately, PMDA developed the Procedures for Review of Generic Prescription Drugs, Procedures for Review of OTC Drugs, Procedures for Review of Insecticides/Rodenticides, and Procedures for Review of Quasi-drugs which state review methods and procedures etc., associated with reviews, and also prepared SOPs for various operations.

  In addition to periodically collecting data on the achievement level of the target review time and informing the reviewers of these levels, meetings of the Progress Management Committee for Reviews and Related Services were held to monitor and examine operational progress. (4 meetings were held in FY 2013.)
- The approval status of generic drugs, OTC drugs and quasi-drugs in FY 2013 are as follows:

Median Regulatory Review Time for Approved Generic Drugs, etc.

Targets

Product	Regulatory review time [months]
Generic drugs	10
OTC drugs	8
Quasi-drugs	5.5

** PMDA aimed to achieve the target review times shown in the table above for 50% (median) of products, by FY 2011.*

Results

	FY 2009	FY 2010	FY 2011	FY 2012	FY 2013
Generic drugs	3,271	2,633	3,091	3,421	3,504
Of which: Number of approved applications filed in or after April 2004	3,245	2,590	3,046	3,388	3,502
Median review time (for the applications filed in or after April 2004) [months]	7.5	6.9	6.5	5.9	5.3
OTC drugs	2,171	1,008	1,031	881	916
Of which: Number of approved applications filed in or after April 2004	2,166	1,007	1,029	881	916
Median review time (for the applications filed in or after April 2004) [months]	4.6	4.0	3.4	4.1	4.9
Quasi-drugs	2,221	1,976	1,938	1,968	2,028
Of which: Number of approved applications filed in or after April 2004	2,220	1,976	1,938	1,968	2,028
Median review time (for the applications filed in or after April 2004) [months]	4.8	5.2	5.0	4.9	4.9
Total	7,663	5,617	6,060	6,270	6,448
Of which: Number of approved applications filed in or after April 2004	7,631	5,573	6,013	6,237	6,446

Note 1: The medians for OTC drugs and quasi-drugs were calculated excluding the period after completion of reviews up to notification of GMP inspection results from authorities such as prefectural governments.

Note 2: The number of approved applications includes priority review products for which the standard regulatory review time is 6 months or less.

Reviews Conducted for Generic Drugs and Others by Fiscal Year

Classification	Fiscal Year	Applications	Approved	Withdrawn etc.	Under review
Generic drugs	FY 2009	2,354	3,271	223	3,343
	FY 2010	3,062	2,633	224	3,540
	FY 2011	2,892	3,091	165	3,175
	FY 2012	4,077	3,421	190	3,644
	FY 2013	3,891	3,504	343	3,688
OTC drugs	FY 2009	1,759	2,171	136	1,890
	FY 2010	1,092	1,008	133	1,841
	FY 2011	1,130	1,031	92	1,848
	FY 2012	1,005	881	90	1,882
	FY 2013	1,013	916	63	1,916
Quasi-drugs	FY 2009	2,572	2,221	82	1,844
	FY 2010	2,297	1,976	135	2,030
	FY 2011	2,212	1,938	82	2,222
	FY 2012	2,117	1,968	74	2,297
	FY 2013	2,298	2,028	174	2,393

Note 1: Values in the Withdrawn etc., column do not include the number of products switched to other review categories during the review

Applications and Approvals for OTC Drugs and Quasi-Drugs by Application Category

OTC drugs

New applications Classification	1	2	3-1	3-2	3-3	4	5-1	5-2	5-3	5-4	6	7-1	7-2	8	Total
FY 2013 Number of products filed	0	2	0	0	0	4	0	4	0	0	4	82	17	805	918
FY 2013 Number of products approved	0	0	0	0	0	12	0	5	0	7	5	32	6	779	846

Category of application	Insecticides	Total
Filed in FY 2013	95	95
Approved in FY 2013	59	59

Former category of application	1	2	3	4-1	4-2	OTC test agents	Total
Approved in FY 2013	0	0	0	0	11	0	11

Quasi-drugs

Category of application	1,3	2	Total
Filed in FY 2013	71	2,227	2,298
Approved in FY 2013	37	1,991	2,028

Note 1: The categories of application for OTC drugs were amended on January 1, 2009. Categories 1, 2, 3, 4-1 and 4-2 provided as "Former category of application" in the table indicate the categories prior to the amendment.

Note 2: Categories of application are as follows:

OTC drugs

Former category of application
- *1: Drugs with new active ingredients (Direct OTC drugs)*
- *2: Drugs with new active ingredients for OTC (Switch OTC drugs)*
- *3: Relatively innovative drugs excluding the above 1 and 2*
- *4-1 Other drugs (Relatively less innovative drugs)*
- *4-2: Other drugs (Drugs that are not innovative)*

New category of application
- *1: Drugs with new active ingredients (Direct OTC drugs)*
- *2: Drugs with new routes of administration*
- *3-1: Drugs with a new indication*
- *3-2: Drugs in a new dosage form*
- *3-3: Drugs with a new dosage*
- *4: Drugs with new active ingredients for OTC (Switch OTC drugs)*
- *5-1: OTC drugs with a new route of administration*
- *5-2: OTC drugs with a new indication*
- *5-3: OTC drugs in a new dosage form*
- *5-4: OTC drugs with a new dosage*
- *6: New OTC combination drugs*
- *7-1: OTC combination drugs with similar prescription*
- *7-2: OTC drugs in a similar dosage form*
- *8: Other drugs (Relatively less innovative drugs and drugs that are not innovative)*

(Quasi-drugs)
- *1: Products that contain new active ingredients*
- *2: Products that are not innovative*
- *3: Innovative products excluding 1*

Note 3: Each application belongs to the category under which it was classified at the time of filing.

Note 4: Each approval belongs to the category under which it was classified at the time of approval.

Note 5: The number of quasi-drugs includes insecticides and rodenticides that were filed as quasi-drugs.

- The median regulatory review times for approved products in FY 2013 were 5.3 months for generic drugs (target, 10 months), 4.9 months for OTC drugs (target, 8 months), and 4.9 months for quasi-drugs (target, 5.5 months), showing that the target was achieved for all categories.

Document-based GLP/GCP etc., Inspections Conducted for Generic Drugs by Fiscal Year

	FY 2009	FY 2010	FY 2011	FY 2012	FY 2013
Generic drugs	1,004	1,040	1,118	1,188	1,086

- For generic drugs, PMDA conducted 1,086 inspections to confirm compliance with GLP, GCP, and other standards for product applications, by collating them with raw data such as test records, laboratory notebook, case report forms, etc.

(iii) Efficient conduct of clinical trial consultations

a. Improvement of pre-application consultations for generic drugs

- Regarding pre-application consultations for generic drugs, in January 2012 PMDA started to provide consultations on quality for generic drugs and on bioequivalence of generic drugs on a trial basis, and 18 consultations were provided in FY 2013. PMDA intends to deal with 2 consultations a month on a trial basis continuously in the first half of FY 2014.

Number of Consultations for Generic Drugs

	FY 2011	FY 2012	FY 2013
Conducted consultations	3	10	17
Withdrawals	0	0	1
Total (conducted and withdrawn consultations)	3	10	18

Note: Consultations for generic drugs were started in FY 2011.

Number of Consultations for Generic Drugs by Consultation Category in FY 2013

Consultation category	Clinical trial consultation Number of cases conducted	Number of cases withdrawn	Total (conducted and withdrawn consultations)
Consultations on bioequivalence of generic drugs	14	1	15
Quality consultation for generic drugs	3	0	3
Total	17	1	18

b. Improvement of pre-application consultations for over-the-counter (OTC) drugs

- PMDA started to offer pre-development and pre-application consultations for OTC drugs in FY 2010 based on opinions from the industry associations. Among them, consultations on appropriateness of development of new OTC drugs were started in FY 2011. Also, pre-application consultations for Switch OTC drugs and consultations on key points of clinical trial protocols were continuously provided on a trial basis. The number of consultations in FY 2012 decreased as compared to those in the previous year, but in FY 2013, PMDA made a marked increase in number of consultation by taking measures such as referring to the opinions from the industry associations. PMDA intends to continuously improve the consultation service.

Number of Pre-development and Pre-application Consultations for OTC Drugs

	FY 2010	FY 2011	FY 2012	FY 2013
Conducted consultations	23	17	4	21
Withdrawals	0	2	0	0
Total (conducted and withdrawn consultations)	23	19	4	21

Note: Pre-development and pre-application consultations for OTC drugs were started in FY 2010.

Number of Pre-development and Pre-application Consultations for OTC Drugs by Consultation Category in FY 2013

Consultation category	Clinical trial consultation Number of cases conducted	Withdrawal Number of cases	Total (conducted and withdrawn consultations)
Pre-application consultation for switch OTC drugs	1	0	1
Consultation on key points of clinical trial protocols for OTC drugs	0	0	0
Consultation on appropriateness of development of new OTC drugs	20	0	20
Total	21	0	21

c. Improvement of pre-application consultations for quasi-drugs

- PMDA exchanged opinions with the Japan Cosmetic Industry Association (JCIA) to identify the needs for pre-application consultations for quasi-drugs. PMDA intends to continue to exchange opinions with the JCIA to implement the consultation system.

Medical devices

- Based on the “Action Program to Accelerate Reviews of Medical Devices” established in December 2008, various measures were implemented or reviewed with the aim of accelerating reviews for new medical devices, with an eye on “Japan Revitalization Strategy -JAPAN is BACK-” and “Healthcare and Medical Strategy” formulated on June 14, 2013.

(i) Appropriate and prompt reviews

a. Structure for clinical trial consultations and reviews

- Based on the “Action Program to Accelerate Reviews of Medical Devices,” PMDA increased the number of reviewers by 14 in FY 2013. There are 104 reviewers in the review system for medical devices as of the end of FY 2014.

  In order to enhance the review system with increased reviewers, more reviewers were allocated to the review categories where otherwise rapid processing was deemed difficult, according to situations such as the status of processing of product applications.

- Under the guidance of office directors and review directors, reviews of new medical devices and improved medical devices were basically conducted by review teams consisting of experts who have academic degrees in pharmaceutical science, physical science, engineering, medicine, dentistry, veterinary medicine, statistics, etc.

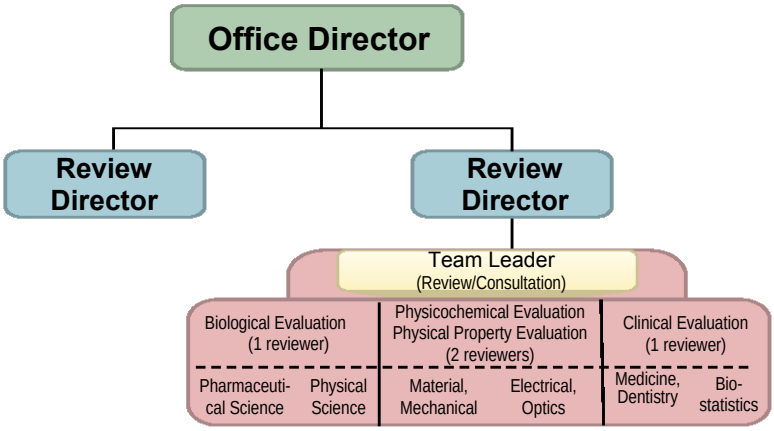
The review team is typically comprised of team leader(s) and reviewers who have specialized in biological evaluations, physicochemical/physical property evaluations, and clinical evaluations.

(Note) *New medical devices:* *Medical devices subject to re-examination (medical devices that have clearly different structure, usage, indications, performance, etc., as compared to existing approved medical devices or certified medical devices).*

Improved medical devices: *Medical devices that do not fall under "new medical devices" or "generic medical devices," and are not so novel as to be subject to re-examination, nor are substantially equivalent to existing medical devices in terms of structure, usage, indications, performance, etc.*

Generic medical devices: *Medical devices that are regarded as substantially equivalent to existing approved medical devices in terms of structure, usage, indications, performance, etc.*

Organization for New/Improved Medical Device Reviews



- Review teams are designated based on the review categories shown in the table below.

Review Categories Covered by the Offices of New/Improved Medical Devices

Office	Review Categories	
Office of Medical Devices I	Category 3-1	Materials aspects of intervention devices mainly in cerebral, cardiovascular, respiratory, and psychoneurologic areas
	Category 3-2	Materials aspects of non-intervention devices mainly in cerebral, cardiovascular, respiratory, and psychoneurologic areas
	Category 4	Mechanical aspects of medical devices mainly in cerebral, cardiovascular, respiratory, and psychoneurologic areas
	Category 8	Mainly for multicategory medical devices, advanced electronic medical devices, other uncategorized medical devices
Office of Medical Devices II	Category 1	Mainly for ophthalmology and otorhinolaryngology
	Category 2	Mainly for dentistry
	Category 5	Mainly for gastrointestinal and urinary systems, obstetrics and gynecology
	Category 6-1	Mainly for medical devices for knee/upper limb joints, hip/digital joints, etc., in orthopedic surgery area
	Category 6-2	Mainly for plates/screws, fixation materials for intramedullary nails/spines and related appliances/machines in orthopedic surgery area, and medical devices for plastic surgery and dermatology
	Category 7	Mainly for laboratory tests (*in vitro* diagnostics)

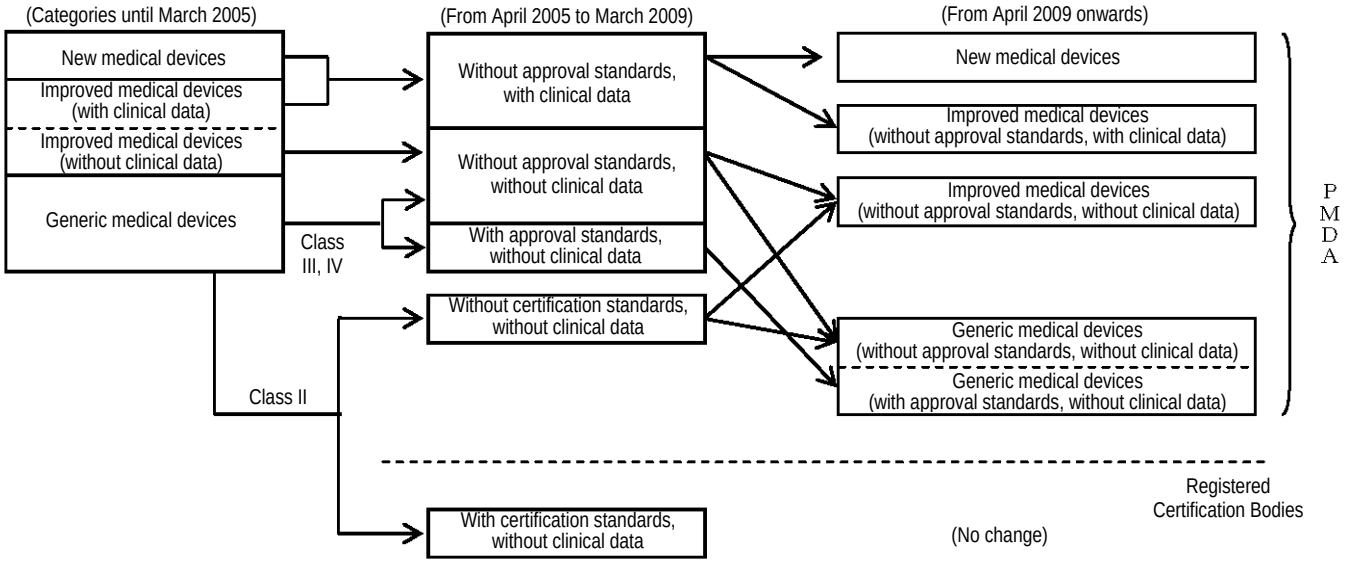
- To hear opinions from external experts in the course of reviews performed by review teams, expert discussions were held where necessary, and also, innovative medical devices etc., were

deliberated at the Committee on Medical Devices and *In-vitro* Diagnostics of Pharmaceutical Affairs and Food Sanitation Council (PAFSC), MHLW.

Review Performance for FY 2013 (medical devices and in vitro diagnostics)

(1) Number of Expert Discussions conducted: 71 (49 document-based discussions, 22 meetings)
(2) Applications deliberated at the Drug Committees (under PAFSC): 19
Applications reported to the Committee on Medical Devices and *in vitro* Diagnostics (under PAFSC): 314 (290 medical devices, 24 *in vitro* diagnostics)

- PMDA conducted clinical trial consultations for new/improved medical devices based on the team-reviewed guidance plan drafted by three staff members, i.e., the Review Director as well as the consultation leader and the deputy consultation leader in charge, who were appointed from among review team members.
- For reviews of generic medical devices, PMDA uses the buddy system in which an experienced reviewer and a novice reviewer are paired to perform a review. Team leaders oversee buddy pairs and Review Directors take control of the whole process.
- Application categories for medical devices were modified at the time of the enforcement of the Pharmaceutical Affairs Act as revised in April 2005, and further modified in April 2009. The current application categories are as shown in the right part of the figure below.



Note: Classes II, III, and IV represent classification of medical devices by risk level. Class II refers to those with relatively low risk to the human body, Class III refers to those with relatively high risk to the human body, and Class IV refers to those that may directly lead to life-threatening conditions.

b. Introduction of the 3-track review system

- As one of the efforts to advance and accelerate reviews of medical devices, the 3-track review system (for new medical devices, improved medical devices, and generic medical devices) has

been put in place in PMDA since FY 2011. In FY 2013, PMDA was committed to further entrenching the system based on the experiences in the previous year.

c. Reinforcement of the progress management of reviews

- In order to conduct reviews and related services promptly and appropriately to achieve the target review time as specified in the Mid-term Plan, PMDA held meetings of the Progress Management Committee for Reviews and Related Services once every 3 months to ensure that the Chief Executive and other executives of PMDA can accurately grasp the progress of reviews and related services and support improvement, as needed. In this way, operational progress was monitored, while particularly relevant information for new medical devices was dealt with comprehensively and approaches for solving operational challenges were considered.
- The Review Segment Committee for Progress Management, with the Director of the Center for Product Evaluation as its head, to control the progress of reviews, was continuously convened in FY 2013. In the meetings, information on the overall review status for new medical devices including QMS inspections etc., and associated issues were shared, and measures addressing challenges and future approaches were examined (11 meetings were held in FY 2013).

  At the Review Segment Committee for Progress Management, taking into account reports from office directors of review divisions, necessary guidance was continuously provided by the Director of the Center for Product Evaluation and the Associate Center Director, and the results of discussion of issues and improvement measures for products with a difficulty that required a prolonged review time were notified within review segments.

d. Standardization and transparency of review

- To clarify review standards, PMDA posted the following three documents on basic considerations for review on its website: "Points to Consider in regard to Applications for New Medical Devices, etc." and "Points to Consider in regard to Applications for Improved Medical Devices," and “Points to Consider in regard to Applications for Generic Medical Devices.” They were first published in FY 2008 and later revised in association with subsequent changes in the regulatory system. PMDA has also explained those points to relevant reviewers and has been using them for reviews etc.
- To promote the transparency and efficiency of reviews, PMDA posted on its website the "Guidelines for Preparation of Summary Technical Documentation (STED) Submitted in Applications for Medical Devices (new medical devices)" which is a revised version of the "Guidelines for Preparation of Summary Technical Documentation (STED) Submitted in Applications for Medical Devices (new medical devices and improved medical device)" published in FY 2009, and introduced at workshops to ensure that it was thoroughly acknowledged. PMDA posted on its website the following guidance documents: "Points to Consider in Preparing Data for Applications of Improved Medical Devices" for improved medical devices, "Points to Consider in Preparing Data for Applications of Generic Medical Devices” and "Guidelines for Preparation of Summary Technical Documentation (STED) Submitted in Applications for Medical Devices in the Category of Generic Medical Devices (without approval standards, without clinical data)" for generic medical devices. PMDA also presented these guidance documents in workshops to thoroughly disseminate them.

e. Consultations and reviews based on medical needs

- PMDA actively exchanged opinions with healthcare professionals by participating in academic conferences in and out of Japan, town hall meetings, requested lectures, etc., to comprehend their

needs. The Agency has conducted consultations and reviews, taking into account the information obtained in this manner.

- In order to encourage MAHs of medical devices to promote the development of medical devices that have been approved in Europe and the U.S. but not yet approved in Japan, the Study Group on the Early Introduction of Medical Devices etc., with High Medical Need (chaired by Dr. Soichiro Kitamura, President Emeritus of National Cerebral and Cardiovascular Center) was established in the MHLW in October 2006. The study group has been actively conducting investigations. PMDA has cooperated for the operation of the study group, and provided clinical trial consultations and review of product applications taking into account the results of investigations by the study group. Through this initiative, 20 medical devices were approved in FY 2013.

f. Consistency between clinical trial consultations and reviews

- In order to ensure the consistency between clinical trial consultations and reviews, review team members are involved in all the clinical trial consultations for products falling under the category to which they are assigned. Coherence from consultations to reviews is maintained and teams are flexibly organized as necessary.

g. Promotion of digitization in reviews

- See (i)-g [New drugs].

(ii) Introduction of new review systems

a. Introduction of prior assessment consultation

- To preliminarily evaluate the quality, efficacy and safety of medical devices from their development stage, PMDA started to offer prior assessment consultations as a pilot scheme in October 2010, and has been formally implementing them from FY 2012. In FY 2013, the request forms were received separately for consultations to be conducted in the first half of the fiscal year and for those in the second half. Consultations were provided for one product falling under Category 3.

b. Short-term review of applications for specified partial changes

- Applications for specified partial changes were reviewed in accordance with "Regarding Acceleration of the Procedure for Specified Changes Made to Medical Devices" (PFSB/ELD/OMDE Notification No. 1110001, dated November 10, 2008). As a result, regulatory review time for 30 products approved in FY 2013 was not more than 2 months excluding the period for GCP/GLP inspections.

c. Support for the development of approval standards, certification standards, and review guidelines for medical devices

- In order to support MHLW in developing approval standards etc., for medical devices, the Committee on Medical Device Approval Standards held five meetings in FY 2013.

  The number of approval or certification standards reported to MHLW in FY 2013 to be established or revised was as follows:

FY (for reporting)	FY 2006	FY 2007	FY 2008	FY 2009	FY 2010	FY 2011	FY 2012	FY 2013	Total
Approval standards	6	7	5	2	6	6	5	4	41
Certification standards	0	14	86	64	294	84	67	82	691
Review guidelines	0	1	2	6	0	0	0	0	9

The number of standards established by MHLW in FY 2013 based on the reports from PMDA is shown below:

Numbers of Approval Standards, Certification Standards, and Review Guidelines Established for Medical Devices and In Vitro Diagnostics

FY (for establishment)	FY 2004	FY 2005	FY 2006	FY 2007	FY 2008	FY 2009	FY 2010	FY 2011	FY 2012	FY 2013	Total
Approval standards	0	17	8	10	-2*	5	3	0	0	4	45
Certification standards	363	9	24	0	17	68	274	67	2	3	827
Review guidelines	0	0	0	0	3	1	4	0	0	0	8

* *In FY 2008, two established approval standards were switched to certification standards, resulting in a negative number.*

List of Approval Standards and Certification Standards for Medical Devices (FY 2013)

Established: 3 Certification standards; 4 Approval standards; 0 Review guidelines	
Date of issue	Name of standard
MHLW Ministerial Announcement No. 230, dated July 1, 2013	Certification Standard for Arthroscopic Fluid Distention Unit etc.
MHLW Ministerial Announcement No. 332, dated October 7, 2013	Certification Standard for Non-intravenous Infusion Pump
MHLW Ministerial Announcement No. 38, dated February 21, 2014	Certification Standard for MR-Combined Positron Emission Tomography
PFSB Notification No. 0204-5, February 4, 2014	Approval Standard for Central Vasculature Angiography Catheter
PFSB Notification No. 0204-8, February 4, 2014	Approval Standard for Central Circulatory Guiding Intravascular Catheter
PFSB Notification No. 0204-11, February 4, 2014	Approval Standard for Central Circulatory Microcatheter
PFSB Notification No. 0204-14, February 4, 2014	Approval Standard for Cardiac/Central Circulatory Catheter Guidewire etc.

- The PMDA website for the information service on medical device standards provides the latest information on the certification standards and approval standards in relation to JIS, ISO/IEC, MHLW Notifications, Japanese Medical Device Nomenclature (JMDN), etc., as their components. The information has also been continuously provided on the dedicated pages of the PMDA English website for overseas users. The information on the website has been updated periodically, at least twice a month.
- PMDA provided advice on each individual product through simple consultations on the scope of changes for which partial change applications are not required, or minor change notifications are required, based on the "Procedures Associated with Partial Change for Medical Devices" (PFSB/ELD/OMDE Notification No.1023001, dated October 23, 2008).
- PMDA dealt with the procedure for changing raw materials for each individual products through simple consultations based on "Regarding the Procedure for Changing Raw Materials of Medical Devices" (PFSB/ELD/OMDE Notification No. 0329-7, dated March 29, 2013), which clarifies the principle of the procedure.

- When MAHs raised questions on whether or not clinical studies are necessary during consultations, PMDA appropriately responded to such questions, for each individual products, based on the notifications etc., issued by MHLW.
- In order to clarify the scope of one product, PMDA conducted simple consultations etc., by referring to the “Partial Revision of ‘Points to Consider for Filing Applications for Medical Devices’” (PFSB/ELD/OMDE No. 1224007, dated December 24, 2010), “Handling of Applications for Dental Implants” (PFSB/ELD/OMDE No. 0713-1, dated July 13, 2012), and “Scope of Descriptions in Application Forms for Filing Application for Medical Devices and Procedures for Partial Change of Medical Devices (for orthopedic implant products)” (PFSB/ELD/OMDE No. 0701-10, dated July 1, 2013).

d. Equivalence review of generic medical devices

- PMDA continuously conducted the equivalence review of generic medical devices filed in FY 2013 based on the notification titled "Points to Consider in Preparing Applications for Generic Medical Devices" (PFSB/ELD/OMDE Notification No.0327004, dated March 27, 2009).

e. Support for the development of certification standards etc.

- PMDA supported the development and revision of certification standards by MHLW. A total of 3 certification standards were established, and a total of 26 certification standards were revised in FY 2013. Also, PMDA supported the preparation of three preliminary drafts for Class III certification standards because some Class III medical devices are to be certified by a registered certification body due to legislative and regulatory changes.

(iii) Efforts to solve the device lag

- The targets for total review time, regulatory review time, and applicant's time were set up for medical device applications filed on or after April 1, 2004, and both the regulatory authorities and applicants have since been making efforts to achieve the targets for review time.
- For new or improved medical devices, PMDA reinforced the progress management while making efforts to reduce the backlog of pending applications. Specifically, reasons were identified for the prolonged review of products for which application was filed years earlier, and reminder notices were frequently sent to applicants if their responses to PMDA's inquiries were delayed.
- For reviews of generic medical devices, PMDA continued the buddy system in which an experienced reviewer and a novice reviewer are paired to perform a review. The buddy pairs are overseen by team leaders and Review Directors take control of the whole process so that the review practices are standardized among review teams. The Office of Medical Devices III, which was established in November 2011, has conducted reviews intensively, and for the review categories with many products under review, PMDA made efforts to flexibly operate the buddy system regardless of review categories in order to accelerate reviews as a whole by having one reviewer of a buddy pair help another reviewer as far as they are reviewing similar products.
- To ensure consistency among review teams and to review medical device applications promptly and appropriately, PMDA developed SOPs relating to various operations, which describe reviews and related procedures for each type of new medical devices, improved medical devices and generic medical devices. These SOPs were explained to relevant reviewers. PMDA also collected monthly data on the achievement level of the target review times and informed the reviewers of the achievement status.

- To achieve the target regulatory review times, PMDA made efforts to process the backlog of pending applications, and also to enhance progress management of reviews of applications submitted newly so that the reviews could be accelerated.

  Meanwhile, to help meet the target times on the applicant's side, PMDA encouraged medical device companies to take measures such as the proactive use of clinical trial consultations prior to regulatory submission, through periodic exchanges of opinions with the industry. Moreover, PMDA showed specific examples of deficiencies often seen at the time of filing application at workshops etc., to call for improvements on the applicant's side.

- For shortening the total review time, it is also important to improve environments for the smooth conduct of global clinical trials. For this purpose, PMDA participated in the Harmonization by Doing (HBD) project which has been undertaken by both Japan and the U.S., and had discussions on the conduct of global clinical trials, the development of common protocols between Japan and the U.S., and the standardization of post-marketing surveillance database. Particularly in this fiscal year, for intravascular treatment devices for critical limb ischemia which is said to be difficult to evaluate, basic principles in global clinical trials was discussed mainly by Japanese and U.S. academia and governments, and the results were presented at the Cardiovascular Research Technologies (CRT) conference held in Washington D.C. in February 2013. In addition, continuously from the previous year, PMDA made efforts to accelerate reviews by exchanging information with the U.S. FDA on review and consultation services. As part of the HBD activities, PMDA participated in scientific sessions held at academic conferences, such as Transcatheter Cardiovascular Therapeutics (TCT) and CRT conferences, to discuss issues such as the challenges in the development of new medical devices and methods of utilizing post-marketing registry with the industry, government, and academia.
- Efforts were made to achieve the target total review time by taking these measures, and then, the status of reviews for medical devices in FY 2013 was as follows:

a. Review times for new medical devices (priority review products)

Median Review Time for New Medical Devices (Priority Review Products)

Targets

Fiscal Year	FY 2009	FY 2010	FY 2011	FY 2012	FY 2013
Total review time [months]	16	16	15	13	10
Regulatory review time [months]	8	8	7	7	6
Applicant's time [months]	9	9	8	6	4

* *PMDA is aiming to achieve the review times shown in the table for 50% (median) of products.*

Results

	FY 2009	FY 2010	FY 2011	FY 2012	FY 2013
Total review time [months]	13.9	15.1	4.3	9.3	9.0
Regulatory review time [months]	6.0	5.3	2.9	7.2	5.1
Applicant's time [months]	7.7	10.7	1.3	3.4	3.5
Number of approved applications	3	3	6	5	14

Note: Products covered were those for which applications were filed in or after FY 2004.

- Priority reviews are conducted for applications for orphan medical devices and other devices that are regarded as having particularly high medical need (medical devices for serious diseases and with distinctly superior efficacy or safety as compared to existing medical devices or therapies). In FY 2013, 14 priority review products (all were new medical devices) were approved.

  Six medical devices regarded as having particularly high medical need were designated for priority review.

- The approval status of priority review products in FY 2013 was as follows: The median total review time was 9.0 months, the median regulatory review time was 5.1 months, and the median applicant's time was 3.5 months, showing that all targets were achieved. FY 2013 saw 14 approvals, showing a marked increase (which was a 2.8-fold rise over FY 2012). The number of approvals was 3.5-fold that in FY 2008 (4 approvals) when the Action Program to Accelerate Reviews of Medical Devices was established.

b. Review times for new medical devices (standard review products)

Median Review Time for New Medical Devices (Standard Review Products)

Targets

Fiscal Year	FY 2009	FY 2010	FY 2011	FY 2012	FY 2013
Total review time [months]	21	21	20	17	14
Regulatory review time [months]	8	8	8	7	7
Applicant's time [months]	14	14	12	10	7

* *PMDA is aiming to achieve the review times shown in the table for 50% (median) of products.*

Results

	FY 2009	FY 2010	FY 2011	FY 2012	FY 2013
Total review time [months]	11.0	16.5	9.7	12.7	6.3
Regulatory review time [months]	6.8	7.1	5.1	5.4	4.0
Applicant's time [months]	7.1	8.2	3.4	5.0	1.6
Number of approved applications	33	15	27	41	80

Note: Products covered were those for which applications were filed in or after FY 2004.

- The approval status of standard review for new medical devices in FY 2013 was as follows: The median total review time was 6.3 months, the median regulatory review time was 4.0 months, and the median applicant's time was 1.6 months, showing that all the time frames were markedly reduced and all targets were achieved. FY 2013 saw 80 approvals, showing a marked increase (which was a 2.0-fold rise over FY 2012). The number of approvals was 6.7-fold that in FY 2008 (12 approvals) when the Action Program to Accelerate Reviews of Medical Devices was established.

  This was probably because many applications for MRI-compatible pacemakers, ICD, etc., concentrated in FY 2013.

- The number of product applications under review at the end of FY 2013 was 41 (including 1 orphan medical device and 1 non-orphan medical device with priority review status), showing a marked reduction from 61 at the end of FY 2012.

Review Status of New Medical Devices by Fiscal Year of Submission

New medical devices (FY of submission)	Applications	Approved	Withdrawn	Under review
In or before FY 2003 ending Mar. 31, 2004	132	54	78	0
FY 2004	56	35	21	0
FY 2005	7	7	0	0
FY 2006	23	19	4	0
FY 2007	37	31	6	0
FY 2008	32	30	2	0
FY 2009	24	20 (1)	4 (1)	0 [-2]
FY 2010	28	24 (1)	2	2 [-1]
FY 2011	42	40 (6)	1	1 [-6]
FY 2012	64	62 (47)	0	2 [-47]
FY 2013	72	36 (36)	0	36 [36]
Total	517	358 (91)	118 (1)	41 [-20]

Note 1: Values in the "Applications" column are the numbers of those submitted as new medical devices.

Note 2: The number of approved products includes those approved as improved medical devices.

Note 3: Figures in parentheses in the columns of "Approved" and "Withdrawn" represent those processed in FY 2013 (included in values on their left).

Note 4: Figures in brackets represent difference from the status reported in FY 2012.

Number of Applications Processed and Time Spent in Each Review Process

	Review process	1. From receipt of applications to product briefing session (formerly initial meeting)	2. From product briefing session to Expert Discussion	3. From Expert Discussion to notification of review result	4. From notification of review result to approval
FY 2013	Number of applications processed	30	26	39	94
	Median total review time [days]	29	162	58	5

Note 1: The median total review times in each process are the sum of the regulatory review time and applicant's time.

Note 2: Expert Discussions were held several times as needed.

Note 3: Values are calculated based on the applications filed in or after April 2004.

c. Review times for improved medical devices (with clinical data)

- The review status of improved medical devices (with clinical data) in FY 2013 was as follows.

Review Times for Improved Medical Devices (with Clinical Data)

Targets

Fiscal Year	FY 2009	FY 2010	FY 2011	FY 2012	FY 2013
Total review time [months]	16	16	14	12	10
Regulatory review time [months]	8	8	7	7	6
Applicant's time [months]	7	7	6	5	4

* *PMDA is aiming to achieve the review times shown in the table for 50% (median) of products.*

Results

	FY 2009	FY 2010	FY 2011	FY 2012	FY 2013
Total review time [months]	17.2	15.5	13.9	17.3	11.6
Regulatory review time [months]	10.4	7.6	7.0	7.9	5.7
Applicant's time [months]	6.6	7.6	7.2	8.8	5.5
Number of approved applications	30	40	55	44	63

Note 1:Products covered were those for which applications were filed in or after FY 2004.

Note 2:Applications filed in or before FY 2008 have been re-categorized in this table according to the new categorization implemented in FY 2009.

- As regards the approval status of improved medical devices (with clinical data) approved in FY 2013, the median total review time was 11.6 months, the median regulatory review time was 5.7 months, and the median applicant’s time was 5.5 months. All the time frames were shortened from the previous year. The target regulatory review time was achieved, but the target applicant’s time was not achieved, resulting in non-achievement of the target total review time. FY 2013 saw 63

approvals, showing a marked increase (1.4-fold increase over FY 2012) and reaching a 5-year high since FY 2009.

- This reflects the intensive efforts particularly for processing the pending applications for improved medical devices (with clinical data) for which many years have passed since the applications were filed. The target total review time and target applicant's time were not reached, but the number of products for which applications, were filed in or before FY 2012 and remained under review was reduced substantially.

  Also, to further reduce the total review time and applicant's time, PMDA requested applicant companies, at industry-PMDA dialogue meetings held regularly, to take following measures: i) To actively utilize clinical trial consultations in the pre-submission stage in order to receive advice or guidance regarding issues such as the adequacy of evaluation and how to compile submission documents, and to ensure that applications are filed after problems are completely resolved in terms of advice or guidance given, and ii) To secure resources in order to promptly respond to inquiries from the regulatory side if an applicant intends to file a number of applications at the same time. Moreover, regarding deficiencies often seen at the time of filing application, specific examples were provided at workshops etc., to call for improvements.

Review Status of Improved Medical Devices (with Clinical Data) by Fiscal Year of Application

Improved medical devices (with clinical data) (FY of submission)	Applications	Approved	Withdrawn	Under review
FY 2009	34	33	1	0
FY 2010	34	33 (1)	1	0 [-1]
FY 2011	26	21 (6)	3 (1)	2 [-7]
FY 2012	42	34 (28)	2	6 [-28]
FY 2013	46	15 (15)	2 (2)	29 [29]
Total	182	136 (50)	9 (3)	37 [-7]

Note 1:The number of applications was counted based on the initial application categories for medical devices submitted and the dates the applications were received.

Note 2:The number of approved products includes those approved under other application categories for medical devices.

Note 3:Figures in parentheses represent those processed in FY 2013 (included in values on their left).

Note 4:Figures in brackets represent difference from the status reported in FY 2012.

d. Review times for improved medical devices (without clinical data)

- The review status of improved medical devices (without clinical data) in FY 2013 was as follows.

Review Times for Improved Medical Devices (without Clinical Data)

Targets

Fiscal Year	FY 2009	FY 2010	FY 2011	FY 2012	FY 2013
Total review time [months]	11	11	10	9	6
Regulatory review time [months]	6	6	6	5	4
Applicant's time [months]	5	5	5	4	2

* *PMDA is aiming to achieve the review times shown in the table for 50% (median) of products.*

Results

	FY 2009	FY 2010	FY 2011	FY 2012	FY 2013
Total review time [months]	13.2	14.5	13.3	9.7	7.5
Regulatory review time [months]	8.5	8.0	5.6	4.8	3.7
Applicant's time [months]	3.9	6.2	6.5	4.7	3.7
Number of approved applications	158	182	218	229	231

Note 1:Products covered were those for which applications were filed in or after FY 2004.

Note 2:Applications filed in or before FY 2008 have been re-categorized in this table in accordance with the new categories implemented in FY 2009.

- As regards the approval status of improved medical devices (without clinical data) approved in FY 2013, the median total review time was 7.5 months, the median regulatory review time was 3.7 months, and the median applicant's time was 3.7 months. All the time flames were shortened from the previous year. The target regulatory review time was achieved, but the target applicant's time was not achieved, resulting in non-achievement of the target total review time. The number of approved applications in FY 2013 was 231, up by 2 over the previous fiscal year, reaching a 5-year high since FY 2009.
- This reflects the intensive efforts particularly for processing the pending applications of improved medical devices (without clinical data) which remained under review although they were filed years earlier. The target total review time and target applicant's time were not reached, but the number of products for which applications were filed in or before FY 2012 and remained under review was reduced substantially.

  Also, to further reduce the total review time and applicant's time, PMDA requested applicant companies, at industry-PMDA dialogue meetings held regularly, to take the following measures: i) To actively utilize clinical trial consultations in the pre-submission stage in order to receive advice or guidance regarding issues such as the adequacy of evaluation and how to compile submission documents, and to ensure that applications are filed after problems are completely resolved in terms of advice or guidance given, and ii) To secure resources in order to promptly respond to inquiries from the regulatory side if an applicant intends to file a number of applications at the same time. Moreover, regarding deficiencies often seen at the time of filing application, specific examples were provided at workshops etc., to call for improvements.

Review Status of Improved Medical Devices (without Clinical Data) by Fiscal Year of Application

Improved medical devices (without clinical data) (FY of submission)	Applications	Approved	Withdrawn	Under review
FY 2009	137	122 (1)	15	0 [-1]
FY 2010	165	137 (12)	23 (2)	5 [-14]
FY 2011	176	155 (19)	13 (3)	8 [-22]
FY 2012	210 (-1)	180 (110)	10 (5)	20 [-116]
FY 2013	189	85 (85)	3 (3)	101 [101]
Total	877 (-1)	679 (227)	64 (13)	134 [-52]

Note 1:The number of applications was counted based on the initial application categories for medical devices submitted and the dates the applications were received.

Note 2:From the number of applications in FY 2011, 1 application was deleted because its category was changed from the one at the time of filing application.

Note 3:The number of approved products includes those approved under other application categories for medical devices.

Note 4:Figures in parentheses represent those processed in FY 2013 (included in values on their left).

Note 5:Figures in brackets represent difference from the status reported in FY 2012.

e. Review times for generic medical devices

- The review status of generic medical devices in FY 2013 was as follows:

Review Times for Generic Medical Devices

Targets

Fiscal Year	FY 2009	FY 2010	FY 2011	FY 2012	FY 2013
Total review time [months]	8	6	5	4	4
Regulatory review time [months]	5	4	4	3	3
Applicant's time [months]	3	2	1	1	1

* *PMDA is aiming to achieve the review times shown in the table for 50% (median) of products.*

Results

	FY 2009	FY 2010	FY 2011	FY 2012	FY 2013
Total review time [months]	12.9	11.0	5.0	4.0	3.9
Regulatory review time [months]	5.9	5.1	2.5	1.6	1.8
Applicant's time [months]	3.6	4.7	2.3	2.3	2.1
Number of approved applications	1,797	1,391	907	1,216	958

Note 1:Products covered were those for which applications were filed in or after FY 2004.

Note 2:Applications filed in or before FY 2008 have been re-categorized in this table in accordance with the new categories implemented in FY 2009.

- As for the approval status of generic medical devices approved in FY 2013, the median total review time was 3.9 months, the median regulatory review time was 1.8 months, and the median

applicant's time was 2.1 months. As compared to the previous year, the total review time and applicant's time were shortened. The target median total review time and target median regulatory review time were achieved. There were 958 approvals. The number of applications reduced from 1,075 in FY 2012 to 924 in FY 2013, resulting in a reduction in number of approvals, but the actual achievement was greater than that in FY 2011. The number of applications under review was reduced by 103 from 561 at the end of FY 2012 to 458 at the end of FY 2013.

- Also, to further reduce the applicant's time for generic medical devices, PMDA requested applicant companies, at industry-PMDA dialogue meetings held regularly, to take following measures: i) To actively utilize consultations in the pre-submission stage in order receive advice or guidance regarding issues such as the adequacy of evaluation and how to compile submission documents, and to ensure that applications are filed after problems are completely resolved in terms of advice or guidance given, and ii) To secure resources in order to promptly respond to inquiries from the regulatory side if an applicant intends to file a number of applications at the same time. Moreover, regarding deficiencies often seen at the time of filing application, specific examples were provided at workshops etc., to call for improvements.

Review Status of Generic Medical Devices by Fiscal Year of Application

Generic medical devices (FY of submission)	Applications	Approved	Withdrawn	Under review
FY 2009	1,126	1,031 (8)	80 (11)	15 [-19]
FY 2010	1,020	895 (26)	87 (16)	38 [-42]
FY 2011	995	911 (47)	56 (13)	28 [-60]
FY 2012	1,075	998 (291)	28 (19)	49 [-310]
FY 2013	924	584 (584)	12 (12)	328 [328]
Total	5,140	4,419 (956)	263 (71)	458 [-03]

Note 1:The number of applications was counted based on the initial application categories for medical devices submitted and the dates the applications were received.

Note 2:The number of approved products includes those approved under other application categories for medical devices.

Note 3:Figures in parentheses represent those processed in FY 2013 (included in values on their left).

Note 4:Figures in brackets represent difference from the status reported in FY 2012.

(iv) Efficient conduct of clinical trial consultations

a. Conduct of priority consultations

- For medical devices, there were no requests for designation for priority consultation or consultation on GLP/GCP compliance for priority consultation products.

b. Acceleration of the procedure for clinical trial consultations

- PMDA firmly achieved the target time of approximately 3 months from request to conduct of clinical trial consultation, by means of establishment of the procedures, appropriate improvements in operations, receipt of consultation requests as needed, etc.

c. Implementation of clinical trial consultations and improvement of the system

Number of Consultations

	FY 2009	FY 2010	FY 2011	FY 2012	FY 2013
Consultations conducted	110	112	141	173	169
(Medical devices)	104	105	136	165	162
(*In vitro* diagnostics)	6	7	5	8	7
Consultations withdrawn	1	1	4	3	12
(Medical devices)	1	1	4	3	11
(*In vitro* diagnostics)	0	0	0	0	1
Total (conducted and withdrawn consultations)	111	113	145	176	181
(Medical devices)	105	106	140	168	173
(*In vitro* diagnostics)	6	7	5	8	8

Number of Prior Assessment Consultations for Medical Devices and In vitro Diagnostics (among the Numbers Listed Above)

	FY 2009	FY 2010	FY 2011	FY 2012	FY 2013
Consultations conducted	–	2	3	3	1
(Medical devices)	–	2	3	3	1
(*In vitro* diagnostics)	–	0	0	0	0
Consultations withdrawn	–	0	0	0	0
(Medical devices)	–	0	0	0	0
(*In vitro* diagnostics)	–	0	0	0	0
Total (conducted and withdrawn consultations)	–	2	3	3	1
(Medical devices)	–	2	3	3	1
(*In vitro* diagnostics)	–	0	0	0	0

Number of Consultations on Pharmacogenomics/Biomarkers (among the Numbers Listed Above)

	FY 2009	FY 2010	FY 2011	FY 2012	FY 2013
Consultations conducted	0	0	0	0	0
Consultations withdrawn	0	0	0	0	0
Total (conducted and withdrawn consultations)	0	0	0	0	0

Note 1: Consultations on pharmacogenomics/biomarkers have been offered since FY 2009.

Note 2: Prior assessment consultations for medical devices and prior assessment consultations for in vitro diagnostics have been conducted since FY 2010.

Note 3: The numbers of prior assessment consultations for medical devices, prior assessment consultations for in vitro diagnostics and consultations on pharmacogenomics/biomarkers were counted on the basis of delivery dates of consultation documents to PMDA.

Note 4: Prior assessment consultations for medical devices and prior assessment consultations for in vitro diagnostics are conducted for the categories of quality, non-clinical and clinical.

- A total of 168 clinical trial consultations (excluding prior assessment consultations and consultations on pharmacogenomics/biomarkers) were carried out in FY 2013. The goal to be achieved by FY 2013 was to secure the yearly capability to process 200 clinical trial consultations and provide all consultations requested. In FY 2013, PMDA basically provided all of the consultations requested.

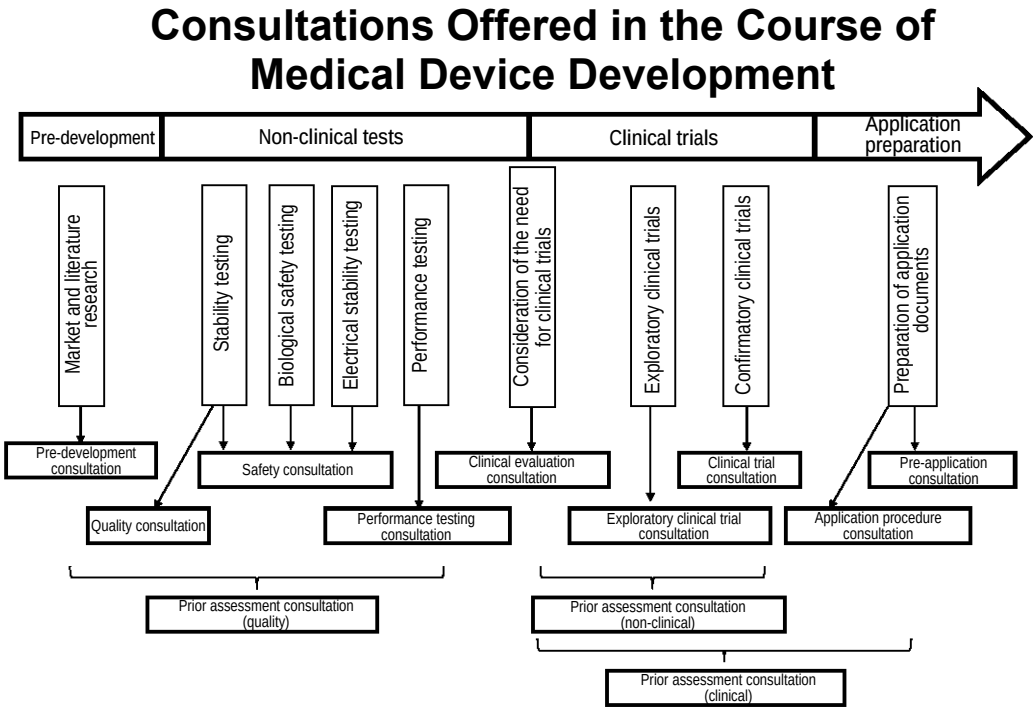
- PMDA aimed to complete the process from clinical trial consultation to finalizing consultation records within 30 business days for 60% of products subject to consultation. In FY 2013, the target was achieved in 154 of 158 consultations (97.5%).

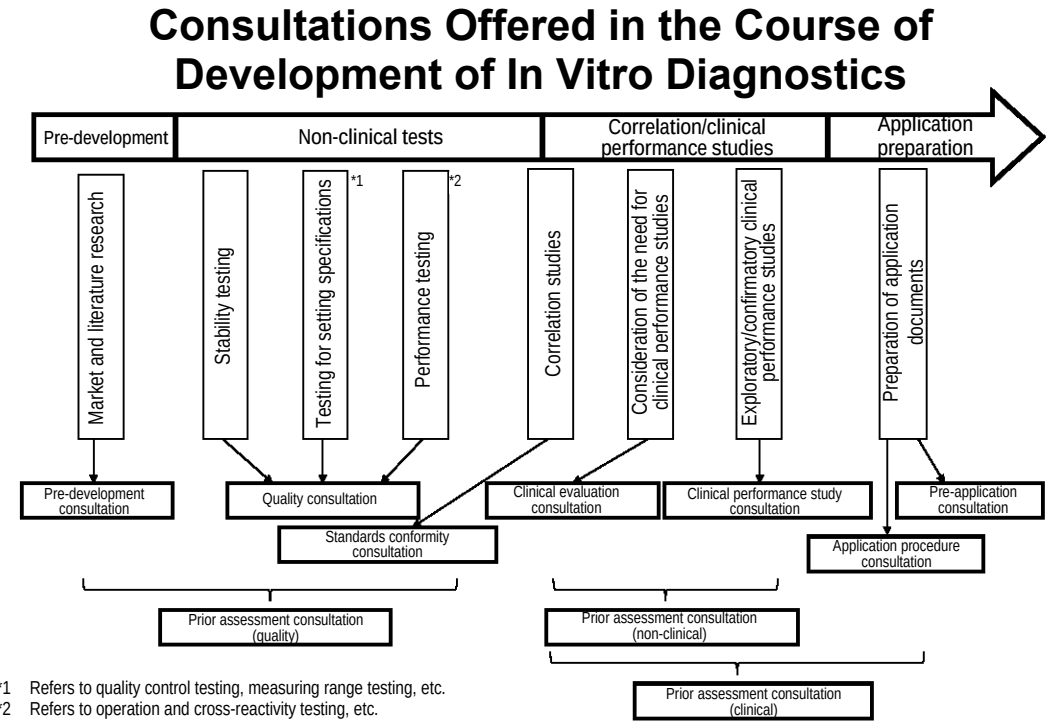
Number of Consultations for Medical Devices by Category in FY 2013

Consultation category	Consultations conducted	Consultations withdrawn	Total (conducted or withdrawn)
Pre-development consultation for medical devices	75	4	79
Safety consultation for medical devices (excluding biological medical devices)	3	0	3
Quality consultation for medical devices (excluding biological medical devices)	0	0	0
Safety consultation for biological medical devices	0	0	0
Quality consultation for biological medical devices	3	0	3
Performance testing consultation for medical devices	7	1	8
Clinical evaluation consultation for medical devices	22	2	24
Exploratory clinical trial consultation for medical devices	2	0	2
Clinical trial consultation for medical devices	29	2	31
Pre-application consultation for medical devices	5	0	5
Application procedure consultation for medical devices	9	1	10
Additional consultation for medical devices	6	1	7
Consultation on GLP/GCP compliance for medical devices	0	0	0
Prior assessment consultation for medical devices (quality)	0	0	0
Prior assessment consultation for medical devices (non-clinical)	1	0	1
Prior assessment consultation for medical devices (clinical)	0	0	0
Pre-development consultation for *in vitro* diagnostics	2	1	3
Quality consultation for *in vitro* diagnostics	1	0	1
Consultation on conformity with standards for *in vitro* diagnostics	1	0	1
Clinical evaluation consultation for *in vitro* diagnostics	1	0	1
Clinical performance study consultation for *in vitro* diagnostics	2	0	2
Pre-application consultation for *in vitro* diagnostics	0	0	0
Application procedure consultation for *in vitro* diagnostics	0	0	0
Additional consultation for *in vitro* diagnostics	0	0	0
Prior assessment consultation for *in vitro* diagnostics (quality)	0	0	0
Prior assessment consultation for *in vitro* diagnostics (non-clinical)	0	0	0
Prior assessment consultation for *in vitro* diagnostics (clinical)	0	0	0
Consultation on pharmacogenomics/biomarkers	0	0	0
Total	169	12	181

d. Review of consultation categories

- Regarding clinical trial consultations for medical devices and *in vitro* diagnostics, PMDA has been considering a review of consultation categories in order to accommodate diverse needs more closely in each stage of development, taking into account demands from the industry and previous experiences.





*1 Refers to quality control testing, measuring range testing, etc.
*2 Refers to operation and cross-reactivity testing, etc.

* *In addition to the consultation menu in the above diagram, other categories such as additional consultation are also available.*

(v) Promotion of evaluation of new technologies

a. Utilization of external experts

- See (v)-a [New drugs].
- The number of Expert Discussions conducted in FY 2013 was 71 (49 document-based discussions, 22 meetings).
- PMDA had discussions with external experts on issues raised in clinical trial consultations and application reviews for cellular and tissue-based products. At the Cellular and Tissue-based Products Subcommittee of the Science Board, PMDA heard opinions from external experts regarding interdisciplinary themes and discussed with them. Principles in the following notifications were utilized in Pharmaceutical Affairs Consultations on R&D Strategy etc.: “Current Perspective on Evaluation of Tumorigenicity of Cellular and Tissue-based Products Derived from induced Pluripotent Stem Cells (iPSCs) and iPSCs as Their Starting Materials” which was finalized at the meeting of the Science Board on August 20, 2013 and “Requirements for ensuring that residual non-proliferative recombinant viruses will not exist when such viruses are used to generate transgenic cells” presented at the meeting of the Subcommittee on Biotechnology of Pharmaceutical Affairs and Food Sanitation Council (PAFSC) on December 16, 2013. In addition, PMDA exchanged opinions with international regulators regarding the regulation of cellular and tissue-based products and topics to be addressed at ICH etc., through telephone conferences with EMA and FDA, gatherings at international conferences, etc.

b. Support for the development of national guidelines

- See (v)-b [New drugs].
- PMDA supported the preparation of the guidance documents for evaluation of autologous retinal pigment epithelial cells derived from iPS cells, physical function restoration systems, and medical devices for treatment of critical limb ischemia disease, which were all included in “Publication of the guidance documents for evaluation of next-generation medical devices” (PFSB/ELD/OMDE Notification No. 0529-1, dated May 29, 2013).

c. Preliminary reviews on gene therapy products, Cartagena Act, etc.

- See (v)-c [New drugs].

d. Implementation of Pharmaceutical Affairs Consultations on R&D Strategy

- See (v)-d [New drugs].

e. Support for the Super Special Consortia for development of advanced medicine

- See (v)-e [New drugs].

f. Support project for promoting consultations/applications for innovative medical devices

- In order to prevent delays in developing innovative medical devices due to financial problems at small- and medium-sized enterprises (SMEs) and venture companies that discovered promising seed-stage technologies, PMDA implemented the “support project for promoting consultations/applications for innovative medical devices” which give a subsidy to SMEs and venture companies that meet certain requirements for the purpose of reducing financial burdens in

consultations/applications for regulatory approval. This scheme reimburses 50% of the user fee for a consultation or a new medical device application after the user fee is paid by the relevant SME or venture company. . Two companies applied for consultation fee subsidy, and the subsidies were accordingly given to the companies in FY 2013.

Inspections

- PMDA conducts a full range of inspections and takes measures to promote proper conduct of laboratory tests and clinical trials for drug and medical device applications for approval, to secure the reliability of application documents, and to properly maintain and manage the product manufacturing processes and quality control systems.

(i) Efficient GLP/GCP/GPSP inspections and data integrity assessments

- PMDA efficiently conducted on-site and document-based inspections and data integrity assessment concerning the studies and data submitted in applications for new drugs and medical devices, to determine whether such data were collected in compliance with the requirements of the Ministerial Ordinance on Good Laboratory Practice (GLP), the Ministerial Ordinance on Good Clinical Practice (GCP), and the data integrity standards for products applications.
- PMDA issued the following four notifications regarding procedures of document-based compliance assessments for product applications and GCP on-site inspections, as well as those of document-based compliance assessments for documents submitted for re-examination and re-evaluation and GPSP on-site inspections (notifications by the Chief Executive of PMDA dated October 12, 2012). PMDA publicized the notifications and conducted inspections based on them.

  Notification on the procedure for inspections related to new drug applications: PMDA Notification No. 1012063

  Notification on the procedure for inspections related to regulatory review of medical device applications: PMDA Notification No. 1012064

  Notification on the procedure for inspections related to re-examinations and re-evaluations of new drugs: PMDA Notification No. 1012065

  Notification on the procedure for inspections related to re-examinations and re-evaluations of medical devices: PMDA Notification No. 1012066
- The checklist of document-based compliance assessments for new drugs (quality/non-clinical) was reviewed to remind sponsors that items such as materials to be confirmed included in the existing checklist are examples. The revised version was posted on the PMDA website and was publicized by issuing the Administrative Notice dated March 31, 2014 “Checklist of Document-based Assessments of New Drugs.” With this, the Administrative Notice dated August 22, 2001 “Checklist of Document-based Assessments of New Drugs” was abolished.
- PMDA conducted 125 GCP on-site inspections (at companies) for new drugs (the number is those of active ingredients used) in FY 2013, and 124 (99.2%) of them were conducted in conjunction with document-based compliance assessments.
- Although a standard administrative processing time for GLP/GCP/GPSP inspections has not been set, PMDA worked hard to ensure that the inspection processing time did not affect the review time of applications for individual products.

a. Promotion of document-based compliance assessment on sites

- PMDA introduced a method in FY 2009 whereby its staff members visit companies for document-based compliance assessments for new drugs. In FY 2013, 124 assessments (88.6%) were conducted in this manner, out of a total of 140 assessments (on the basis of the number of active ingredients).

b. Introduction of the GCP system inspection

- As part of investigation on the GCP system inspection, a survey using the EDC management sheet (PMDA/CPE Notification No. 0327001, dated March 27, 2013, issued by the Director of Center for Product Evaluation, PMDA) was started in full scale in October 2013.
- The survey using this management sheet was considered to be a useful method, and the implementation of such a survey for other operations was considered. In FY 2013, a pilot survey using the management sheet was conducted for operations related to collection, evaluation, and provision of safety information etc.
- Currently, the mandatory submission of electronic clinical trial data in compliance with the CDISC standards at the time when application is filed is under consideration at PMDA. Consequently, clinical trial data are expected to be increasingly based on the CDISC standards. The introduction of a new method of survey was decided accordingly, and then a survey on actual use was conducted for member companies of relevant industry associations in order to accurately comprehend the current status and future schedule of CDISC standards adoption.

c. Improvement of the efficiency of GLP/GCP/GPSP inspections and data integrity assessments for medical devices

- In Consultations on R & D Strategy conducted to discuss clinical studies of medical devices, PMDA made efforts for facilitating the proper conduct of clinical studies in compliance with GCP and the improvement of the integrity of submission data, by conducting consultations on GCP (pre-consultation meetings, consultations).
- In FY 2013, a total of 1,160 document-based assessments/data integrity assessments and 5 GCP on-site inspections were completed.

d. International contributions in relation to GLP compliance assessments

- The Organisation for Economic Co-operation and Development (OECD), the only organization that performs international harmonization activities for GLP, holds a training course for GLP inspectors once every 2 or 3 years in OECD member countries. The host country of the training course is supposed to practically prepare and organize the course, and the 11th course session held in October 2013 was hosted by PMDA as the first session in Asia. On that occasion, the course program had 83 participants from 27 countries, and lectures and case studies were provided centering on the methods of inspection for computer system validation and quality assurance. Participants appreciated the high level of prior preparation and program handling during the course period in addition to the contents of the course.

(ii) Efficient GPSP/GPMSP inspections and data integrity assessments for re-examination

- PMDA conducts document-based and on-site inspections and data integrity assessments as to whether or not data submitted for re-examination of approved new drugs and new medical devices had been collected and prepared in compliance with the data integrity standards for product

applications and the requirements of the Ministerial Ordinance on Good Post-Marketing Study Practices (GPSP) or the Ministerial Ordinance on Good Post-Marketing Surveillance Practice (GPMSP).

In FY 2013, the number of completed assessments was 71 for new drugs and 9 for new medical devices.

- PMDA conducts data integrity assessments as to whether or not data submitted for re-evaluation of approved drugs had been collected and generated in compliance with the data integrity standards for product applications etc., but there were no products subject to the data integrity assessments for re-evaluation in FY 2013.

Number of GLP/GCP/GPSP Compliance Assessments

		FY 2009	FY 2010	FY 2011	FY 2012	FY 2013
Document-based assessments		2,140	2,359	2,437	2,737	2,610
	New drugs	246	251	280	286	364
	Generic drugs	1,004	1,040	1,118	1,188	1,086
	Medical devices	890	1,068	1,039	1,263	1,160
GCP on-site inspections		175	171	149	197	242
	New drugs	164	158	140	187	222
	Generic drugs	10	10	8	9	15
	Medical devices	1	3	1	1	5
Document-based assessments for re-examination		66	138	111	127	80
	New drugs	66	135	109	112	71
	New medical devices	-	3	2	15	9
GPSP inspections		65	135	109	112	71
	New drugs	65	135	109	112	71
	New medical devices	–	–	–	–	–
Document-based assessments for re-evaluation		–	–	–	–	–
GLP inspections		26	30	32	39	21
	Drugs	18	26	23	29	18
	Medical devices	8	4	9	10	3

Note: The numbers of document-based assessments (excluding those for medical devices), GCP on-site inspections (excluding those for medical devices), document-based assessments for re-examination (excluding those for medical devices), GPSP inspections (excluding those for medical devices), document-based assessments for re-evaluation and GLP inspections represent numbers of products for which inspection/assessment was completed. The numbers of document-based assessments, GCP on-site inspections, document-based assessments for re-examination and GPSP inspections (all for medical devices) represent the numbers of products for which inspection/assessment and review was completed. (Products for which inspection/assessment is completed from January 2014)

(iii) Efficient GMP/QMS inspections

a. Background of GMP/QMS inspections

- Based on the amended Pharmaceutical Affairs Act that came into effect on April 1, 2005, compliance of methods for manufacturing control and quality control at manufacturing sites for drugs etc., with requirements specified in the Ministerial Ordinance on GMP for Drugs and Quasi-drugs*, and/or Ministerial Ordinance on QMS for Medical Devices and *In vitro* Diagnostics* is a pre-requisite for approval. Therefore, in addition to the manufacturing sites already licensed by the Minister of Health, Labour and Welfare, the following manufacturing sites became subject to

inspection by PMDA: (1) foreign manufacturing sites related to all products that require regulatory approval; and (2) domestic manufacturing sites for new drugs, new medical devices or Class IV medical devices (high-risk medical devices such as pacemakers).

* *Ministerial Ordinance on Good Manufacturing Practice (GMP) for Drugs and Quasi-drugs (MHLW Ministerial Ordinance No.179 of 2004)*
* *Ministerial Ordinance on Quality Management System (QMS) for Medical Devices and In vitro Diagnostics (MHLW Ministerial Ordinance No.169 of 2004)*

Note 1: GMP (Good Manufacturing Practice): Standards for manufacturing control and quality control
Note 2: QMS (Quality Management System): A quality management/supervision system

b. Establishment of the inspection system

- PMDA continued to recruit GMP/QMS inspectors and the number of inspectors was 48 as of April 1, 2013. In the areas of drugs and quasi-drugs, PMDA carried forward the establishment of the system to supervise quality management, such as by setting up an inspection quality assurance group, with an eye on the accession to the Pharmaceutical Inspection Cooperation Scheme (PIC/S: An international organization on GMP inspections, centering on European countries). In addition, PMDA enriched training programs through the use of external workshops etc., in order to strengthen the inspection system for cellular and tissue-based products.
- The administrative processing status of GMP/QMS inspections in FY 2013 is shown below:

GMP/QMS Inspections under the Pharmaceutical Affairs Act

	FY 2008					FY 2009				
	Applications	Completed		Withdrawn	In progress	Applications	Completed		Withdrawn	In progress
Drugs *	1,158	738	(214)	52	812	2,228	2,000	(297)	71	969
In vitro diagnostics	70	78	(1)	3	33	115	107	(3)	5	36
Quasi-drugs	2	3	(0)	0	2	3	3	(0)	0	2
Medical devices	971	915	(42)	44	360	1,201	1,285	(66)	39	237
Total	2,201	1,734	(257)	99	1,207	3,547	3,395	(366)	115	1,244

	FY 2010					FY 2011				
	Applications	Completed		Withdrawn	In progress	Applications	Completed		Withdrawn	In progress
Drugs *	1,159	1,324	(131)	120	684	1,538	1,283	(185)	31	908
In vitro diagnostics	66	81	(0)	2	19	73	85	(0)	1	6
Quasi-drugs	1	0	(0)	1	2	0	0	(0)	0	2
Medical devices	896	944	(54)	40	149	697	765	(36)	24	57
Total	2,122	2,349	(185)	163	854	2,308	2,133	(221)	56	973

	FY 2012					FY 2013				
	Applications	Completed		Withdrawn	In progress	Applications	Completed		Withdrawn	In progress
Drugs *	1,582	1,593	(198)	40	857	1,508	1,415	(168)	75	875
In vitro diagnostics	64	48	(0)	0	22	52	67	(1)	0	7
Quasi-drugs	6	2	(0)	2	4	3	3	(1)	0	4
Medical devices	999	954	(81)	3	99	988	883	(61)	11	193
Total	2,651	2,597	(279)	45	982	2,551	2,368	(231)	86	1,079

* *Excluding in vitro diagnostics.*

Note: Figures in parentheses represent the numbers of on-site inspections out of completed inspections.

- The administrative processing times of GMP/QMS inspections in FY 2013 are shown below:

Median Processing Time of GMP/QMS Inspections

	FY 2008		FY 2009		FY 2010	
	Median total processing time	Median PMDA processing time	Median total processing time	Median PMDA processing time	Median total processing time	Median PMDA processing time
Drugs*	155 days	100 days	162 days	91 days	118 days	63 days
In vitro diagnostics	117 days	46 days	110 days	56 days	117 days	62 days
Quasi-drugs	156 days	29 days	154 days	108 days	–	–
Medical devices	131 days	59 days	142 days	56 days	145 days	69 days
	FY 2011		FY 2012		FY 2013	
	Median total processing time	Median PMDA processing time	Median total processing time	Median PMDA processing time	Median total processing time	Median PMDA processing time
Drugs*	147 days	77 days	176 days	90 days	118 days	71 days
In vitro diagnostics	83 days	38 days	100 days	36 days	106 days	66 days
Quasi-drugs	–	–	219 days	71 days	272 days	71 days
Medical devices	113 days	21 days	84 days	44 days	106 days	56 days

* *Excluding in vitro diagnostics.*

- The processing status of inspections of manufacturing facilities conducted in FY 2013 at domestic manufacturing sites licensed by the Minister, as based on the Regulations for Buildings and Facilities for Pharmacies, Manufacturing Sites, etc., is shown below:

Number of Inspections of Buildings and Facilities for Domestic Manufacturing Sites

	FY 2009		FY 2010		FY 2011		FY 2012		FY 2013	
Drugs*	40	(25)	20	(19)	25	(19)	15	(9)	9	(4)
In vitro diagnostics	4	(2)	1	(1)	3	(3)	1	(1)	3	(3)
Medical devices	2	(1)	3	(3)	0	(0)	2	(1)	0	(0)
Total	46	(28)	24	(23)	28	(22)	18	(11)	12	(7)

* *Excluding in vitro diagnostics.*

Note: Values include withdrawn applications. Figures in parentheses represent the numbers of on-site inspections out of completed inspections.

- PMDA conducts for-cause inspections, questioning, and sampling with regard to domestic manufacturers etc., under instructions from the MHLW. The number of for-cause inspections conducted in FY 2013 is shown below:

Number of For-cause Inspections (Domestic Manufacturers)

	FY 2009	FY 2010	FY 2011	FY 2012	FY 2013
Drugs*	12	6	12	13	6
In vitro diagnostics	3	2	3	1	1
Medical devices	0	1	0	0	0

* *Excluding in vitro diagnostics.*

- PMDA conducts simple consultations on GMP/QMS inspections. The number of simple consultations on GMP/QMS inspections conducted in FY 2013 is shown below:

Number of Simple Consultations Conducted for GMP/QMS Inspections

	FY 2009	FY 2010	FY 2011	FY 2012	FY 2013
Drugs*	39	36	44	38	44
In vitro diagnostics	1	0	0	0	0
Quasi-drugs	0	1	0	0	0
Medical devices	17	6	6	8	3
Total	57	43	50	46	47

* *Excluding in vitro diagnostics.*

c. Promotion of on-site inspections of foreign manufacturing sites

- The number of on-site inspections of foreign manufacturing sites that were initiated in FY 2005 is shown below:

On-site Inspections of Foreign Manufacturing Sites of Drugs by Region

	Europe	North, Central and South America	Asia/Oceania	Africa	Total
FY 2005	2	8	2	0	12
FY 2006	13	20	2	1	36
FY 2007	22	22	8	0	52
FY 2008	31	19	32	0	82
FY 2009	39	20	47	0	106
FY 2010	12	24	29	0	65
FY 2011	9	7	45	0	61
FY 2012	14	14	38	0	66
FY 2013	12	10	42	0	64

Note: Breakdown of FY 2013:
(Europe) France, Ireland, UK, Italy, Romania, Belgium, Iceland, Sweden, Denmark;
(North, Central and South America) the United States (including Puerto Rico), Canada, Brazil;
(Asia, Oceania) China, India, South Korea, Taiwan, Singapore, Thailand

On-site Inspections of Foreign Manufacturing Sites of Medical Devices by Region

	Europe	North, Central and South America	Asia/Oceania	Africa	Total
FY 2005	1	1	0	0	2
FY 2006	5	10	0	0	15
FY 2007	1	10	0	0	11
FY 2008	13	17	0	0	30
FY 2009	3	28	5	0	36
FY 2010	8	19	1	0	28
FY 2011	4	15	1	0	20
FY 2012	11	22	4	0	37
FY 2013	4	12	10	0	26

Note: Breakdown of FY 2013:
(Europe) UK, Switzerland, Turkey;
(North, Central and South America) the United States (including Puerto Rico), Canada;
(Asia, Oceania) Israel, Singapore, Taiwan, South Korea, China, United Arab Emirates (UAE)

- The number of inspections of manufacturing facilities conducted in FY 2013 at foreign manufacturing sites based on the Regulations for Buildings and Facilities for Pharmacies and Manufacturing Establishments is shown below:

Number of Inspections of Buildings and Facilities for Foreign Manufacturing Sites

	FY 2009	FY 2010	FY 2011	FY 2012	FY 2013
Drugs*	390	230	579	530	383
In vitro diagnostics	40	27	60	68	79
Quasi-drugs	41	26	72	62	58
Medical devices	910	677	1,187	1,751	1,453
Total	1,381	960	1,898	2,411	1,973

* *Excluding in vitro diagnostics.*

Note: Values include withdrawn applications. All inspections were done on a document basis.

- PMDA conducts for-cause inspections, questioning, and sampling with regard to foreign manufacturers etc., under instructions from MHLW. The number of for-cause inspections conducted in FY 2013 is shown below:

Number of For-cause Inspections (Foreign Manufacturing Sites)

	FY 2009	FY 2010	FY 2011	FY 2012	FY 2013
Drugs*	1	1	1	4	2
In vitro diagnostics	0	0	0	0	0
Medical devices	0	4	1	1	0
Total	1	5	2	5	2

* *Excluding in vitro diagnostics.*

Number of On-site GMP Inspections of Foreign Manufacturing Sites of Drugs by Country

Region	Country	FY 2007	FY 2008	FY 2009	FY 2010	FY 2011	FY 2012	FY 2013	Total
Europe	France	6	5	6	1	3	2	1	24
	Denmark	3	2	2	0	0	0	2	9
	Ireland	2	5	3	2	0	1	1	14
	UK	4	1	3	0	0	1	1	10
	Netherlands	1	1	5	0	0	2	0	9
	Spain	3	1	1	0	0	0	0	5
	Italy	2	5	3	2	0	1	2	15
	Belgium	1	2	4	3	1	0	2	13
	Austria	0	2	2	0	1	2	0	7
	Finland	0	0	2	0	0	1	0	3
	Germany	0	3	7	0	3	1	0	14
	Sweden	0	1	0	0	0	0	1	2
	Romania	0	1	0	0	0	0	1	2
	Czech	0	0	0	0	0	1	0	1
	Ukraine	0	0	0	0	0	1	0	1
	Lithuania	0	0	0	0	0	1	0	1
	Slovenia	0	2	1	0	0	0	0	3
	Portugal	0	0	0	3	0	0	0	3
	Greece	0	0	0	0	1	0	0	1
	Turkey	0	0	0	1	0	0	0	1
	Iceland	0	0	0	0	0	0	1	1
	Subtotal	22	31	39	12	9	14	12	139
North, Central and South America	USA	22	14	18	23	6	14	8	105
	Canada	0	2	2	1	0	0	1	6
	Mexico	0	1	0	0	1	0	0	2
	Argentina	0	2	0	0	0	0	0	2
	Brazil	0	0	0	0	0	0	1	1
	Subtotal	22	19	20	24	7	14	10	116
Asia/Oceania	China	5	11	25	10	20	16	18	105
	India	1	12	4	7	4	4	3	35
	Singapore	2	4	0	0	0	0	2	8
	South Korea	0	3	9	10	18	14	11	65
	Indonesia	0	0	0	0	0	1	0	1
	Taiwan	0	2	6	1	1	2	6	18
	Thailand	0	0	2	0	1	0	2	5
	Vietnam	0	0	0	1	1	0	0	2
	Israel	0	0	0	0	0	1	0	1
	New Zealand	0	0	1	0	0	0	0	1
	Subtotal	8	32	47	29	45	38	42	241
Grand Total		52	82	106	65	61	66	64	496

Note 1: Not including for-cause inspections at foreign manufacturing sites under Article 75-4 of the Pharmaceutical Affairs Act.

Note 2: Puerto Rico was included in the USA.

Number of On-site QMS Inspections of Foreign Medical Devices Manufacturing Sites by Country

Region	Country	FY 2007	FY 2008	FY 2009	FY 2010	FY 2011	FY 2012	FY 2013	Total
Europe	Ireland	0	6	0	4	1	3	0	14
	UK	0	1	0	0	1	0	1	3
	Italy	0	2	0	2	1	1	0	6
	Netherlands	0	1	0	1	0	0	0	2
	Switzerland	0	1	1	0	0	0	1	3
	Spain	0	1	0	0	0	1	0	2
	France	1	1	1	1	1	4	0	9
	Denmark	0	0	1	0	0	0	0	1
	Austria	0	0	0	0	0	1	0	1
	Belgium	0	0	0	0	0	1	0	1
	Turkey	0	0	0	0	0	0	1	1
	Subtotal	1	13	3	8	4	11	3	43
North, Central and South America	USA	10	16	27	19	12	21	8	113
	Mexico	0	1	0	0	1	0	0	2
	Brazil	0	0	1	0	0	0	0	1
	Canada	0	0	0	0	1	1	4	6
	Costa Rica	0	0	0	0	1	0	0	1
	Subtotal	10	17	28	19	15	22	12	123
Asia	China	0	0	3	0	0	1	1	5
	South Korea	0	0	0	1	0	0	5	6
	Thailand	0	0	0	0	0	1	0	1
	Singapore	0	0	2	0	0	0	2	4
	Philippines	0	0	0	0	0	2	0	2
	Israel	0	0	0	0	1	0	1	2
	Taiwan	0	0	0	0	0	0	1	1
	UAE	0	0	0	0	0	0	1	1
	Subtotal	0	0	5	1	1	4	11	22
Grand Total		11	30	36	28	20	37	26	188

Note 1: Not including for-cause inspections at foreign manufacturing sites under Article 75-4 of the Pharmaceutical Affairs Act.

Note 2: Puerto Rico was included in the USA.

d. Coordination between GMP/QMS inspections and reviews

- During the review process of drug and quasi-drug applications, the Office of GMP/QMS Inspections holds periodic meetings (once a month with Offices of New Drug) to involve reviewers in GMP inspections and to update the progress status of reviews, in order to conduct inspections at appropriate timings in the review process.
- For applications for Class IV medical devices such as high-risk cellular and tissue-derived medical devices and pacemakers, QMS inspectors collaborate with reviewers as needed to ensure that there are no discrepancies between important product specifications that are included in the application and specifications actually employed at manufacturing sites. Such collaboration is also maintained for reviewing medical devices designated for priority review or expedited review, where the progress is managed to ensure that QMS inspections do not affect the progress of reviews.

3.2.(2) Improvement of reliability of reviews and related services and safety measures

(i) Enriching training program

a. Consideration of the method of training evaluations

- PMDA evaluated new recruit training and on-site training programs (e.g., observation visits to facilities) based on the method of training evaluations developed in FY 2009. The training programs earned high marks in terms of participant satisfaction and acquisition of knowledge/skills.

b. Development of training programs for reviews of medical devices and safety measures

- A hands-on training using medical devices in the areas of cardiovascular surgery, orthopedics, etc., was also provided. For the acquisition of basic knowledge about medical devices, first-class and second-class ME technical trainings were also provided (19 employees).

  Also, in the new recruit training program, special training on Risk Management Plan (RMP) and training on health damage including adverse drug reactions were conducted in addition to training on operations for safety measure.

c. Lectures and guidance given by skilled experts

- In order to educate the staff from the broad perspective required for reviews and safety measures, PMDA provided its employees with the following training opportunities: special training programs including lectures in which experts invited from in and out of Japan presented product development activities, design/management of medical devices, etc., at companies, and training on respective review parts with the cooperation of the National Institute of Health Sciences (NIHS) (34 times); training programs on laws and regulations such as the Pharmaceutical Affairs Act to learn the regulatory system etc. (6 times); and training programs on clinical study design to learn biostatistics (12 times).

d. Education and training of GMP/QMS inspectors

- GMP/QMS inspectors of PMDA participated in programs such as the Regulatory Affairs and Hygienic Control Training Program at the National Institute of Public Health, a training program hosted by the Parenteral Drug Association (PDA), and a training program hosted by AAMI (Advancing Safety in Medical Technology), and also participated in a joint GMP/QMS mock inspection training program provided by MHLW, a workshop on sterilization validation of medical devices, etc. PMDA dispatched its inspectors for training programs provided by the inspection divisions of the Ireland Medicine Board (IMB) and the Medicines and healthcare products Regulatory Agency (MHRA, UK)) in PIC/S member nations. PMDA also conducted long-term GMP on-site training programs (for 2 months) at drug manufacturing facilities etc., and dispatched two inspectors to two facilities with cooperation of relevant organizations.

e. Improvement of training in clinical practice

- In order to ensure that safety measures are planned in line with the clinical practice, PMDA dispatched five staff members to two medical institutions for them to be trained in the same way as for hospital pharmacists.

f. Visits to manufacturing facilities

- PMDA conducted on-site training programs, such as observation visits to drug/medical device manufacturing facilities (9 facilities) and research institutions (2 facilities).

(ii) Promotion of interaction with outside researchers and investigative research

a. Promotion of collaborative graduate school program

- In order to contribute to the diffusion of regulatory science and provision of information, PMDA promoted the Collaborative Graduate School Program and approached universities. PMDA concluded the collaborative graduate school agreement with 2 universities (Note 2) in FY 2013, in addition to the 17 partner universities.(Note 1) From April 2011 to November 2013, PMDA accepted one graduate student from Gifu Pharmaceutical University Graduate School as a pre-doctoral fellow to provide research guidance etc. As a fruit of it, an original paper was published. A PMDA internal debriefing session on the research results by the student was held (March 2014). The student earned a doctorate degree (pharmaceutical sciences) (March 2014).

  (Note 1) University of Tsukuba (Graduate School of Comprehensive Human Sciences), Yokohama City University (Graduate School of Medicine), Yamagata University (Graduate School of Medical Science), Gifu Pharmaceutical University (Graduate School of Pharmaceutical Science), Kobe University (Graduate School of Medicine) and Chiba University (Graduate School of Medical and Pharmaceutical Sciences/Graduate School of Medicine), Musashino University (Graduate School of Pharmaceutical Sciences), Gifu University (United Graduate School of Drug Discovery and Medical Information Sciences), Teikyo University (Graduate School of Medicine/Graduate School of Pharmaceutical Sciences), Shujitsu University (Graduate School of Clinical Pharmacy), University of Shizuoka (Graduate School of Integrated Pharmaceutical and Nutritional Sciences), Osaka University (Graduate School of Medicine/Graduate School of Pharmaceutical Sciences), Kyoto Pharmaceutical University (Graduate School of Pharmaceutical Sciences), Okayama University (Graduate School of Medicine, Dentistry and Pharmaceutical Sciences), Nagoya University (Graduate School of Medicine), Nagoya City University (Graduate School of Pharmaceutical Sciences), Hokkaido University (Graduate School of Medicine)

  (Note 2) Kanazawa University (College of Medical, Pharmaceutical and Health Sciences), Kumamoto University (Graduate School of Medical Sciences/Graduate School of Pharmaceutical Sciences)

- As a part of efforts to increase the recognition of regulatory science, PMDA made arrangement and sent PMDA staff to give lectures upon request from universities etc. (FY 2013: 29 universities, 51 lectures).

b. Development of internal rules associated with the collaborative graduate school program

- PMDA developed its internal rules in FY 2009 to accept students from partner university graduate schools, and accepted one student from a partner university graduate school as a pre-doctoral fellow from April 2011 to November 2013. PMDA established a regulatory science promotion liaison meeting and a committee on the collaborative graduate school agreement and improved compensation and working conditions for visiting lecturers, and also prepared the “Implementation Guidelines for Acceptance of Pre-Doctoral Fellow at PMDA for FY 2014” to start creating environments to appropriately accept students for the partner university graduate school.

c. Promotion of initiative to facilitate development of innovative drugs, medical devices, and cellular and tissue-based products

- PMDA has worked to foster personnel familiar with regulatory science through personnel exchanges with research institutions including universities based on the initiative to facilitate development of innovative drugs, medical devices, and cellular and tissue-based products (a project funded by MHLW), and has also promoted cooperation in research projects on methods for evaluating the efficacy and safety of products developed using advanced technologies. In FY 2013, PMDA conducted personnel exchanges with 24 universities etc., accepted 20 researchers as specially-appointed experts (including non-regular employees), and dispatched 34 employees (including non-regular employees).

(iii) Promotion of responding to advanced technologies through cross-sectional projects etc. (Refer to 2. (1) [5] b).

a. Support for the development of evaluation guidelines

- In FY 2013, PMDA provided cooperation for affairs such as the preparation of government's evaluation guidelines through activities of 11 standards development projects and working groups as the Projects Across Multi-offices in PMDA for the purpose of promoting product development, promoting international collaborations for review standards etc., and accelerating reviews by making clear scientific principles for reviews of drugs and medical devices. Specifically, PMDA provided cooperation for the preparation of three notifications and two Q&A documents from the *In vitro* Companion Diagnostic Device Project, one Q&A document from the Post-approval Manufacturing Changes Project, two notifications and Q&A documents from the Microdose Trials Project and the Nanomedicine Initiative Project, and one notification and Q&A document from the Nanomedicine Initiative Project.
- PMDA gave presentations on activities of the cross-sectional projects at academic conferences, the Science Board, etc., for PR purposes, and also exchanged opinions with experts regarding evaluation policies etc.

b. Contribution to establishment of internationally harmonized methods

- In FY 2013, in order to investigate individual issues addressed by ' Projects Across Multi-offices in PMDA including Pediatric Drugs Working Group, Orphan Drug Working Group, QbD Assessment Project, Nanomedicine Initiative Project, PMDA exchanged opinions with experts from regulatory authorities in the EU and the U.S. through telephone conferences, preliminary meetings, etc. The members of the Nanomedicine Initiative Project of PMDA contributed to preparation of a joint reflection paper with overseas regulatory authorities which was issued in FY 2013. Members of most projects also participated in presentation sessions and panel discussions in workshops and international academic conferences, and thus contributed to the processes toward international harmonization.

(iv) Promoting proper conduct of clinical trials

- PMDA exchanged opinions on GCP or the conduct of clinical trials with healthcare professionals at medical institutions etc., which underwent inspection, after completion of the GCP on-site inspection.
- In order to enhance understanding of the proper conduct of clinical trials, PMDA held GCP Workshops in Tokyo and Osaka targeting drug development and regulatory affairs personnel, auditors of pharmaceutical companies and site management organizations (SMOs) as well as

healthcare professionals. In the Workshops, PMDA representatives presented issues that are frequently pointed out as findings in document-based compliance assessment or GCP on-site inspections. The workshop materials were posted on PMDA's website for concerned parties to be informed of. Also, PMDA staff members gave presentations at academic conferences, etc., attended by healthcare professionals to exchange opinions with concerned parties.

Number of GCP Workshop Participants

Location	FY 2009	FY 2010	FY 2011	FY 2012	FY 2013
Tokyo	1,165	1,048	1,086	1,254	1,189
Osaka	461	455	418	471	404
Total	1,626	1,503	1,504	1,725	1,593

(v) Promoting provision of information such as review reports

a. Improving provision of information

- In promoting proper use of drugs and medical devices and ensuring transparency of reviews, PMDA has, with the understanding and cooperation of relevant companies, released information on reviews of new drug applications, including review reports, on the Medical Product Information page of its website, in collaboration with MHLW.
- PMDA worked with MHLW to develop Notifications (draft) etc., to publicly release re-examination reports, and started posting re-examination reports on its website of new drugs in FY 2009 and of new medical devices in FY 2010.
- In order to make available information on PMDA's reviews and safety measures to foreign users, PMDA has created and released the English version of review reports on its English website. In FY 2013, the Agency created and released the English translations of 20 review reports.

b. Releasing information related to review reports

(Review reports on new drugs)

- Based on the submitted information, new drugs fall into 2 categories: those that are to be deliberated in the Drug Committees of the Pharmaceutical Affairs and Food Sanitation Council (PAFSC) (hereinafter referred to as "deliberation products"); and those that are to be reported to the Drug Committees of PAFSC (hereinafter referred to as "report products"). For “deliberation products,” both "review reports" that describe details and results of reviews and "summaries of product applications" that summarize submitted data are subject to public release, whereas for “report products,” "review reports" are subject to public release. The information is posted on the PMDA website after conferring with the relevant companies regarding the content released for each product, based on a Notification Issued from ELD, PFSB at MHLW.
- In FY 2013, PMDA released 120 review reports (median time from approval to release, 4 days), 81 summaries of product applications (median time from approval to release, 35 days) and 38 re-examination reports (median time from result notification to release, 8 days).

  The percentage of review reports released within one month after approval was 99.1% (100% in FY 2012) and the percentage of summaries of product applications released within 3 months after approval was 95.0% (100% in FY 2012).

(Review reports on new medical devices)

- In FY 2013, PMDA released 19 review reports (median time from approval to release, 28 days), 18 summaries of product applications (median time from approval to release, 89 days) and 9 re-examination reports (median time from result notification to release, 5 days).

  The percentage of review reports released within one month after approval was 73.7% (81.8% in FY 2012) and the percentage of summaries of product applications released within 3 months after approval was 77.8% (73.3% in FY 2012).

(Review reports on OTC drugs and quasi-drugs)

- It was decided that PMDA should publicly release review reports on OTC drugs and quasi-drugs, following the issuance of the PFSB/ELD Notification dated March 31, 2006, which specified publication procedures etc. This Notification was amended on October 31, 2008 so that summaries of product applications are also published. In FY 2013, PMDA released 5 review reports and 4 summaries of product applications on OTC drugs. There were no released reports for quasi-drugs.

c. Securing of impartiality in the utilization of external experts

- It is necessary to secure impartiality and transparency of judgment given by the commissioned external experts. The "Rules for Convening Expert Discussions etc., by the Pharmaceuticals and Medical Devices Agency" (December 25, 2008) has been set forth with the aim to ensure the transparency of PMDA's services by releasing review reports and the information on the conflict of interests of commissioned external experts, thereby allowing outside parties to verify the decision-making process. In accordance with the rule, PMDA reports to the Advisory Council and the Committee on Review and Safety Operations regarding cash contributions and contract money received by the external experts commissioned by PMDA for Expert Discussions on reviews and safety measures.

(vi) Promotion of international activities

- PMDA has been proactively promoting international activities in line with the PMDA International Strategic Plan developed in February 2009, aiming to proceed with the activities in a planned and systematic manner in cooperation with MHLW. In October 2011, PMDA established the PMDA International Vision to clarify the concrete goals to be attained in the next 5 to 10 years while achieving the PMDA International Strategic Plan. Based on the PMDA International Vision and PMDA International Strategic Plan, PMDA intends to meet the needs of the Japanese citizen and people around the world for drugs and medical devices, thereby contributing to international society. PMDA also arranged these concrete efforts as the Road map for the PMDA International Vision and aims to steadily implement the road map by following it up in a timely manner.

a. Strengthening of cooperation with the U.S., the EU, Asian countries, and relevant international organizations

- In order to exchange information concerning consultations, reviews, and post-marketing safety measures with the U.S. and the EU, PMDA has had discussions with the U.S. FDA and the EC/EMA, gathered information on review systems, safety measures, etc., and also exchanged opinions for international cooperation, in collaboration with the MHLW.

- PMDA dispatched its employees as liaison officers to the U.S. Pharmacopeial Convention, the EMA, and Swissmedic, in order to gather information and exchange views.
- PMDA participated in the 1st meeting of Global Coalition for Regulatory Science Research (GCRSR) held in Little Rock (the U.S.) in August 2013, and exchanged opinions on regulatory science research with regulatory authorities and academia in related countries including the U.S., Canada, and Australia.
- PMDA participated in the 8th International Summit of Heads of Medicines Regulatory Agencies held in Amsterdam (the Netherlands) in December 2013, and exchanged opinions on pharmaceutical regulatory affairs with regulators from various countries including the U.S. FDA and the EMA. PMDA had deliberations for establishing the International Coalition of Medicines Regulatory Authorities (ICMRA), an international collaborative organization to strategically control/coordinate various issues of international cooperation and harmonization by executives of regulatory authorities from various countries and to support enhance capabilities of regulatory authorities, and Dr. Kondo, Chief Executive of PMDA, was elected as the vice-chair of the Management Committee.
- In October 2013, PMDA held the Thailand-Japan Symposium with the ThaiFDA, and exchanged opinions on pharmaceutical regulation, safety measures, Pharmacopoeia, and GMP inspections in both countries. At the same time, the two regulatory agencies held a bilateral conference and agreed to the development of close cooperative relationship in the future.
- In December 2013, PMDA participated in the Joint Conference of Taiwan and Japan held in Taiwan, and exchanged opinions on pharmaceutical regulations and reviews, generic products, and GMP in both countries. At the same time, PMDA held a bilateral conference and agreed to the creation of close collaborative relationship in the future.
- In February 2014, PMDA held bilateral conferences with the EMA, Singapore HSA, Indonesia NADFC, and WHO, and exchanged information and opinions. PMDA also deliberated the progress status of ongoing items of cooperation and the future direction toward further advancement.
- PMDA held an OECD's GLP training course in Japan. PMDA also has made efforts to reinforce collaboration with OECD member countries through measures such as participating in the OECD's GLP working group and dispatching trainees to the OECD's secretariat. In addition, PMDA shared information on the inspection status etc., by exchanging lists for inspections with OECD member countries.

  Regarding GCP, PMDA informed the EMA and the inspection agencies of the relevant EU countries of inspection schedule etc., in compliance with the agreed procedures when conducting inspections in EU countries.

b. Strengthening of activities for international harmonization

- In FY 2013, PMDA continued to actively participate in international harmonization initiatives for drugs such as ICH*. PMDA improved the consistency of Japanese standards with international standards, such as those for data prepared for regulatory submission, which were agreed upon among Japan, the U.S., and the EU in ICH Meetings, thereby promoting further international harmonization.
- Toward the development of international standards and the international regulatory harmonization, PMDA actively participated in Steering Committee Meetings and Expert Working Group Meetings of ICH, Steering Committee Meetings and Expert Working Group Meetings of IGDRP*, Steering Committee Meetings of APEC LSIF RHSC*, and the Expert Working Group Meetings of PDG*.

Also, at the 1st conference of the IPRF* which has been newly set up for exchanging opinions/information among drug regulatory authorities, PMDA served as the vice-chair and cooperated with the chair Swissmedic, contributing to efforts for reinforcing international harmonization among regulatory authorities.

* ICH: International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use
* IPRF: International Pharmaceutical Regulators Forum
* IGDRP: International Generic Drug Regulators Pilot
* APEC LSIF RHSC: Asia Pacific Economic Cooperation, Life Science Innovation Forum, Regulatory Harmonization Steering Committee
* PDG: Pharmacopoeial Discussion Group (Japan, U.S. and Europe)

- In FY 2013, in the area of medical devices, PMDA continued to actively participate in Management Committee Meetings and Working Group Meetings of IMDRF*, Steering Committee Meetings and Working Group Meetings of HBD*, ISO*, etc.
  * HBD: Harmonization by Doing (for regulations on medical devices in Japan and the U.S.)
  * ISO: International Organization for Standardization
  * IMDRF: International Medical Devices Regulators Forum

- For HBD, PMDA supported activities of each working group as a co-chair with the US academia, and contributed to regulatory harmonization on a practical level through teleconferences or meetings of respective working groups. Also, in July, PMDA held HBD Think Tank East 2013 in Tokyo, and delivered a presentation of 10-year activity results and future prospects. Through the HBD project titled "Collaborative Consultations and Review of Premarketing Applications Pilot Program," PMDA made efforts to resolve the "device lag" between Japan and the U.S. by sharing information with the U.S. FDA regarding specific issues raised in the process of product review.

Main international harmonization conferences on drugs in which PMDA participated (relating to reviews and post-marketing safety measures)

*ICMRA (International Coalition of Medical Regulatory Authorities)
*GCRSR (Global Coalition for Regulatory Science Research)
*ICH: Brussels meeting and Osaka meeting
- •Carcinogenicity (S1)
- •Photosafety Evaluation of Pharmaceuticals (S10)
- •Impurities: Guideline for Metal Impurities (Q3D)
- •Q&A on GMP for Active Pharmaceutical Ingredients (Q7 IWG)
- •Informal Safety Brainstorming
- •Electronic Standards for Transmission of Regulatory Information (M2)
- •Assessment and Control of DNA Reactive (Mutagenic) Impurities in Pharmaceuticals to Limit Potential Carcinogenic Risk (M7)
- •Electronic Common Technical Document (M8)
- •Data Elements for Transmission of Individual Case Safety Reports (E2B [R3])
- •Clinical Safety Data Management: Periodic Safety Update Reports (PSUR) for Marketed Drugs (E2C [R2])

*PDG: Pharmacopoeial Discussion Group (Japan, the U.S. and Europe): Tokyo conference and Strasbourg conference
*MedDRA (Medical Dictionary for Regulatory Activities) Steering Committee Meeting
*ISO TC/215 (Health informatics)
*HL7 (standards for interoperability of health information technology)
*ICCR (International Cooperation on Cosmetics Regulation)
*IGDRP: International Generic Drug Regulators Pilot: Canberra meeting and Geneva meeting
*CIOMS (Council for International Organizations of Medical Sciences) Working Group
*Working Group on Good Laboratory Practice (GLP) of OECD
*WHO INN (International Nonproprietary Names) meeting
*APEC LSIF RHSC (Life Science Innovation Forum, Regulatory Harmonization Steering Committee): Medan meeting and Ningbo meeting

Main international harmonization conferences on medical devices in which PMDA participated (relating to reviews and post-marketing safety measures)

*ISO
- •ISO/TC/194 (Biological evaluation of medical devices)
- •ISO/TC/106 (Dentistry)

*Regulatory Affairs Professionals Society (RAPS)
*Harmonization by Doing (HBD)
*APEC LSIF RHSC (Life Science Innovation Forum, Regulatory Harmonization Steering Committee)
*IMDRF: International Medical Device Regulators Forum
- •RPS (Regulated Product Submission)
- •MDSAP (Medical Device Single Audit Program)
- •UDI (Unique Device Identification)
- •NCAR (National Competent Authority Report)
- •Recognized Standards

*AHWP (Asian Harmonization Working Party)
*GMDN (Global Medical Device Nomenclature)

- PMDA participated in an internal discussion on efforts for establishing the steering committee and expert committee of IGDRP, and used it as the foothold for the materialization in the future.
- PMDA held a total of 4 Expert Discussion meetings on drug names and reported 45 Japanese accepted names (JAN) to MHLW. Four consultations on applications for international nonproprietary names (INN) were also conducted. PMDA participated in the WHO-hosted conferences on INN in April and October 2013.

JAN: Japanese Accepted Names

INN: International Non-proprietary Names

- PMDA participated in the Second International Meeting of World Pharmacopoeias which was held by WHO in India in April, and the Global Summit of the Pharmacopoeias which was held by the U.S. Pharmacopeia Convention and the Chinese Pharmacopoeia Commission in the U.S. in September, and exchanged opinions on common issues.

  Particularly, in the former conference, Good Pharmacopoeial Practices to specify items, contents, standards and so on, necessary for Pharmacopeia that are to be formulated in different countries/regions, are being prepared. PMDA has provided continuous cooperation for the WHO's international activities as a member of the draft formulation group.

c. Promotion of personnel exchanges

- Based on the Administrative Rules on Overseas Training, centering on training programs implemented by overseas regulatory authorities, PMDA selected and dispatched employees after soliciting personnel who were willing to be dispatched (27 employees).
- PMDA received three foreign trainees from the Indonesia NADFC, two from the Taiwan CDE, and 1 from the U.S. FDA. PMDA also accepted government research teams from China and Taiwan and explained an overview of PMDA's organization and services.
- PMDA held a training seminar for people from overseas regulatory authorities, and provided training on the services of the Agency, post-marketing safety measures and relief system for drugs and medical devices, case study, etc.
- As a preliminary research on whether or not Swissmedic dispatches employees to PMDA, the Head of Communication and Networking at Swissmedic visited PMDA for one week. During the visit, operations at each office/division were explained to the Swiss officer.

d. Development of internationally minded human resources with excellent communication skills

- PMDA considered a human resource development program while hearing experiences from related organizations, in order to develop human resources with adequate linguistic ability and human network, professional expertise in related areas of specialty, appropriate decision-making capability according to the situations in and out of Japan, and international credibility.

e. Improvement and strengthening of international publicity and provision of information

- PMDA made efforts to provide information in English by taking measures such as posting news releases every month on its English website.
- In order to provide information on its reviews and related services and safety measures to international audiences, PMDA has prepared and released English translations of the review reports and safety information on its website. In FY 2013, the Agency prepared and published English translations of 20 review reports. PMDA also created the English version lists of approved new drugs/new medical devices, and released them approximately quarterly.
- At the DIA Annual Meetings, RAPS Annual Meetings, etc., held in Japan, the US, and Europe, PMDA's speakers gave presentations on the Agency's reviews and safety measures to raise

international recognition of PMDA's services, while PMDA staff members used an exhibition booth for publicity purposes.

- The information on activities of Projects Across Multi-offices in PMDA has been posted on the English website. Particularly, PMDA disseminated information on activities of projects such as the Nanomedicine Initiative Project in which PMDA contributed to the preparation of guidance in FY 2013, the Orphan Drug Working Group in which activities were conducted with overseas regulatory authorities, the Pediatric Drugs Working Group, and the QbD Assessment Project. In addition, PMDA plans to publish English translations of notifications and guidance issued in FY 2013 which the team of the *In vitro* Companion Diagnostic Device Project prepared or provided cooperation for. Currently, the translation of the guidance documents and related work are under way.

f. Promotion of global clinical trials

- In order to reduce the drug lag, PMDA has promoted global clinical trials, and has conducted consultations and reviews based on guidance documents titled "Basic Principles on Global Clinical Trials" (PFSB/ELD Notification, dated September 28, 2007), which clarifies basic concepts to conduct global clinical trials, and "Basic Principles on Global Clinical Trials (reference cases)" (Administrative Notice of ELD, PFSB at MHLW, dated September 5, 2012).

  Of 601 clinical trial notifications submitted in FY 2013, 169 were for global clinical trials.

Number of Clinical Trial Notifications of Global Clinical Trials

	FY 2009	FY 2010	FY 2011	FY 2012	FY 2013
Number of cases	113	134	121	130	169

- PMDA intends to take an active approach to global clinical trials. In FY 2013, it carried out 59 consultations on global clinical trials for drugs with new active ingredients.

Number of Consultations on Global Clinical Trials for Drugs with New Active Ingredients

	FY 2009	FY 2010	FY 2011	FY 2012	FY 2013
Number of cases	56	66	73	64	59

3.2.(3) Enhancement of post-marketing safety measures (reinforcement of information management and risk management system)

(i) Proper assessment of reports on adverse drug reactions and medical device malfunctions

- In order to improve the safety of marketed drugs and medical devices, and to enable patients and healthcare professionals to use them properly, PMDA collects and examines safety information efficiently, processes the information speedily, plans appropriate safety measures and provides easy-to-understand safety information promptly, to ensure that reviews and safety measures function in an inseparable manner.
- There were approximately 310,000 reports on adverse reactions and infections caused by drugs and approximately 27,000 reports on medical device malfunctions and infections caused by medical devices submitted to PMDA from in and out of Japan in FY 2013. PMDA inputs the collected information into a database and shares such information with MHLW. In addition, PMDA monitors information on new measures taken for medical products by foreign regulatory agencies, including FDA and EMA, to consider and evaluate its responses to domestic products on a daily

basis, while reviewing academic literature to analyze, share and evaluate information on adverse drug reactions. In addition, PMDA is making efforts to take comprehensive safety measures for drugs and medical devices in the post-marketing stage by enhancing cooperation between the review offices and safety offices, as well as between the relief office and safety offices.

- Based on daily reviews conducted by the product safety teams, PMDA assesses and reviews such reports on adverse drug reactions etc., and reports on medical device malfunctions etc., with the Safety Division of MHLW every week, seeks opinions from external experts and companies, and proposes necessary safety measures, such as revision of precautions in package inserts, to MHLW. Particularly urgent issues are responded to immediately in cooperation with MHLW.
- The numbers of reports (in terms of the number of active ingredients for the drugs, and the number of generic names for the medical devices) submitted to MHLW for the products judged to require safety measures, such as revision of package inserts, were as follows.

	FY 2009	FY 2010	FY 2011	FY 2012	FY 2013
Drugs	260	339	185	198	160
Medical devices	62	19	17	15	14
Medical safety*	4	5	6	6	6

* *"Medical safety" indicates the number of reports on near-incident cases, which are collected by the Japan Council for Quality Health Care. PMDA analyzes the data in the light of expertise for drugs and medical devices, after seeking opinions from experts, and reports the analysis results for safe use of drugs and medical devices to MHLW.*

- Post-marketing safety measures taken by MHLW based on reports from PMDA were as follows (includes duplicated measures).

		FY 2009	FY 2010	FY 2011	FY 2012	FY 2013
Drugs	Directions for revision to precautions in package insert	254	339	185	198	160
	Posting articles and cases on PMDSI*	29	32	41	36	40
Medical devices	Directions for revision to precautions in package insert or issuance of notifications on self-check	4	3	5	4	3
	Posting articles on PMDSI*	5	3	4	1	4

* *PMDSI stands for Pharmaceuticals and Medical Devices Safety Information.*

- As collaborative activities with the review offices, the Offices of Safety I and II evaluate adverse drug reactions reported via early post-marketing phase vigilance (EPPV) together with the reviewers of the product applications. Staff members of the safety offices also participate in the review process (clinical trial consultations, assessment of post-marketing surveillance plans, review of draft package inserts, Expert Discussions, etc.) of new drugs and new medical devices. As for the collaboration with the Office of Relief Fund, information such as names of drugs and adverse drug reactions in judged cases for payment/non-payment of benefits is provided to the safety offices and is reflected to the safety measures.
- In FY 2013, PMDA made the following efforts to appropriately collect, organize, and examine the reports on adverse drug reactions etc., and reports on medical device malfunctions etc., submitted by MAHs and medical institutions:

  a. Upgraded the information management system for adverse drug reactions and the safety measures support system

b. Updated the master files in terms of names of drug products, adverse drug reactions and MAHs

c. Encouraged staff members to attend academic conferences (a total of 342 participants) to gather information

d. Held liaison meetings regularly on both drugs and medical devices with MHLW (every week)

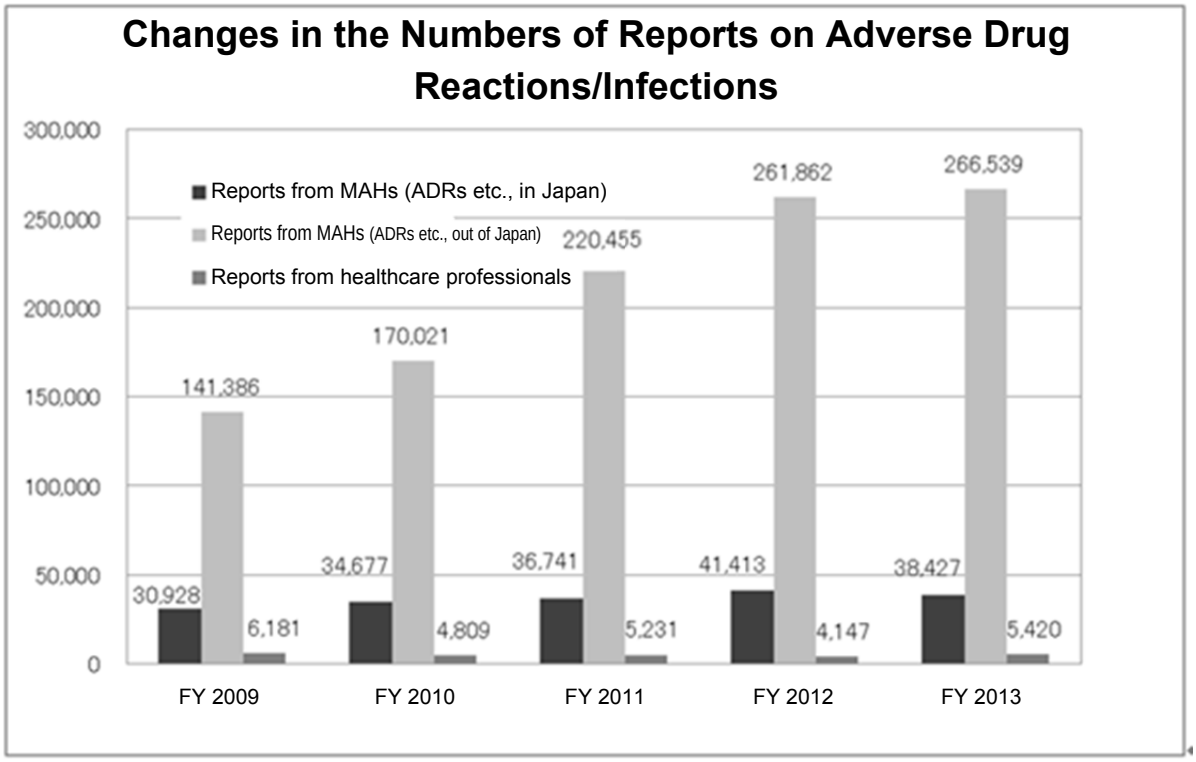
- PMDA's information management system for adverse drug reactions and the safety measures support system will need to be in compliance with the ICH-E2B (R3) guideline, which is the next international data exchange standard for adverse drug reaction reporting. In FY 2013, PMDA performed the final verification continuously from FY 2012, and started to develop the reception system based on its results.

Collection of adverse reaction reports etc.

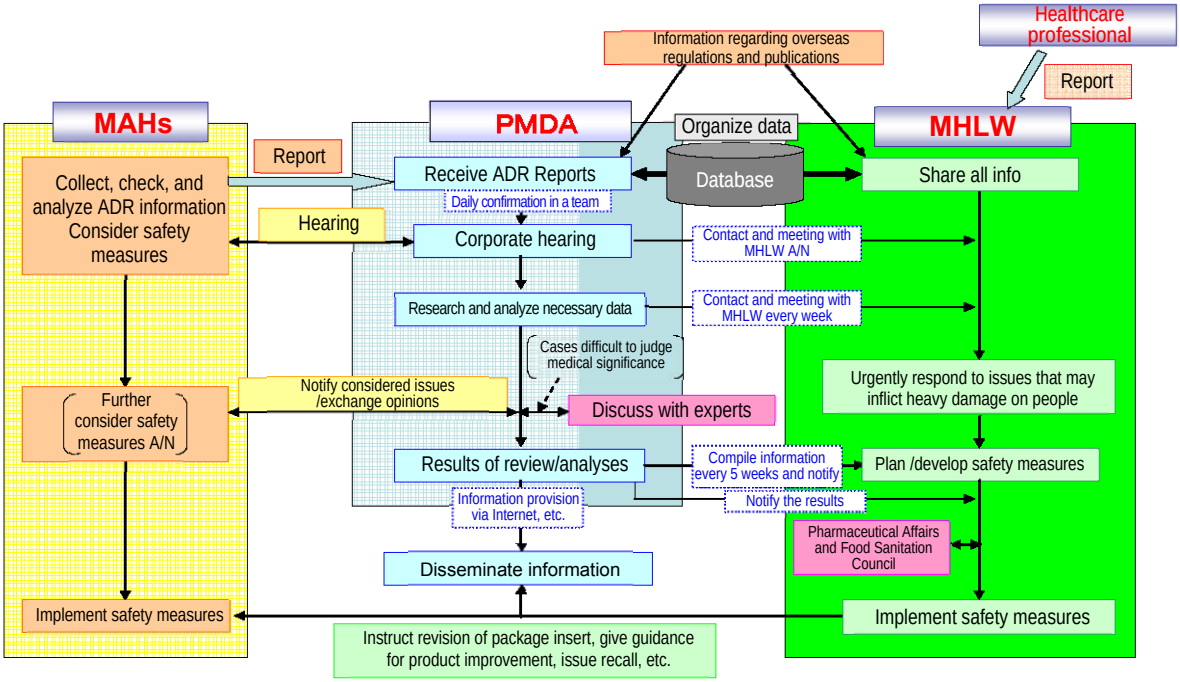
1-1) Number of reports relating to drugs

	FY 2009	FY 2010	FY 2011	FY 2012	FY 2013
Reports from MAHs	175,285	207,772	260,473	306,410	308,383
(adverse drug reactions, in Japan)	(30,814)	(34,578)	(36,641)	(41,254)	(38,329)
(infections caused by drugs, in Japan)	(114)	(99)	(100)	(159)	(98)
(adverse drug reactions, out of Japan)	(141,364)	(169,994)	(220,410)	(261,823)	(266,506)
(infections caused by drugs, out of Japan)	(22)	(27)	(45)	(39)	(33)
(research reports)	(933)	(940)	(841)	(884)	(962)
(foreign safety measure reports)	(930)	(1,033)	(1,347)	(1,134)	(1,317)
(periodic infection reports)	(1,108)	(1,101)	(1,089)	(1,117)	(1,138)
Reports from healthcare professionals	6,181	4,809	5,231	4,147	5,420
(1) Safety information reporting system	3,721	3,656	3,388	3,304	4,067
(2) Vaccines*	2,460	1,153	1,843	843	1,353
Total	181,466	212,581	265,704	310,557	313,803

* *This table includes the numbers of reports on adverse reactions following vaccination with cervical cancer vaccine, Hib vaccine, pediatric pneumococcal conjugate vaccine, and influenza vaccines in the numbers of "reports from healthcare professionals" after FY 2011, but the numbers were not included in the similar table in the Annual Reports for FY 2009 and 2010. From FY 2013 onward, reports on adverse reactions following vaccination with all vaccines are included in the numbers of "reports from healthcare professionals."*



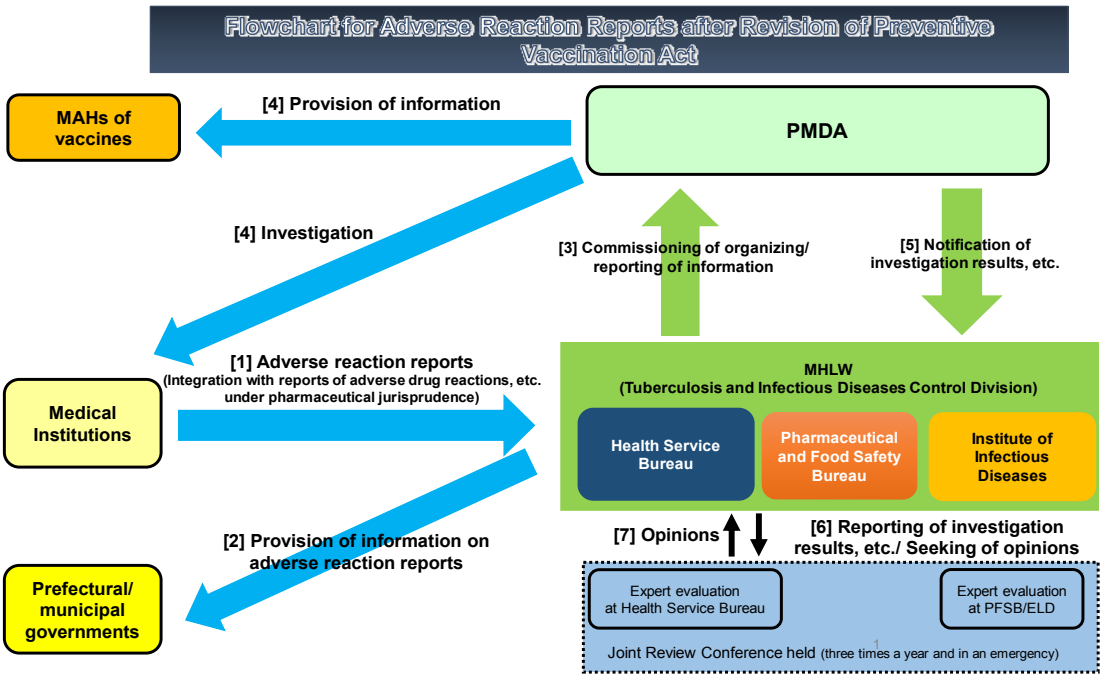
Flowchart for Processing Adverse Drug Reaction Reports



1-2) Reports on adverse reactions following vaccination with influenza vaccines

Pursuant to Article 14, Paragraphs 1 and 2 of the Preventive Vaccination Act (Act No. 68 of 1948), PMDA started a project for organizing information of vaccination adverse reaction reports and a project for investigation on those reports on April 1, 2013 (see the following scheme). The number of vaccination adverse reaction reports collected according to this scheme in FY 2013 was 1,353. After receiving

vaccination adverse reaction reports that were accepted at the Tuberculosis and Infectious Diseases Control Division, Health Service Bureau, MHLW, PMDA provides information to MAHs of suspected vaccines, and also gives an instruction to properly deal with the events under the Pharmaceutical Affairs Act. Regarding reported cases of vaccination adverse reactions, PMDA conducted an interview with doctors who diagnosed the adverse reactions and those who gave the vaccination, as needed. In the cases of deaths and particular serious adverse reactions (e.g., anaphylactic reaction), PMDA sought opinions from experts regarding matters such as the validity of diagnosis for the adverse reactions and causal relationship between the adverse reactions and vaccines, thereby contributing to safety assessment of vaccines at MHLW.



1-3) Adverse drug reaction reports from patients

The final recommendations drawn up in April 2010 by the Committee for Investigation of Drug-induced Hepatitis Cases and Appropriate Regulatory Administration to Prevent Similar Sufferings highlighted the necessity of establishing a system which utilizes information from patients for safety measures. Also in the report submitted in January 2012 by the Investigational Sub-committee on Revision of Pharmaceutical Regulatory Systems of the Health Science Council, it was suggested that information on adverse drug reactions self-reported by patients should be utilized.

Based on these recommendations, PMDA set up the Direct Patient Reporting System for Adverse Drug Reactions on March 26, 2012 with reference to the outcomes of a study supported by the Health and Labour Sciences Research Grants from FY 2009 to FY 2011 ("Research on System for Receiving Adverse Drug Reaction Reports from Patients"), and has been conducting a project for receiving adverse drug reaction reports from patients on a trial basis via the Internet. In this project, adverse drug reaction reports are to be collected from patients who developed drug-induced adverse reactions or their family. Those reports are to be used to improve safety measures for drugs such as identifying trends in occurrence of adverse reactions to drugs. Based on reports and questionnaire results collected during the trial period, PMDA intends to revise the reporting system and then formally start receiving reports.

The number of adverse drug reaction reports from patients collected by FY 2013 is shown in the following table. In FY 2013, PMDA also released cases reported between March 2012 and the end of March 2013.

	FY 2011	FY 2012	FY 2013
Adverse drug reaction reports from patients	30	154	116

1-4) PMDA's detailed investigation on reports from medical institutions (excluding vaccination adverse reaction reports)

In the final recommendations drawn up in April 2010 by the Committee for Investigation of Drug-induced Hepatitis Cases and Appropriate Regulatory Administration to Prevent Similar Sufferings, it was indicated that a system to conduct necessary investigations such as direct inquiries to healthcare professionals should be developed for death/serious cases among adverse drug reactions etc., reported from medical institutions.

PMDA developed a system to conduct follow-up investigations of reports from medical institutions. In addition, PMDA considered the mechanism for feedback to MAHs etc., prepared necessary notifications, and then made inquiries to medical institutions regarding fatal cases starting on July 29, 2010. After that, PMDA has expanded cases subject to follow-up investigation in a step-by-step manner, and currently not only fatal cases but also cases of serious adverse reactions are subject to detailed investigation.

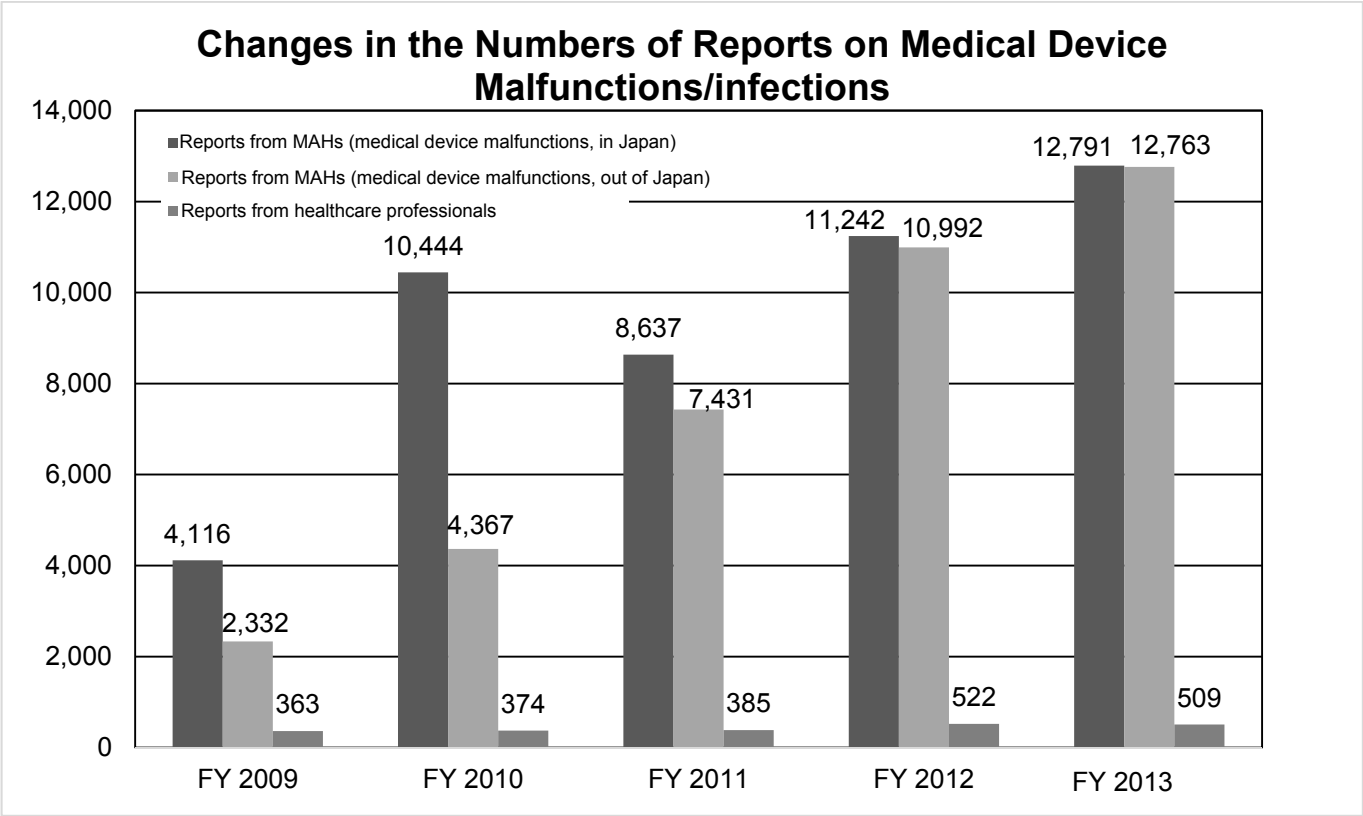
The number of cases in which PMDA has conducted detailed investigation by the end of FY 2013 is shown in the following table.

	FY 2011	FY 2012	FY 2013
Number of cases in detailed investigation	613	663	862

Regarding the adverse drug reactions/infections which PMDA investigated by making inquiries among the cases reported from healthcare professionals to the Minister of Health, Labour and Welfare, PMDA started sharing the information on individual cases via the Internet using a dedicated server in November 2011 with MAHs of the primary suspected drugs of the reported cases.

2) Number of reports relating to medical devices

	FY 2009	FY 2010	FY 2011	FY 2012	FY 2013
Reports from MAHs	7,344	15,874	17,192	23,643	27,303
(medical device malfunctions, in Japan)	(4,114)	(10,444)	(8,637)	(11,242)	(12,791)
(medical device malfunctions, out of Japan)	(2,332)	(4,367)	(7,431)	(10,992)	(12,763)
(infections caused by medical devices, in Japan)	(2)	(0)	(0)	(0)	(0)
(research reports)	(6)	(27)	(2)	(3)	(5)
(foreign safety measure reports)	(831)	(978)	(1,060)	(1,337)	(1,669)
(periodic infection reports)	(59)	(58)	(62)	(69)	(75)
Reports from healthcare professionals	363	374	385	522	509
Total	7,707	16,248	17,577	24,165	27,812

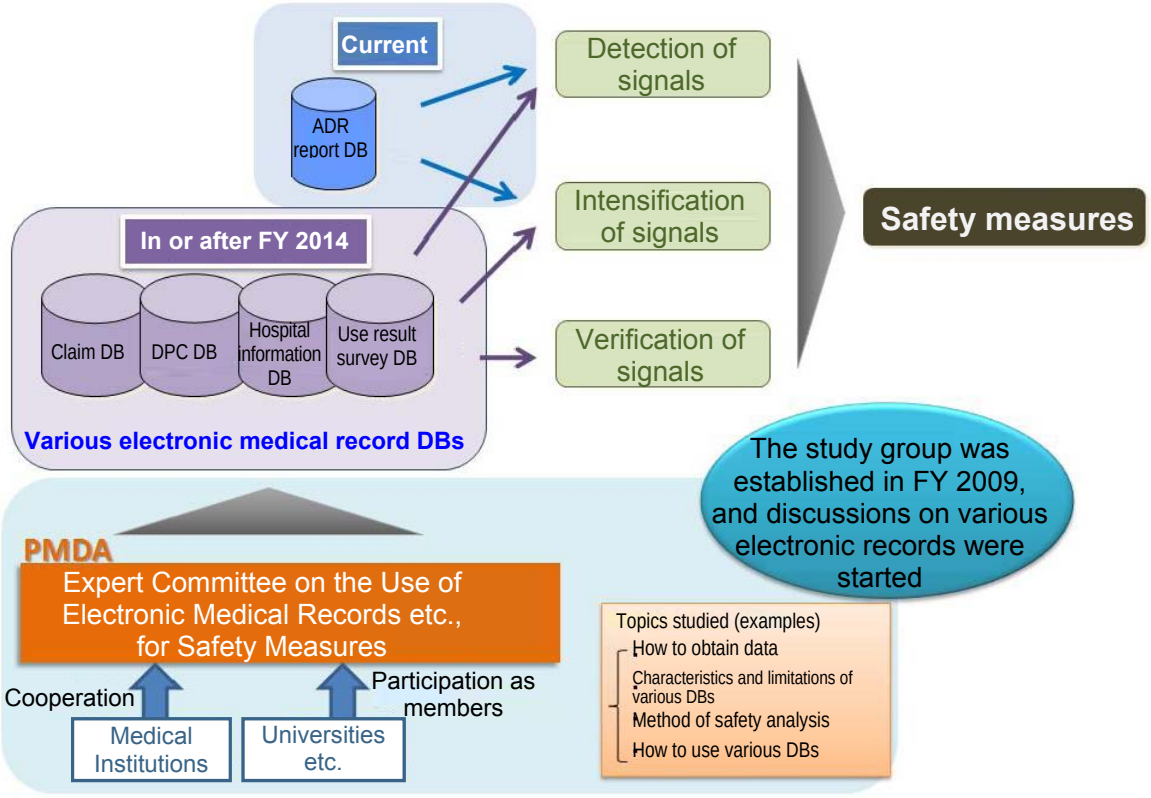


(ii) Sophistication of safety measures

a. Use of electronic medical records etc.

- In accordance with the Second Mid-term Plan, PMDA planned to build an infrastructure to access the databases of medical records including health insurance claim data (hereinafter referred to as "claim data") by FY 2013, and then to perform pharmacoepidemiological analyses to evaluate pharmaceutical risks quantitatively. The Agency intended to start making use of such infrastructure on a trial basis in FY 2011, and to establish a system for conducting investigations on the incidence of adverse drug reactions and pharmacoepidemiological analyses by FY 2013.
- PMDA named the investigation to utilize electronic medical records etc., for safety measures "MIHARI Project," and started evaluating each type of data such as claim data and hospital information system data in terms of their advantages/disadvantages and feasibility and limitations in FY 2009. PMDA established the Expert Committee on the Use of Electronic Medical Records, etc., for Safety Measures as the evaluation body composed of external experts, and conducted various pilot studies while obtaining the advice from the Committee. In FY 2013, the pilot studies were continuously conducted mainly to explore appropriate analytical methods and to evaluate the usability, limitations, etc., of each data source (see the following table). PMDA has been sequentially releasing reports on various trial surveys conducted during the period of the Second Mid-term Plan on the Medical Product Information web page.

Study for Introducing New Databases (DBs) for Drug Safety Evaluation Process



Data Source	Study started in	Study	Breakdown
Receipt Data (post-marketing DB, small-scale)	FY 2009	Data characterization	Patients with anaphylaxis were identified by using ICD-10 codes and analyses were performed by sex, age, primary disease, procedure, therapeutic agent, etc. (The report has already been posted on the Medical Product Information web page.)
	FY 2010	Actual condition of prescription of drugs	Patients who were prescribed any one of the following four drugs were identified and analyses of respective drugs were performed. 1. Amantadine 2. Thiamazole 3. Paroxetine 4. Anti-influenza agents (The report has already been posted on the Medical Product Information web page. Partly presented in an academic conference)
	FY 2010	Survey on effects of safety measures	Patients who were prescribed any one of the following four drugs were identified and analyses were performed for safety measures taken during the follow-up period. 1. Amantadine (contraindicated in dialysis patients) 2. Thiamazole (periodic blood tests) 3. Paroxetine (prescription limited in patients under 18 years) 4. Anti-influenza agents (prescription limited in patients under age) (The report has already been posted on the Medical Product Information web page. Partly presented in an academic conference)

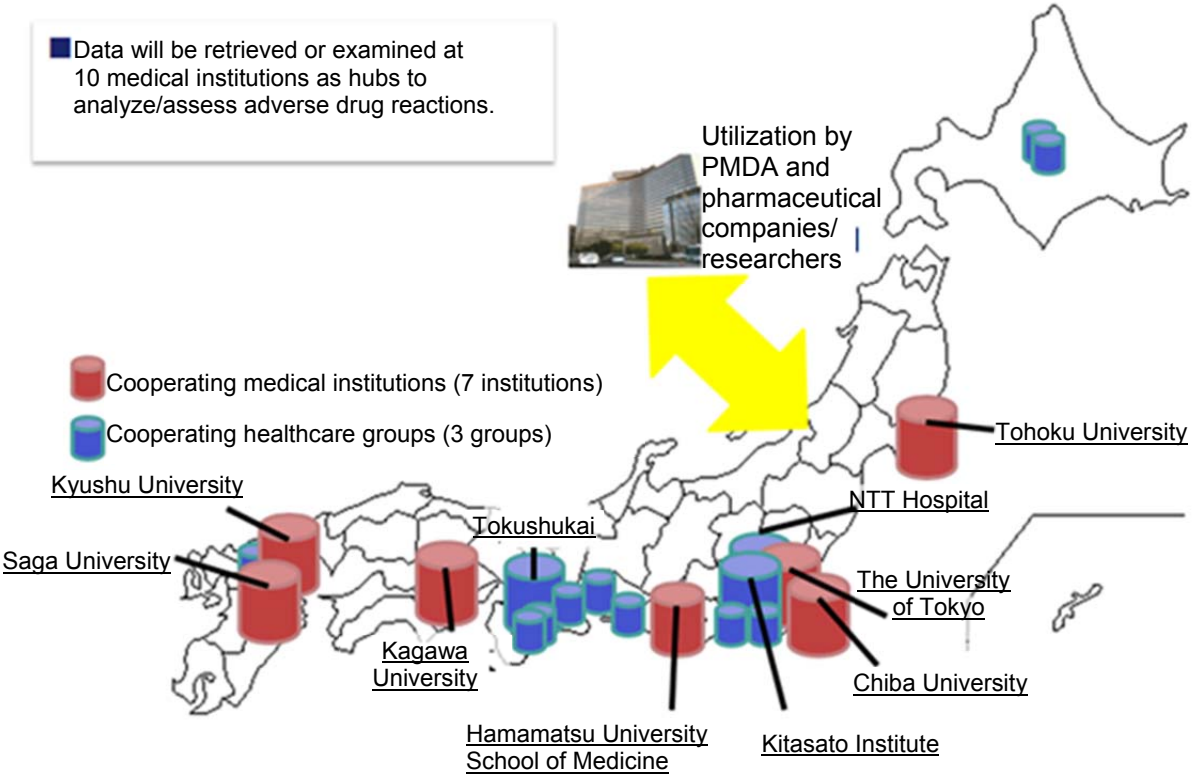
Data Source	Study started in	Study	Breakdown
	FY 2010	Risk assessments of adverse drug reactions	Risk assessments were performed for the following two known associations of drugs and adverse reactions (presented in academic conference). 1. Osteoporosis associated with steroids (Cohort study/ Nested Case-Control study) 2. Drug-induced Parkinsonism associated with antipsychotic drugs (Nested Case-Control study) (The report has already been posted on the Medical Product Information web page.)
	FY 2010	Signal detection by pharmacoepidemiological method	Signal detection was performed by using SSA† for a known association between a drug and an adverse reaction (drug-induced parkinsonism associated with antipsychotic agents) (presented in an academic conference). 1. Drug-induced parkinsonism associated with antipsychotic agents †SSA: Sequence Symmetry Analysis (The report has already been posted on the Medical Product Information web page. Presented in an academic conference)
	FY 2010	Signal detection by data mining	Signal detection by using the data mining method was examined in collaboration with an external contractor. (The report has already been posted on the Medical Product Information web page.)
	FY 2011	Actual condition of prescription of drugs	Patients who were prescribed any one of the following three drugs/drug groups were identified and analyses of respective drugs/drug groups were performed. 1. Antimicrobial drugs (for pediatrics) 2. Doxorubicin 3. Monobasic sodium phosphate monohydrate/ anhydrous dibasic sodium phosphate
	FY 2011	Survey on effects of safety measures	Patients who were prescribed monobasic sodium phosphate monohydrate and anhydrous dibasic sodium phosphate were identified and analyses were performed for safety measures taken during the follow-up period.
	FY 2011 - 2012	Risk assessments	Risk assessments were performed for the following two associations of drugs and adverse reactions (presented in an academic conference). 1. Association between the use of atypical antipsychotic drugs and glucose metabolism disorder (Cohort study/ Nested Case-Control study) 2. Association between the use of thiazide diuretics and glucose metabolism disorder (Nested Case-Control study) (The report has already been posted on the Medical Product Information web page.)
	FY 2011 - FY 2012	Signal detection by data mining	Signal detection (hypothesis extraction) by using the data mining method was examined in collaboration with an external contractor.
	FY 2012 - FY 2013	Signal detection by pharmacoepidemiological method (SSA, SCCS)	Detection of signals by SSA or Self Controlled Case Series (SCCS) were done for the following known adverse events: 1. Depression associated with interferon preparations (SSA), 2. Hyperlipidemia associated with olanzapine (SSA), 3. Occurrence of acute asthma attack after prescription of NSAIDs (SCCS)

Data Source	Study started in	Study	Breakdown
DPC (Diagnosis Procedure Combination) Data	FY 2010	Data characterization	Patients with anaphylaxis were identified by using ICD-10 codes and analyses were performed by sex, age, primary disease, prescription, procedure, etc. (The report has already been posted on the Medical Product Information web page.)
	FY 2011	Actual condition of prescription of drugs	Patients who were prescribed any one of the following three drugs/drug groups were identified and analyses of respective drugs/drug groups were performed. 1. Antimicrobial drugs (for pediatrics) 2. Doxorubicin 3. Sorafenib
	FY 2011	Survey on effects of safety measures	Patients who were prescribed sorafenib were identified and analyses were performed for safety measures taken during the follow-up period.
Hospital information Data (HIS)	FY 2009 - FY 2011	Data characterization	The data was characterized with the cooperation of five medical institutions. Six types of adverse drug reactions were identified and analyzed (Partly presented in an academic conference).
	FY 2010 - FY 2011	Examination of validity of outcome definition	Cases of an adverse drug reaction were identified from the database and checked by a medical record review, with the cooperation of two medical institutions, and the validity of outcome definition was evaluated (Presented in academic conference).
	FY 2012	Survey on effects of safety measures	Patients who were prescribed sitagliptin were identified, and safety measures related to combined use with sulfonylurea were analyzed. (Presented in academic conference)
	FY 2012	Risk assessments	Risk assessments were performed for the following two associations of drugs and adverse reactions with the cooperation of 6 medical institutions. 1. Association between the use of vancomycin and liver disorder 2. Association between the use of sitagliptin and acute renal failure
	FY 2012	Examination of validity of outcome definition	Validity of definition from outcome was examined using clinical laboratory values for the following four outcomes with the cooperation of 6 medical institutions: 1. Diabetes mellitus 2. Hyperlipidemia 3. Hyperthyroidism 4. Acute renal failure/Acute renal disorder Validity of outcome definition was examined using medical records on "Acute renal failure/Acute renal disorder" with the cooperation of 2 medical institutions.

- In FY 2011, the "Project for developing infrastructure for medical information database (MID-NET®)" was started. The purpose of this project is to build a database at 10 cooperating medical institutions nationwide such as university hospitals, selected by MHLW through open recruitment, of electronic medical information retained by the medical institutions. The project aims at establishing a link system of the medical information databases covering 10 million patients nationwide in the future. In this project, PMDA assumes the role of establishing the system among the cooperating medical institutions. The Agency also intends to develop its internal analysis system to utilize this database for safety measures (see the diagram).

Project for Developing the Medical Information Database

Hubs of the medical information database will be established at 10 university hospitals/group hospitals, etc., nationwide, with the aim of collecting large amount of data.



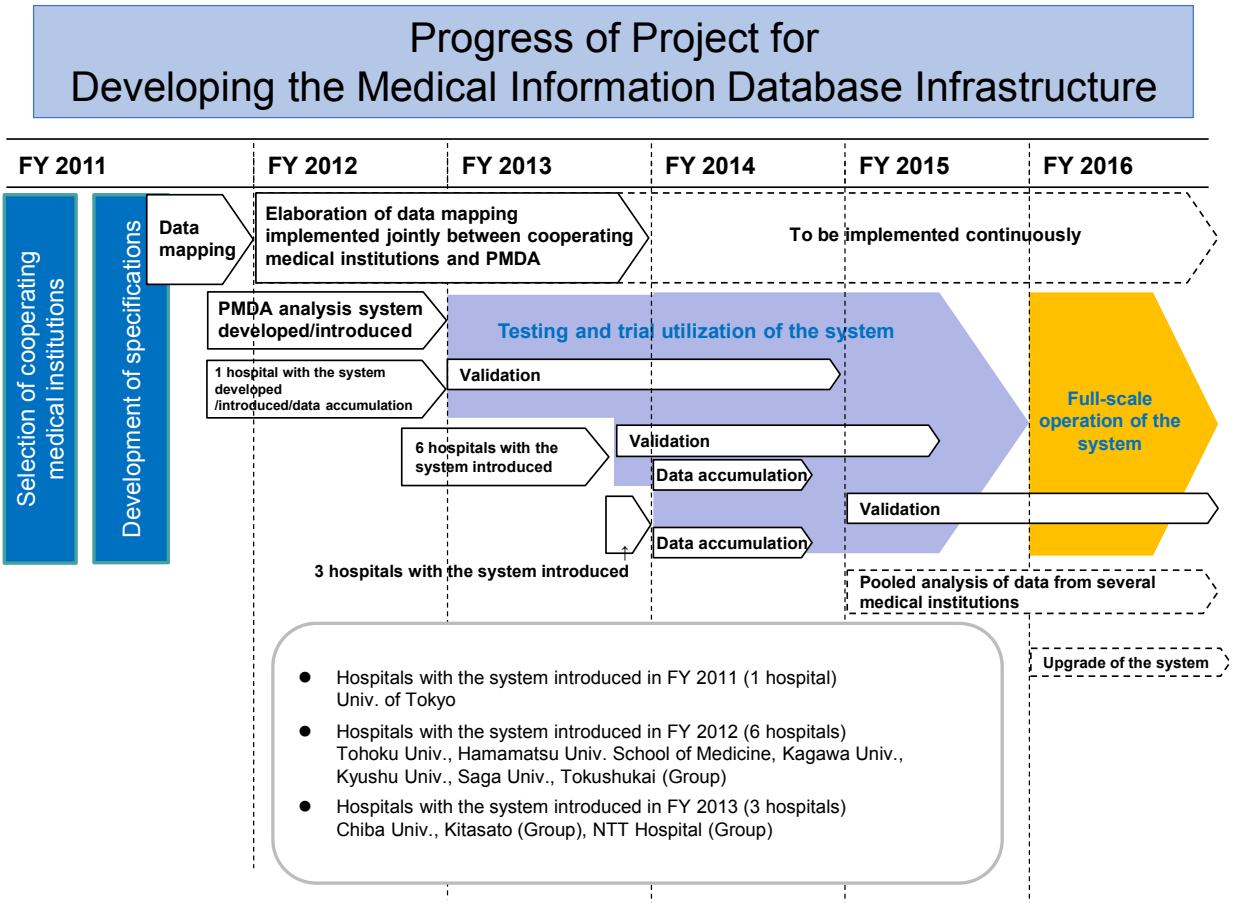
- The medical information database was developed sequentially from FY 2011 to FY 2013. The medical database were established at 7 cooperating medical institutions in FY 2012 and the database development was almost completed at the remaining 3 medical institutions in FY 2013.

  In FY 2011, PMDA started developing its internal systems such as the analysis interface system as well as systems for hub at the University of Tokyo Hospital, one of the cooperating medical institutions. The Agency also upgraded the existing hospital information system at the University of Tokyo Hospital as a preparation for the introduction of the planned database system. In FY 2012, the development of PMDA's system and the hospital information system were completed and the respective systems were introduced to PMDA and the University of Tokyo Hospital. PMDA also started upgrading hospital information systems in the 6 cooperating medical institutions. In FY 2013, PMDA started introducing the hospital system to 3 cooperating medical institutions (see the diagram). For local codes used at each medical institution, PMDA also started a mapping confirmation work to assign a unified standard code used among the cooperating medical institutions. In FY 2014, data accumulation in the database as well as trial utilization of medical information stored in the database will be propelled.

- In FY 2013, PMDA started a data validation project to sophisticate analytical methods for the medical information database as a step for utilizing the medical information database system. This project is intended to evaluate the validity of outcome or exposure data extracted under certain conditions by cross-checking with medical records, etc., that are actually kept by each hospital. Examination of them wil also lead to confirmation of the reliability of the medical information database toward full-scale utilization. The project was conducted for 7 medical institutions in FY 2013, and is scheduled to be continuously conducted in and after FY 2014.

- Also, in FY 2012 and FY 2013, as a project sophisticate analytical methods for the medical information database, the draft "guideline for implementation of pharmacoepidemiological research for safety assessment of drugs by using the medical information database, etc." was organized and prepared at a study group composed of external knowledgeable persons, and public comments on the draft guidelines were invited for one month from July 9, 2013. After that, the guideline was modified in response to these comments, and released on the Medical Product Information web page in March 2014.

  This guideline includes points to note from an academic standpoint so that appropriate pharmacoepidemiological research can be conducted when PMDA, pharmaceutical companies, or academic researchers, etc., perform safety assessments of a drug with secondary use of the medical information database. The guideline is expected to be very useful also when MID-NET® is utilized.



b. Digitization of information on adverse drug reactions and its utilization for safety measures

- In accordance with the Second Mid-term Plan, PMDA intended to computerize information on adverse reactions, such as adverse drug reaction reports and information from drug use-results surveys, and to build databases in order to utilize digitized information in the development of safety measures.
- Regarding the database of drug user-result surveys, MHAs, who will submit the data, made a request that the database be used only within PMDA and not released publicly. The request was initially under consideration at PMDA, but the database development plan itself was not materialized in FY 2013 because the use of the data was considered to be closely related to the system of "advanced review and consultation with electronic data," where electronic data

submission will be mandatory and the data will be utilized for future reviews and consultations. The full-scale study of the system has been underway since September 2013.

c. Sophistication of the data mining method

- In accordance with the Second Mid-term Plan, PMDA planned to proactively make use of the data mining method in organizing, evaluating, and analyzing information on adverse drug reactions, in order to detect adverse drug reactions at an early stage and to take measures to prevent further events. PMDA also intends to improve the approach as needed by referring to overseas examples.

> Reference: What Is the Data Mining Method?
> The data mining method is technology that extracts, from among a large amount of data accumulated in the database, events that frequently occur simultaneously as highly correlated events. The term "data mining" refers to the process of retrieving, or "mining," only useful information from the database.
> Specifically, the data mining method is used for detecting "combinations of drugs and adverse drug reactions that are likely to have a causal relationship (signals)" from the database of individual cases of adverse drug reactions.

- The data mining method has been utilized for the process of evaluating adverse reaction reports. In FY 2013, the method was continuously reviewed.

d. Collection and evaluation of data on medical devices subject to tracking (implantable ventricular-assist devices [IVADs])

- In accordance with the Second Mid-term Plan, PMDA intended to build a system for collecting and evaluating time-series data on the operational status of IVADs, which was adopted from among high-risk implantable medical devices subject to tracking, as a pilot study. Data to be collected include the incidence rate of malfunctions of the devices. PMDA planned to appropriately use the system for developing safety measures etc.

> Reference: What are Medical Devices Subject to Tracking?
> Medical devices for which it is obligatory for a MAH etc., to create and store records of contact information of the users so that prompt and appropriate responses can be taken easily if a malfunction occurs with the medical device. Under the Pharmaceutical Affairs Act, such devices are categorized as designated medical devices.

- In FY 2013, PMDA continued the "Japanese Registry for Mechanically Assisted Circulatory Support (J-MACS)" project based on the protocols that were developed under the industry-government-academia collaboration in the First Mid-term Plan. PMDA developed a web-based entry system and implementation structures at participating medical institutions, and started data collection in June 2010. As of March 12, 2014, a total of 287 patients (216 for IVAD, 71 for extracorporeal VAD) have been enrolled at 26 participating institutions. The number of enrolled patients and other data has been updated on the PMDA's Medical Product Information web page.

e. Evaluation of medical device malfunctions

- In accordance with the Second Mid-term Plan, PMDA intended to develop methods for scientific evaluation of medical devices by ascertaining the incidence of device malfunctions that may unavoidably occur at a certain rate due to the nature of the device rather than its structural defects.
- As a part of this development, PMDA has been continuously conducting a pilot study on coronary stents from the effective period of the First Mid-term Plan. Data from a study (26 institutions, 16,463 enrolled patients, 3- to 5-year follow-up period) in patients who underwent percutaneous coronary intervention (PCI) or coronary artery bypass graft (CABG) operation have been collected through an external contract organization.
- In FY 2013, PMDA completed data collection over a follow-up period of five years. Ultimately, data were collected from a total of 15,792 patients (13,592 patients with PCI, 2,220 patients with CABG [excluding patients who did not give their consent]) at 26 institutions.
- PMDA plans to enrich safety measures by carrying forward “predictive/preventive” safety measure operations through more active scientific evaluation/analysis with the utilization of electronic medical information.

(iii) Establishment of a post-marketing safety system through information feedback

a. Access by MAHs to reports on adverse drug reactions etc., associated with their products

- PMDA investigates information of adverse drug reactions etc., which has been reported to the regulatory authorities but not to the relevant MAHs by medical institutions. The Agency has shared the investigation results with the MAHs by operating a system which enables the MAHs to access and download ICH-E2B-compliant SGML files of such adverse drug reactions from the PMDA website so that the MAHs can analyze the information and take measures accordingly.

b. Responses to consultation requests from MAHs

- In order to contribute to improving post-marketing safety measures in MAHs, PMDA conducted various consultations (on drugs, medical devices, and medical safety) requested by MAHs. These medical safety consultations were in particular related to revisions to package inserts, post-marketing risk management plans, creation of drug guides for patients, naming and labeling of drugs to prevent medical accidents, and improvements in products to prevent medical accidents based on analyses of near-incident cases.
- The number of provided consultations by category for FY 2013 is shown below:

	FY 2009	FY 2010	FY 2011	FY 2012	FY 2013
Drugs	619	752	670	704	776
Medical devices	247	171	163	179	95
Medical safety	142	83	59	80	31

- Consultations for medical safety conducted in FY 2013 are mainly on the names of new drugs, packaging/labeling, and near-incident cases for drugs/medical devices. PMDA responded to all consultations in an appropriate and prompt manner.

c. Release of information on drug risk under evaluation

- From the viewpoint of further enhancing safety measures for drugs, PMDA releases (1) risk information which PMDA monitors closely because it could lead to revision of precautions in package inserts etc., and (2) risk information which has attracted attention from foreign regulatory authorities, academic societies, etc., and are under evaluation by MHLW/PMDA. These types of information have been posted on the Medical Product Information web page as appropriate since July 2011, as preliminary information that may lead to safety measures such as revision of precautions.

d. Public release of adverse drug reaction cases

- PMDA has publicly released adverse drug reaction reports that were submitted by MAHs in and after April 2004 on its Medical Product Information web page sequentially since January 2006. In March 2012, PMDA expanded the scope of data items and reports to be released so that the contents can be more easily utilized by related parties.

  Currently, PMDA is releasing all domestic adverse drug reaction reports 4 months after their reporting in principle. The following data items from the reports are released: "fiscal year and quarter of a year reported," "reporting category," "job category of reporter," "investigation status," "gender," "age," "primary disease," "body height," “body weight," "suspected drug/brand name," "reason for use," "route of administration," "a single-dose," "start date of administration," "end date of administration," "action against suspected drug," "adverse events (onset date)," "presence/absence of recurrence due to re-administration," "outcome," "suspected concomitant drug," and "other concomitant drug."

  PMDA has also released reports of adverse drug reactions/infections about which PMDA conducted investigations such as making inquiries, from among those reports submitted from healthcare professionals to the Minister of Health, Labour and Welfare.

  By the end of FY 2013, PMDA posted 292,720 reports submitted up until November 2013.

- In addition, in April 2012, PMDA started providing the data sets of adverse reaction reports (including expanded items/reports) exported into the CSV format for public release. The database had been available only in line listing format. As a result, the data can be used for research and studies.

- The time period from receiving adverse reaction reports to public release was maintained at a 4-month period, showing that the target period for FY 2013 was achieved.

e. Public release of medical device malfunction cases

- From among the contents of all reports on medical device malfunctions that were submitted by MAHs in or after April 2004, PMDA has publicly released their “fiscal year reported,” “gender,” “age,” “outcome,” “generic name,” “condition of the medical device,” and “adverse event experienced by patient” on its Medical Product Information web page, since March 2006. By the end of FY 2013, PMDA posted 84,766 reports submitted up until September 2013.

f. Prompt release of package inserts and related notifications directing their revision for prescription drugs on the PMDA website

- By the end of FY 2013, PMDA posted 12,921 package inserts of prescription drugs on the Medical Product Information web page. Upon the issuance of notifications regarding directions for e revision of a package insert by the government, PMDA posted the notifications on its website

within 2 days of the issuance of such information, and provided a link to the corresponding package insert.

g. Provision of information relating to instructions for use of medical devices

- For medical devices, PMDA has made instructions for use publicly available since FY 2005. The Agency released 19,309 instructions for use by the end of FY 2013. Also, the Agency has posted notifications directing the revision of instructions for use within 2 days of the issuance of such information, and routinely provided links to the corresponding instructions for use.

h. Provision of information relating to package inserts of OTC drugs

- Changes were made to the regulatory system for OTC drugs in accordance with the Pharmaceutical Affairs Act, as revised in June 2009. Prior to the enforcement of the revised Act, the government developed systems for providing advice and consultation according to the risk level of OTC drugs, secured qualifications of professionals engaged in selling drugs, and improved the environment that supports provision of adequate information and consultation. As a part of the efforts, PMDA started posting package inserts of OTC drugs on its website in March 2007. A total of 10,234 package inserts are available on the website as of the end of FY 2013.

i. Package insert information for *in vitro* diagnostics

- As described above, information on package inserts of prescription drugs, medical devices, and OTC drugs are provided on the Medical Product Information web page to ensure proper use of such products. Package insert information for *in vitro* diagnostics has also been available since FY 2008. A total of 4,076 package inserts are available on the website as of the end of FY 2013.

j. Provision of manuals for management of individual serious adverse drug reactions

- The manuals for management of individual serious adverse drug reactions prepared by MHLW in its initiative of comprehensive actions for serious adverse drug reactions have been made available on the PMDA website since November 2006. As of the end of FY 2011, manuals for a total of 75 adverse drug reactions were posted on the website.

  These manuals contain information for patients and their family members, which allow early detection of serious adverse drug reactions based on subjective symptoms, and also contain methods of their diagnosis and management for healthcare professionals.

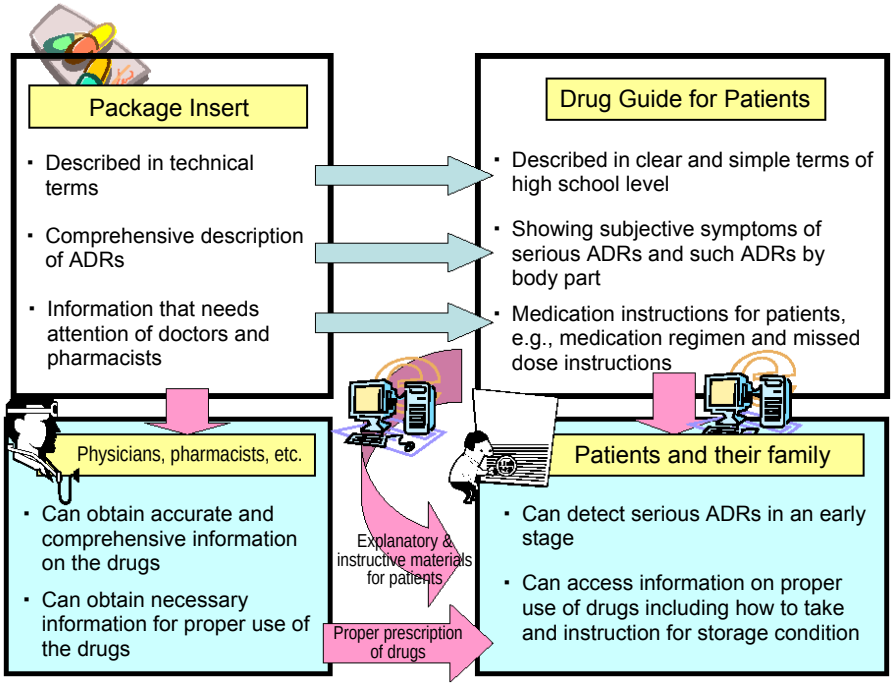
  The MHLW's initiative of comprehensive actions for serious adverse drug reactions was terminated in FY 2010, and consequently, no information was added to the manual in FY 2013, but the manuals are being reviewed for a future revision.

k. Provision of Drug Guide for Patients

- To promote proper understanding of prescription drugs among patients and to enable detection of serious adverse reactions at an earlier stage, The Drug Guide for Patients has been available on the PMDA website since January 2006. In FY 2013, the drug guides for 75 active ingredients (for which a drug guide had to be developed following the Revision of PRECAUTIONS, or which were newly marketed) were added to the Drug Guide for Patients database, and a total of 492 active ingredients in 3,409 products (2,155 package inserts) were posted by the end of FY 2013.
- In accordance with the "Guidelines for Developing the Drug Guide for Patients" (PFSB Notification dated June 30, 2005), PMDA has reviewed and revised the Drug Guide for Patients while

continuously obtaining advice from experts ("Research on How to Provide Patients and People with Drug Safety Information," a study supported by the Health and Labour Sciences Research Grant).

Package Inserts for Prescription Drugs and Drug Guide for Patients



l. Provision of information from the PMDA's Medical Product Information web page

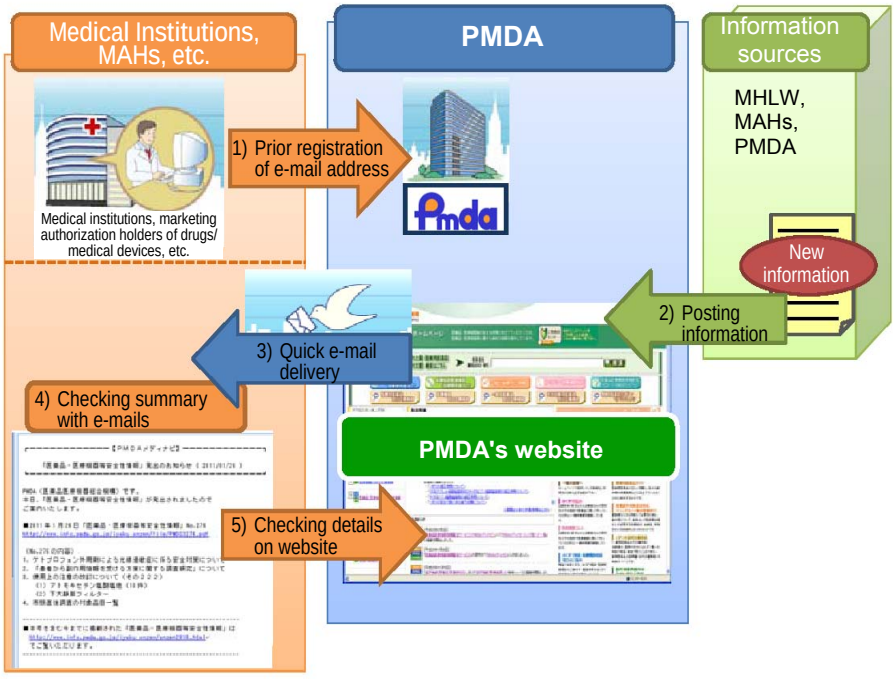
- Among safety information that is issued on a daily basis, PMDA promptly posts important information such as revision of PRECAUTIONS on its Medical Product Information web page (http://www.info.pmda.go.jp/), and distributed the information by e-mail (PMDA medi-navi) to healthcare professionals and relevant people in companies upon issuing the information. PMDA also posts various safety information including package inserts, on the Medical Product Information web page to enhance and reinforce the provision of safety information.
- In FY 2013, PMDA improved and enhanced its website by adding new contents such as RMP, thereby making it more user-friendly.

m. Provision of Pharmaceuticals and Medical Devices Information E-mail Service (PMDA medi-navi)

- The Pharmaceuticals and Medical Devices Information E-mail Service (PMDA medi-navi) which provides safety information such as revisions to package inserts and Class I recalls, is distributed via e-mail to healthcare professionals who subscribe to the service. To enhance public recognition of the service and increase the number of subscribers, PMDA reinforced the PR activities by conducting magazine advertisement using its character, search advertising, and academic conference presentations. In FY 2013, PMDA opened a new registration page for smartphone users to improve recipients' convenience. Also, PMDA newly distributed leaflets at the time of issuance of pharmacist licenses in each prefecture in April 2013, and distributed materials to pharmacy students who were to undergo practical training and their instructor pharmacists in September 2013.

- A total of 102,790 e-mail addresses were registered as of the end of FY 2013 (increased by about 18,600 in FY 2013), of which approximately 33,500 subscribers were with hospitals and clinics, 31,100 were pharmacies, 7,200 were dental clinics or other medical facilities, and 14,700 were MAHs or distributors.
- In June 2011, PMDA started to provide "My Drug List for Safety Update" as an additional function of PMDA medi-navi. As of the end of FY 2013, a total of 7,366 subscribers have been registered.
- This service "My Drug List for Safety Update" enables users to prepare a customizable drug list on the website. When users register necessary drugs (My Drugs), a list of links to web pages of package inserts, Interview Forms, Drug Guides for Patients, etc., for My Drugs is displayed. Furthermore, there are functions such as displaying a warning mark in the case where any safety information such as Dear Healthcare Professional Letters is issued for any registered drug.

Pharmaceuticals and Medical Devices Information E-mail Service (PMDA medi-navi)



Breakdown of Contents of PMDA medi-navi Distributed in FY 2013

Contents of e-mails	Number of cases
Dear Healthcare Professional Letters of Rapid Safety Communications (Blue Letter)	2
Recalls (Class I)	27
Pharmaceuticals and Medical Devices Safety Information	12
Drug Safety Update (DSU)	11
Revision of PRECAUTIONS of drugs	12
Revision of PRECAUTIONS of medical devices	3
Notification on self-check (medical devices)	0
PMDA Medical Safety Information	7
Approval information (medical devices)	14
Approval information (prescription drugs)	52
Notifications on drugs, Notifications on medical devices	21
Information on proper use of drugs	12
Information on drug risk under evaluation	10
Information on products submitted for public knowledge-based applications that are covered by insurance	6
Notice of decision on payment/non-payment of adverse reaction relief benefits	12
Others	14
Total	215

n. Provision of medical safety information

- PMDA has been extracting, evaluating, and examining near-incident cases associated with drugs and medical devices from the "Project Report on Collection of Medical Incident Information," "Annual Report of the Project to Collect and Analyze Near-incident Cases from Pharmacies," etc. published by the Japan Council for Quality Health Care. In FY 2013, 2,680 cases associated with drugs and 368 cases associated with medical devices were evaluated, and the results were reported to MHLW. The details of 3,048 cases, for which deliberations had been completed by MHLW, were posted on the PMDA's Medical Product Information web page and also shown in the following table.

Cases	Drugs	Medical Devices
Total applicable cases: 3,048 cases	2,680	368
1) Cases in which safety measures for the use of drugs/medical devices taken by the MAHs etc. were considered necessary or possible.	0	0
2) Cases in which measures have already been taken, or are currently under consideration, by the MAHs etc.	12	31
3) Cases in which information is insufficient for the MAHs to consider safety measures, or cases that were likely to have resulted from human errors or human factors.	2,668	337

- Since November 2007, PMDA has issued PMDA Medical Safety Information, which is prepared by reference to opinions given by healthcare professionals such as physicians, pharmacists, nurses, and clinical engineers and specialists in fields such as ergonomics. It provides precautions with not just text but easy-to-understand charts for healthcare professionals to use medical products safely. The information addresses events that were reported repeatedly or that led to issuance of revisions to package inserts, among near-incident cases, adverse drug reaction reports, and malfunction reports. In FY 2013, the following 7 issues of PMDA Medical Safety Information were posted on the Medical Product Information web page

No.	Posted on	PMDA Medical Safety Information titles
No.37	April 2013	Precautions in Handling of Insulin Injectors
No.38	May 2013	Improper Assembly of Resuscitator Bags
No.39	September 2013	Precautions in Handling of Tracheal Masks
No.40	October 2013	Precautions in Handling of Vaccines
No.41	January 2014	Precautions in Handling of Epidural Catheters
No.42	February 2014	Precautions in Handling of Nasogastric Tubes
No.43	March 2014	Risks in Handling of Gastrostomy Tubes

o. Information provision in English

- In order to promote the dissemination of information on safety measures to foreign countries, PMDA translated into English the summary of the Risk Management Plan scheme and posted it on PMDA's English website. The Agency also continued to translate into English the PMDA Risk Communications, the PMDA Medical Safety Information and the Pharmaceuticals, and Medical Devices Safety Information issued by MHLW and to post them on its English website.

p. Post-marketing safety measures workshops

- At various workshops and academic conferences, PMDA gave presentations on its approaches to improving and strengthening safety measures, the safety measures including recent revisions of precautions in package inserts, the effective use of the Medical Product Information web page, and PMDA's consultation services.

q. Consultations on drugs/medical devices

- In order for general consumers and patients to use drugs and household medical devices safely and securely, PMDA offers a telephone consultation service.
- In FY 2013, the number of persons receiving consultations was 10,244 (12,617 calls) for drugs, and 547 (591 calls) for medical devices.
- PMDA has extracted consultation cases on generic drugs from consultations on drugs and provided them to the secretariat of the Generic Drug Quality Information Review Group (a review group consisting of experts established at the National Institute of Health Sciences [NIHS]).

Number of Consultations on Drugs/Medical Devices

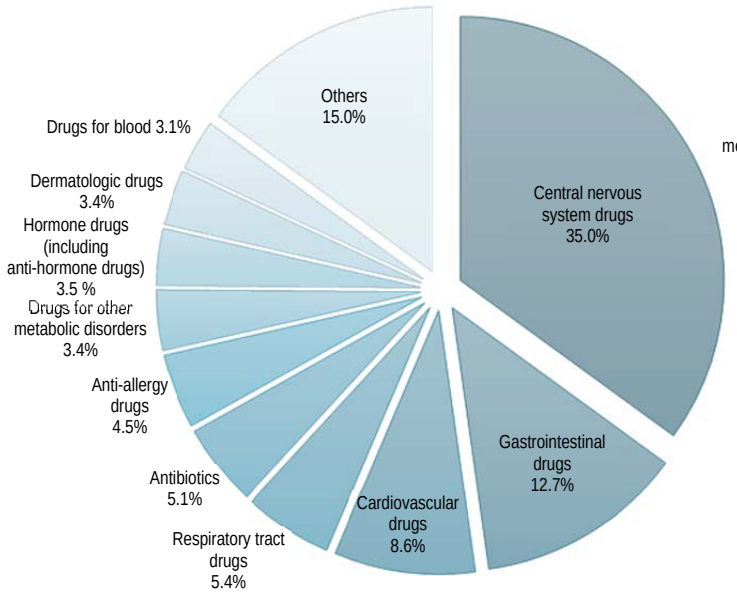
	FY 2009	FY 2010	FY 2011	FY 2012	FY 2013
Consultations on drugs [cases/day] (of which consultations on generic drugs)	9,316 [38.5] (687)	8,846 [36.4] (617)	8,945 [36.7] (453)	9,679 [39.5] (493)	10,244 [42.0] (626)
Consultations on medical devices [cases/day]	558 [2.3]	574 [2.4]	660 [2.7]	700 [2.9]	547 [2.2]

Contents of Consultations on Drugs

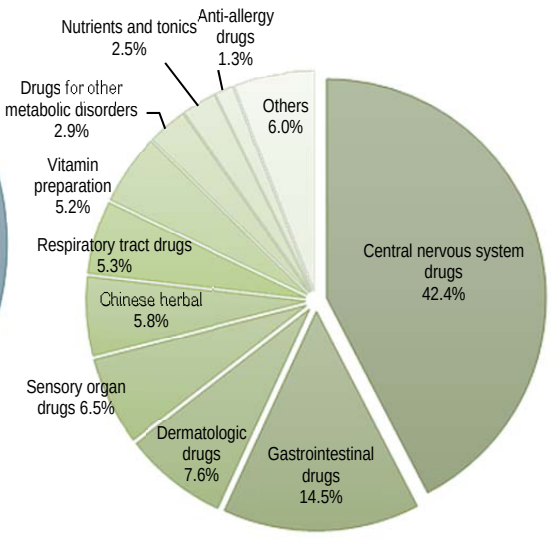
Contents of consultation	FY 2009	FY 2010	FY 2011	FY 2012	FY 2013
(1) Safety	5,727 (42.4%)	5,553 (45.0%)	5,146 (41.3%)	5,267 (41.9%)	4,437 (35.2%)
(2) Indications	1,079 (8.0%)	890 (7.2%)	1,147 (9.2%)	1,158 (9.2%)	1,302 (10.3%)
(3) Dosage and Administration	746 (5.5%)	784 (6.4%)	981 (7.9%)	1,259 (10.0%)	1,278 (10.1%)
(4) Interactions	753 (5.6%)	784 (6.4%)	986 (7.9%)	1,206 (9.6%)	1,426 (11.3%)
(5) Ingredients	251 (1.9%)	181 (1.5%)	199 (1.6%)	222 (1.8%)	255 (2.0%)
Others	4,960 (36.7%)	4,144 (33.6%)	4,014 (32.1%)	3,446 (27.5%)	3,919 (31.1%)
Total	13,516 (100.0%)	12,336 (100.0%)	12,473 (100.0%)	12,558 (100.0%)	12,617 (100.0%)

Percentages of Consultations on Drugs by Therapeutic Category in FY 2013

Prescription drugs (n = 21,113)

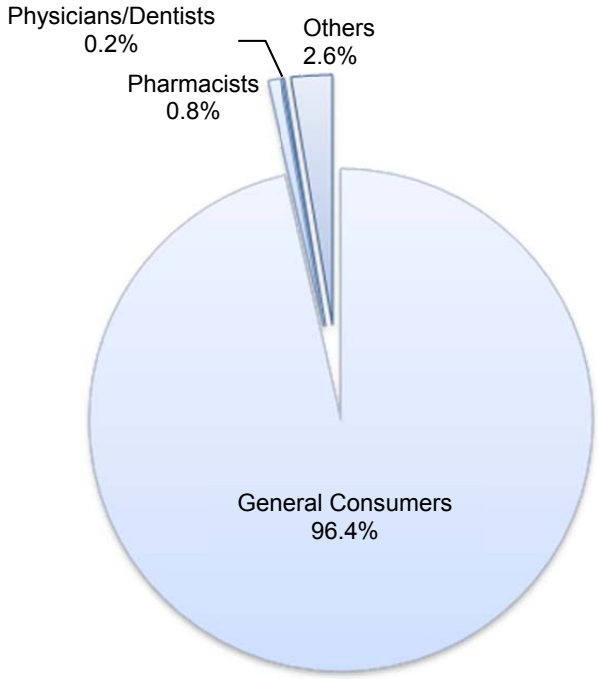


Over-the-counter drugs (n = 828)

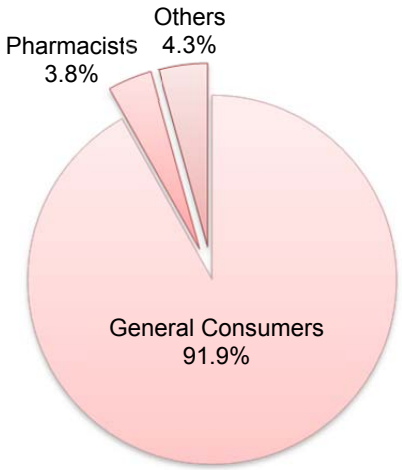


Breakdown of Persons Receiving Consultations on Drugs in FY 2013 (by Profession etc.)

Consultations on drugs (n = 10,244)

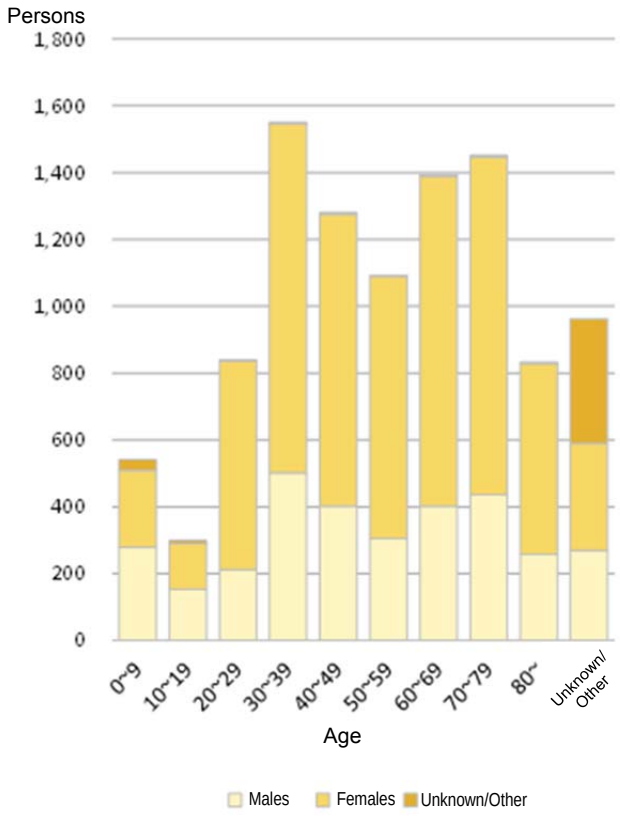


Consultations on generic drugs (n = 626)

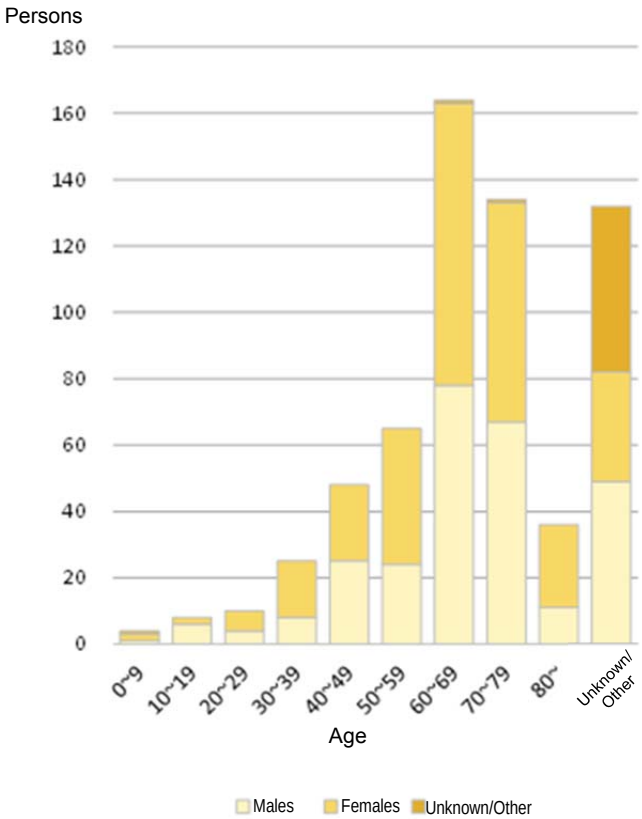


Breakdown of Persons Receiving Consultations on Drugs in FY 2013 (by Age/Gender*)

Consultations on drugs (n = 10,244)



Consultations on generic drugs (n = 626)

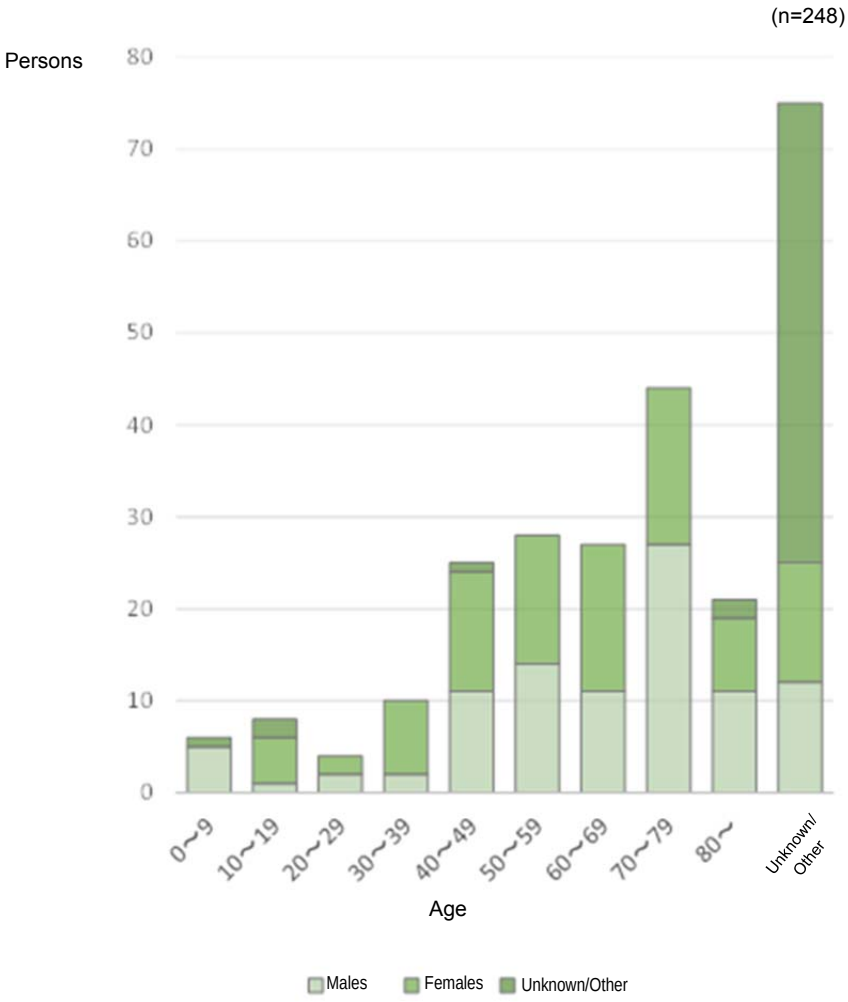


* Persons taking/using drugs were counted by age/gender

Contents of consultations on medical devices

Contents of consultation	FY 2009	FY 2010	FY 2011	FY 2012	FY 2013
(1) Safety	74 (12.0%)	78 (12.5%)	85 (12.4%)	106 (14.5%)	68 (11.5%)
(2) Indications	59 (9.6%)	61 (9.8%)	69 (10.1%)	62 (8.5%)	43 (7.3%)
(3) Performance	27 (4.4%)	17 (2.7%)	24 (3.5%)	36 (4.9%)	13 (2.2%)
(4) Method of use	15 (2.4%)	12 (1.9%)	10 (1.5%)	7 (0.9%)	9 (1.5%)
Others	441 (71.6%)	454 (73.0%)	498 (72.5%)	522 (71.2%)	458 (77.5%)
Total	616 (100.0%)	622 (100.0%)	686 (100.0%)	733 (100.0%)	591 (100.0%)

Breakdown of Persons Receiving Consultations on Medical Devices in FY 2013 (by Age/Gender**)



** Persons using medical devices, who had had consultations for general consumers and at consumer centers, were counted by age/gender.

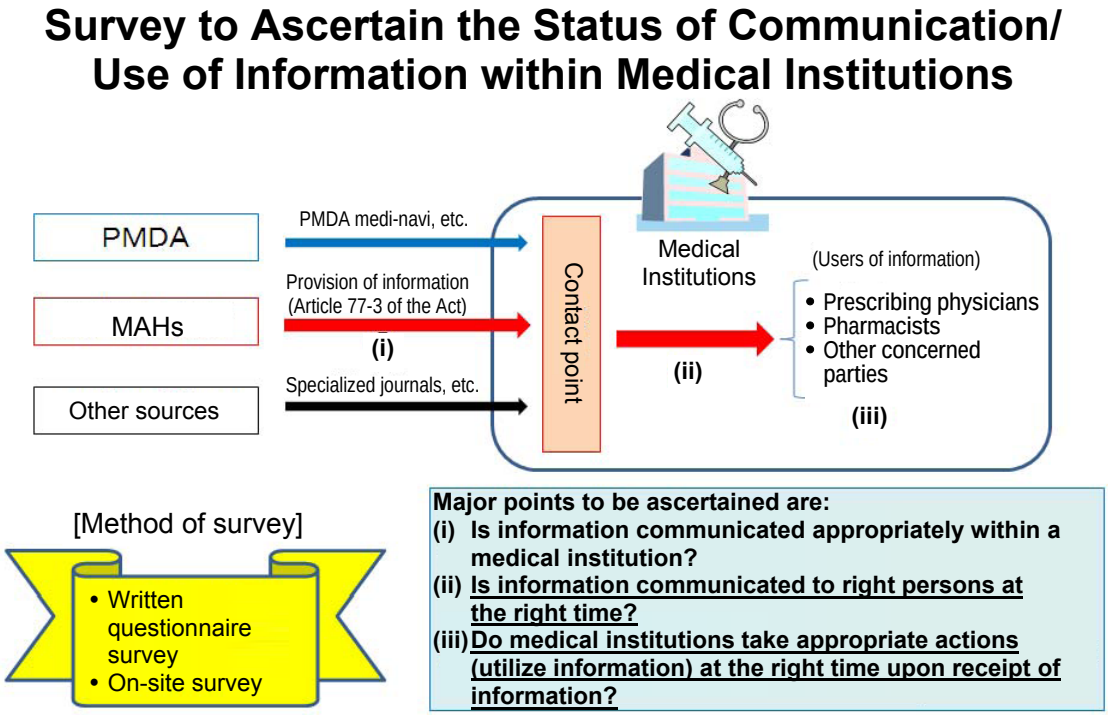
r. Status of communication and use of transmitted safety information within medical institutions

When safety measures are taken, it is important that necessary safety information is appropriately communicated to and used by healthcare professionals in clinical settings. Accordingly, in FY

2010, PMDA started an investigation to ascertain the status of communication and use of safety information on drugs, etc., in medical institutions.

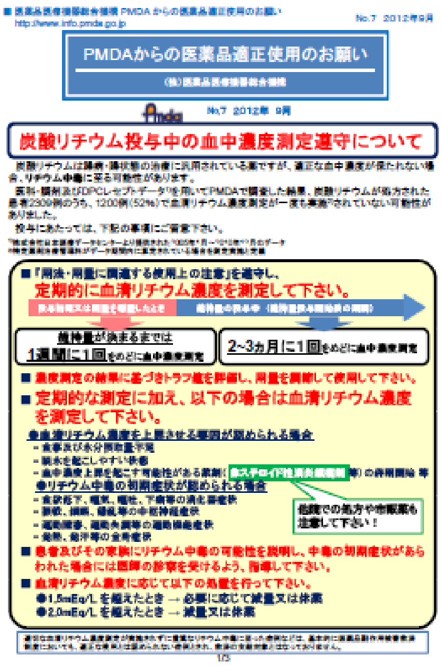
PMDA conducted one mail-in questionnaire survey among hospitals (8,679 institutions) nationwide in FY 2010, and subsequent surveys with different questions among hospitals (8,640) nationwide in FY 2011 and among hospitals (8,536) and half of pharmacies (26,738) nationwide in FY 2012. The survey results up to FY 2012 are available on the PMDA website.

In FY 2013, PMDA mainly conducted door-to-door surveys, including the following three surveys: 1) a survey on good practices for drug safety information, 2) a basic survey on medical device safety information, and 3) a survey on handling of drug safety information overseas. Survey results will be released upon completion of compilation, while awareness-raising materials for the good practices of handling drug safety information will be prepared. PMDA plans to use the results and materials to promote proper communication/use of information at medical institutions and pharmacies.



s. Provision of the PMDA Request for Proper Use of Drugs

If proper use (including dose and frequency as well as frequency of testing for adverse reaction monitoring) of a drug has already been recommended in its package insert or the company's document but the drug is not used properly or testing is not properly conducted, patients' claims for relief benefits for adverse drug reactions may be rejected. In order to avoid such a case, PMDA started providing relevant information to healthcare professionals and related academic societies to promote proper use of drugs in FY 2010.



(Request for Proper Use of Drugs to patients)

Number of Information Documents Released on the PMDA's Medical Product Information Web Page as of the End of March 2014

Posted information		FY 2008	FY 2009	FY 2010	FY 2011	FY 2012	FY 2013
Package insert information[*1]							
	Prescription drugs	13,287	13,050	12,256	12,064	12,435	12,921
	Medical devices	8,164	11,213	13,979	15,584	17,539	19,309
	OTC drugs	8,356	9,513	9,884	10,136	10,158	10,234
	In vitro diagnostics	2,237	3,301	3,984	3,994	4,054	4,076
Drug Guide for Patients[*1]		294 active ingredients (1,958 products)	312 active ingredients (1,920 products)	330 active ingredients (2,311 products)	363 active ingredients (1,951 products)	417 active ingredients (2,453 products)	492 active ingredients (3,409 products)
Safety information issued by MHLW		350	376	409	438	464	494
• Directions for revision of package inserts							257
• Pharmaceuticals and Medical Devices Safety Information							168
• Press release							69
Urgent safety information (by pharmaceutical companies)[*2]		24	24	24	24	25	27
Drug Safety Update (by Federation of Pharmaceutical Manufacturers' Associations of Japan [FPMAJ])		51	61	71	81	91	101
Notification of safety measures for medical devices							
	Notification on self-check	47	49	50	50	51	51
	Notification of revisions of labeling	30	32	33	41	45	48
	Other related notification	57	66	74	83	93	111
Information about case reports on suspected ADR		110,879	142,084	175,360	210,412	254,392	292,720
Information about case reports on suspected malfunction		42,405	46,551	51,169	62,898	73,012	84,766
Notification related to preventive measures for medical accidents		44	56	68	77	87	96
PMDA Medical Safety Information		9	15	22	29	36	43
Manuals for management of individual serious adverse drug reactions		38	63	63	75	75	75
Information on approved new drugs		373 active ingredients	445 active ingredients	513 active ingredients	592 active ingredients	666 active ingredients	700 active ingredients
• Review reports, summaries of product applications		(763 products)	(895 products)	(1,034 products)	(1,189 products)	(1,314 products)	(1,416 products)
A list of prescription drugs on which Quality Information Package (Orange Book) was published		811 active ingredients/ formulations	811 active ingredients/ formulations	811 active ingredients/ formulations	811 active ingredients/ formulations	811 active ingredients/ formulations	811 active ingredients/ formulations
		(3,900 products)	(3,900 products)	(3,900 products)	(3,900 products)	(3,900 products)	(3,900 products)
Information on recalls of drugs or medical devices[*3]		3,448	1,979	1,977	2,299	1,907	1,913
Pharmaceuticals and Medical Devices Information E-mail Service (PMDA medi-navi)							
	E-mails issued[*4]	107	188	203	259	207	215
	Subscribers	20,707	27,410	35,719	55,372	84,146	102,790
Number of web site visitors[*5]		642 million	754 million	873 million	949 million	994 million	1,080 million

**1 Added or deleted as necessary*

**2 In and after October 2011, the total number of Dear Healthcare Professional Letters of Emergent Safety Communications (Yellow Letter) and Dear Healthcare Professional Letters of Rapid Safety Communications (Blue Letter) issued is indicated.*

**3 Added as necessary; and deleted after two years in principle.*

**4 Accumulated total number of e-mails issued in each year*

**5 Total number of files viewed in each year*

Part 4 Development of the Third Mid-term Plan

4.1. Background to the Third Mid-term Plan

- The Third Mid-term Target sets out goals for the management of operations to be achieved by PMDA for the period between April 2014 and March 2019. Regarding the Third Mid-term Targets, an overall review of the organization and operations of PMDA was discussed at the meeting of the Medical Care and Welfare Group of the Evaluation Committee for Incorporated Administrative Agencies of MHLW (held on August 13, 2013), and the targets were assigned to PMDA by the Minister of Health, Labour and Welfare on March 7, 2014, after a final deliberation at the Group's meeting (held on March 3, 2014).
- While hearing opinions from concerned parties such as members of the Advisory Council of PMDA and of the Evaluation Committee for Incorporated Administrative Agencies of MHLW, as well as representatives from the pharmaceutical and medical device industries and the Japan Confederation of Drug-induced Sufferers Organizations, PMDA received preliminary information from MHLW regarding the proposed mid-term targets. Under the guidance of MHLW, PMDA prepared and submitted the draft Third Mid-term Plan to the Minister of Health, Labour and Welfare on March 7, 2014, after deliberations at the Advisory Council Meeting (3rd meeting, held on February 4, 2014) and the meeting of the Medical Care and Welfare Group of the Evaluation Committee for Incorporated Administrative Agencies (held on March 3, 2014). Ultimately, the Third Mid-term Plan was authorized on March 31, 2014.

4.2. Main Points of the Third Mid-term Plan

The main points of the Third Mid-term Plan are as follows:

○ Taking into account the Japan renaissance strategy "JAPAN is BACK" (adopted by the Cabinet on June 14, 2013), the Health and Medicine Strategy (agreed upon by the Chief Cabinet Secretary, the Minister of Health, Labour and Welfare, the Minister of Internal Affairs and Telecommunications, etc. on June 14, 2013), the Act on Securing of Quality, Efficacy and Safety of Pharmaceuticals, Medical Devices, etc. (Act No. 145 of 1960), the Act on Securing of Safety of Regenerative Medicine, etc. (Act No. 85 of 2013), etc., efforts will be made for further acceleration and quality improvement of reviews while taking safety measures such as securing the post-marketing quality of products and preventing the occurrence and expansion of health and hygiene hazards, in order to promote the practical applications of innovative drugs, medical devices, and regenerative medicine products, etc. first in the world.

○ Personnel Affairs

- The number of employees is planned to be increased from 751 at the end of the period covered by the Second Mid-term Plan (the end of March 2013) to 1,065 in FY 2018. For this purpose, PMDA will employ capable personnel with great expertise mainly through open recruitment.
- PMDA will establish policies on the number of technical employees with expertise and on a review of the employment conditions in order to create attractive working environments, and will make efforts to achieve them in a planned manner.
- To employ highly capable personnel with expertise, PMDA will consider strategic ways of securing human resources, including the introduction of an annual salary system.

○ Rationalization of Operation Management

- The Mid-Term Plan budgets for general administrative expenses and operating expenses (excluding personnel expenses, etc.) for which the administrative subsidies are to be allocated will be reduced by 15% and 5%, respectively, as compared to the levels for FY 2014 at the end of the period of the Mid-term Targets.
- A financial base appropriate for the roles of PMDA will be considered and necessary measures will be taken.

○ Relief Services for Adverse Health Effects

- PMDA will enhance public relations and dissemination of information regarding the relief systems.
- The target administrative processing time from receipt of the claim until the decision on payment (at least 60% of judged cases will be processed within 6 months) will be maintained even in situations where the number of claims is expected to increase.

○ Reviews and Related Services

PMDA will:

- Make efforts to achieve “zero” review lag and to improve the quality of review. In order to achieve these goals, strengthen its structure as necessary.
- Regarding the targets for total review time from filing of application to approval for new drugs, achieve the target total review times of 9 months for priority review products up to the 80th percentile and 12 months for standard review products up to the 80th percentile by FY 2018.
- Achieve the target regulatory review time of 10 months for the 50th percentile of new generic drugs by FY 2018.
- Achieve the target total review time of 10 months for the 50th percentile of generic drugs etc., (standard review products) submitted for partial change approval by FY 2018.
- Regarding generic drugs, etc. (those other than standard review products) submitted for partial change approval, achieve the target total review time of 6 months for the 50th percentile of products submitted for changes in test methods, etc. and the target total review time of 3 months for the 50th percentile of products with expedited review status by FY 2018.
- Achieve the target regulatory review time of 7 months for the 50th percentile of behind-the-counter (BTC) drug (switch over-the-counter [OTC] and powerful drugs)/OTC drugs is by FY 2018.
- Achieve the target regulatory review time of 5.5 months for the 50th percentile of quasi-drugs by FY 2018.
- Achieve the target total review time of 10 months for new medical devices (priority review products) up to the 80th percentile by FY 2018.
- Achieve the target total review time of 14 months for new medical devices (standard review products) up to the 80th percentile by FY 2018.
- Achieve the target total review time of 10 months for improved medical devices (with clinical data) up to the 60th percentile by FY 2018.
- Achieve the target total review time of 6 months for improved medical devices (without clinical data) up to the 60th percentile by FY 2018.

- Achieve the target total review time of 4 months for generic medical devices up to the 60th percentile by FY 2018.
- For cellular and tissue-based products, strengthen the structure to respond appropriately to time-limited conditional approval and achieve the target standard review time (regulatory review time) of 9 months for those products.
- Make efforts to keep concerned parties thoroughly informed about the utilization of various types of consultations PMDA offers.
- Increase the efficiency of inspections by using the assessment results provided by regulatory agencies of other member countries under the PIC/S etc., in risk evaluation.
- Improve the quality of registered certification bodies by ensuring the quality of the auditors and by conducting appropriate training, etc., for those certification bodies.
- Regarding Pharmaceutical Affairs Consultations on R&D Strategy, conduct consultations where advice is given on development processes (road map) and confirmatory study protocol.

○ Safety Measures

PMDA will

- Launch direct patient reporting system for adverse drug reactions (ADRs) formally in order to strengthen the collection of ADR or medical device malfunction reports.
- Organize, evaluate, and analyze information on ADRs etc., in a systematic manner.
- Develop medical information database, etc.
- Establish a system for post-marketing safety measures by providing information feedback, etc.: Regarding line listing of adverse reactions, the time from adverse reactions reporting to disclosure will remain as within 4 months. For Pharmaceuticals and Medical Devices Information E-mail Alert Service (PMDA medi-navi), aim at increasing the number of registries at the earliest possible time before the end of FY 2018 by at least 1.5 times that at the end of FY 2013.
- Enhance dissemination of information to the public regarding the safety of drugs and medical Devices, etc.
- Conduct appropriate post-marketing safety measures based on the Risk Management Plan for drugs.
- Enhance safety measures in response to the introduction of the new review system, and a safety management system allowing for consistency from the review to post-marketing stages: Enhance the system of safety management in order to maintain consistency from the review to post-marketing stages, by allocating multiple risk managers for each review category.
- Enhance follow-ups of the safety measures taken.
- Promote data collection, investigation, and analysis on vaccination adverse reactions reports in accordance with the Preventive Vaccination Act.

○ Promotion of regulatory science and globalization, etc.

PMDA will

- Proactively utilize the Science Board comprising external experts from fields such as medical science, dentistry, pharmaceutical science, and engineering, thereby strengthening cooperation and communication with universities, research institutions, etc., and healthcare professionals

regarding evaluation methods for innovative drugs, medical devices, and cellular and tissue-based products, while making approaches to advanced technology products more adequately, for example, by promoting the Pharmaceutical Affairs Consultation on R&D Strategy.

- Enhance regulatory science research.
- Enhance training programs.
- Promote interaction and investigative research with external researchers.
- Respond to globalization.
- Measures for intractable diseases, orphan diseases, etc.
- Provide information such as review reports.
- Ensure impartiality in utilizing external experts.
- Improve the quality of review and safety services by enhancing the information system.

III. SUPPLEMENTARY INFORMATION

Table1. Products Approved in FY 2013: New Drugs

Review Category	Approval Date	No.	Brand Name (Applicant Company)	New Approval/ Partial Change	Active Ingredient(s) (underlined: new active ingredient)	Notes
1	Apr. 30, 2013	1	Potassium Iodide Pills 50 mg "Nichi-iko" (Nichi-Iko Pharmaceutical Co., Ltd.)	Change	Potassium iodide	A drug with a new additional indication and a new dosage for the prevention and reduction of internal exposure to radioactive iodine in the thyroid gland. [Expedited review]
1	May 16, 2013	2	Humira 40 mg for S.C. Injection Syringe 0.8 mL (Abbvie G.K.)	Change	Adalimumab (genetical recombination)	A drug with a new additional indication and a new dosage for the treatment of intestinal Behcet's disease in patients who have not responded sufficiently to conventional treatments.
1	Jun. 14, 2013	3	Humira 40 mg for S.C. Injection Syringe 0.8 mL (Abbvie G.K.)	Change	Adalimumab (genetical recombination)	A drug with a new additional indication and a new dosage for the treatment of moderate to severe ulcerative colitis (for use only in patients who have not responded sufficiently to conventional treatments).
1	Aug. 20, 2013	4	Ora-Bliss Gargle Gran. 11% (Showa Yakuhin Kako Co., Ltd.) Miranor Granule 11% (Oriental Pharmaceutical and Synthetic Chemical Co., Ltd.)	Change Change	Sodium fluoride	Drugs with a new dosage indicated for the prevention of dental caries.
1	Aug. 20, 2013	5	Fosrenol Chewable Tablets 250 mg Fosrenol Chewable Tablets 500 mg Fosrenol Granules 250 mg Fosrenol Granules 500 mg (Bayer Yakuhin, Ltd.)	Change Change Change Change	Lanthanum carbonate hydrate	Drugs with a new indication to extend the indication for the improvement of hyperphosphatemia in patients with chronic kidney disease.
1	Sep. 13, 2013	6	Lipiodol 480 Injection 10 mL (Guerbet Japan K.K.)	Change	Iodine addition products of the ethylesters of the fatty acids obtained from poppyseed oil	A drug with a new route of administration and a new dosage for a new additional indication for the adjustment of drugs or medical devices. [Public knowledge-based application after preliminary assessment by the Pharmaceutical Affairs and Food Sanitation Council (PAFSC)]
1	Sep. 13, 2013	7	Nesp Injection 10 μg Plastic Syringe Nesp Injection 15 μg Plastic Syringe Nesp Injection 20 μg Plastic Syringe Nesp Injection 30 μg Plastic Syringe Nesp Injection 40 μg Plastic Syringe Nesp Injection 60 μg Plastic Syringe Nesp Injection 120 μg Plastic Syringe Nesp Injection 180 μg Plastic Syringe (Kyowa Hakko Kirin Co., Ltd.)	Change Change Change Change Change Change Change Change	Darbepoetin alfa (genetical recombination)	Drugs with a new additional pediatric dosage. These drugs are indicated for the treatment of renal anemia.
1	Sep. 13, 2013	8	Soliris for Intravenous Infusion 300 mg (Alexion Pharma G.K.)	Change	Eculizumab (genetical recombination)	A drug with a new additional indication and a new dosage for the treatment of patients with atypical hemolytic uremic syndrome (aHUS) to inhibit complement-mediated thrombotic microangiopathy.
1	Sep. 20, 2013	9	Nesp Injection 5 μg Plastic Syringe (Kyowa Hakko Kirin Co., Ltd.)	Approval	Darbepoetin alfa (genetical recombination)	A drug with a new additional pediatric dosage in an additional dosage form. The drug is indicated for the treatment of renal anemia.
1	Sep. 20, 2013	10	Oblean Tablets 120 mg (Takeda Pharmaceutical Company Limited)	Approval	Cetilistat	A drug with a new active ingredient indicated for the treatment of obesity (for use only in patients who have both type 2 diabetes mellitus and dyslipidaemia and whose BMI level is 25kg/m^2 or more even with diet and exercise therapies).
1	Jan. 17, 2014	11	Riona Tab. 250 mg (Japan Tobacco Inc.)	Approval	Ferric citrate hydrate	A drug with a new active ingredient indicated for the improvement of hyperphosphatemia in patients with chronic kidney disease.
1	Jan. 17, 2014	12	Savene Injectable 500 mg (Kissei Pharmaceutical Co., Ltd.)	Approval	Dexrazoxane	A drug with a new active ingredient indicated for the treatment of anthracycline extravasation.
1	Feb. 21, 2014	13	Regpara Tablets 25 mg Regpara Tablets 75 mg (Kyowa Hakko Kirin Co., Ltd.)	Change Change	Cinacalcet hydrochloride	Drugs with a new additional indication and a new dosage for the treatment of hypercalcemia in patients with parathyroid carcinoma, and hypercalcemia in patients with primary hyperparathyroidism (HPT) who are unable to undergo parathyroidectomy or who experience recurrent primary HPT after the surgery. [Orphan drug]

Review Category	Approval Date	No.	Brand Name (Applicant Company)	New Approval/ Partial Change	Active Ingredient(s) (underlined: new active ingredient)	Notes
2	May 31, 2013	15	Ancaron Inj. 150 (Sanofi K.K.)	Change	Amiodarone hydrochloride	A drug with a new additional indication and a new dosage indicated for the treatment of cardiac arrest due to ventricular fibrillation/pulseless ventricular tachycardia, resistant to electrical cardioversion.
2	Jun. 14, 2013	17	Maintate Tablets 2.5 mg Maintate Tablets 5 mg (Mitsubishi Tanabe Pharma Corporation)	Change Change	Bisoprolol fumarate	Drugs with a new additional indication and a new dosage for the treatment of tachycardiac atrial fibrillation.
2	Jun. 28, 2013	18	Bisono Tape 4 mg Bisono Tape 8 mg (Toa Eiyo Ltd.)	Approval Approval	Bisoprolol	Drugs with a new active ingredient indicated for the treatment of essential hypertension (mild to moderate).
2	Jun. 28, 2013	19	Irtra Combination Tablets LD Irtra Combination Tablets HD (Shionogi & Co., Ltd.)	Approval Approval	Irbesartan/ trichlormethiazide	New combination drugs indicated for the treatment of hypertension.
2	Aug. 20, 2013	20	Trerief Tablet 25 mg (Dainippon Sumitomo Pharma Co., Ltd.)	Change	Zonisamide	A drug with a new dosage indicated for the improvement of wearing-off phenomenon in symptoms of Parkinson's disease.
2	Sep. 13, 2013	21	Samsca Tablets 7.5 mg (Otsuka Pharmaceutical Co., Ltd.)	Change	Tolvaptan	A drug with a new additional indication and a new dosage for the treatment of fluid retention in patients with hepatic cirrhosis who have not responded sufficiently to other diuretics such as loop diuretics.
2	Sep. 20, 2013	22	Complavin Combination Tablets (Sanofi K.K.)	Approval	(1) Clopidogrel sulfate (2) Aspirin	A new combination drug indicated for the treatment of ischemic heart diseases (acute coronary syndrome [unstable angina, non-ST-segment elevation myocardial infarction, ST-segment elevation myocardial infarction], stable angina, old myocardial infarction) to which percutaneous coronary intervention (PCI) is applicable.
2	Sep. 20, 2013	23	Preminent Tablets HD (MSD K.K.)	Approval	(1) Losartan potassium (2) Hydrochlorothiazide	A drug with a new dosage in an additional dosage form. The drug is indicated for the treatment of hypertension.
2	Nov. 22, 2013	24	Onoact 50 for injection (Ono Pharmaceutical Co., Ltd.)	Change	Landiolol hydrochloride	A drug with a new additional indication and a new dosage for the treatment of tachyarrhythmia including atrial fibrillation/flutter in patients with low cardiac function.
2	Jan. 17, 2014	25	Adempas Tablets 0.5 mg Adempas Tablets 1.0 mg Adempas Tablets 2.5 mg (Bayer Yakuhin, Ltd.)	Approval Approval Approval	Riociguat	Drugs with a new active ingredient indicated for the treatment of persistent/recurrent chronic thromboembolic pulmonary hypertension (CTEPH) after surgical treatment or inoperable CTEPH. [Orphan drug]
2	Mar. 24, 2014	26	Takelda Combination Tablets (Takeda Pharmaceutical Company Limited)	Approval	Lansoprazole/aspirin	A new combination drug indicated for the postoperative inhibition of thrombus and thrombus formation (limited to patients with previous history of gastric or duodenal ulcer) in patients with angina (chronic stable angina, unstable angina), myocardial infraction, ischemic cerebrovascular disorder (transient ischemic attack [TIA], cerebral infarction), and patients who have undergone coronary artery bypass grafting (CABG) or percutaneous transluminal coronary angioplasty (PTCA).
2	Mar. 24, 2014	27	Atedio Combination Tab. (Ajinomoto Pharmaceutical Co., Ltd.)	Approval	Valsartan/cilnidipine	A new combination drug indicated for the treatment of hypertension.
2	Mar. 24, 2014	28	Rasimlo Combination Tablet LD Rasimlo Combination Tablet HD (Novartis Pharma K.K.)	Approval Approval	Aliskiren fumarate/amlodipine besylate	New combination drugs indicated for the treatment of hypertension.
2	Mar. 24, 2014	29	Zacras Combination Tablets LD Zacras Combination Tablets HD (Takeda Pharmaceutical Company Limited)	Approval Approval	Azilsartan/amlodipine besilate	New combination drugs indicated for the treatment of hypertension.
2	Mar. 24, 2014	30	Treprost 20 mg for injection Treprost 50 mg for injection Treprost 100 mg for injection Treprost 200 mg for injection (Mochida Pharmaceutical Co., Ltd.)	Approval Approval Approval Approval	Treprostinil	Drugs with a new active ingredient indicated for the treatment of pulmonary arterial hypertension (WHO functionalclassification; Class II, III and IV).
2	Mar. 24, 2014	31	Samsca Tablets 7.5 mg Samsca Tablets 15 mg Samsca Tablets 30 mg (Otsuka Pharmaceutical Co., Ltd.)	Change Change New	Tolvaptan	Drugs with a new additional indication and a new dosage, and a drug with a newly-added dosage form indicated for inhibiting the progression of autosomal dominant polycystic kidney disease in patients whose kidney volume already have increased and enlarged at a rapid rate. [Orphan drug]

Review Category	Approval Date	No.	Brand Name (Applicant Company)	New Approval/ Partial Change	Active Ingredient(s) (underlined: new active ingredient)	Notes
(1) - (3) 2 (4) - (6) 2 3-1	Sep. 13, 2013	33	[1] Predonine 10 mg [2] Predonine 20 mg [3] Predonine 50 mg [4] Predonine Tablets 5 mg (Shionogi & Co., Ltd.) [5] Prednisolone Tablets 1 mg (Asahi Kasei) [6] Prednisolone Tablets 5 mg (Asahi Kasei) (Asahi Kasei Pharma Corporation)	Change Change Change Change Change Change	[1] - [3] Prednisolone sodium succinate [4] - [6] Prednisolone	Drugs with a new additional indication and a new dosage for the treatment of acute-phase Kawasaki's disease (cases where the disease is severe and at risk for coronary artery disorder) ([1] - [6]) and Duchenne muscular dystrophy ([4] - [6]). Duchenne muscular dystrophy: [Public knowledge-based application after PAFSC's preliminary assessment]
3-1	May 31, 2013	34	E Keppra Tablets 250 mg E Keppra Tablets 500 mg (UCB Japan Co., Ltd.)	Change Change	Levetiracetam	Drugs with a new additional pediatric dosage indicated for use as an adjunctive therapy with other antiepileptic drugs to treat partial seizures (including secondary generalized seizures) in patients with epilepsy who have not responded sufficiently to other antiepileptic drugs.
3-1	Jun. 14, 2013	35	Abilify Tablets 3 mg Abilify Tablets 6 mg Abilify Tablets 12 mg Abilify OD Tablets 3 mg Abilify OD Tablets 6 mg Abilify OD Tablets 12 mg Abilify Powder 1% Abilify Oral Solution 0.1% (Otsuka Pharmaceutical Co., Ltd.)	Change Change Change Change Change Change Change Change	Aripiprazole	Drugs with a new additional indication and a new dosage for the treatment of depression (for use only in patients who have an inadequate response to antidepressant therapy).
3-1	Jun. 28, 2013	36	E Keppra Dry Syrup 50% (UCB Japan Co., Ltd.)	Approval	Levetiracetam	A drug with a new additional pediatric dosage in an additional dosage form indicated for use as an adjunctive therapy with other antiepileptic drugs to treat partial seizures (including secondary generalized seizures) in patients with epilepsy who have not responded sufficiently to other antiepileptic drugs.
3-1	Sep. 20, 2013	37	Xeplion Aqueous Suspension for Intramuscular Injection 25 mg Syringe Xeplion Aqueous Suspension for Intramuscular Injection 50 mg Syringe Xeplion Aqueous Suspension for Intramuscular Injection 75 mg Syringe Xeplion Aqueous Suspension for Intramuscular Injection 100 mg Syringe Xeplion Aqueous Suspension for Intramuscular Injection 150 mg Syringe (Janssen Pharmaceutical K.K.)	Approval Approval Approval Approval Approval	Paliperidone palmitate	Drugs with a new active ingredient indicated for the treatment of schizophrenia.
3-1	Sep. 20, 2013	38	Vyndaqel Capsules 20 mg (Pfizer Japan Inc.)	Approval	Tafamidis meglumine	A drug with a new active ingredient indicated for delaying the peripheral neurologic impairment in transthyretin familial amyloid polyneuropathy. [Orphan drug]
3-1	Nov. 22, 2013	39	Paxil Tablets 5 mg Paxil Tablets 10 mg Paxil Tablets 20 mg (GlaxoSmithKline K.K.)	Change Change Change	Paroxetine hydrochloride hydrate	Drugs with a new additional indication and a new dosage for the treatment of posttraumatic stress disorder.
3-1	Nov. 22, 2013	40	Anafranil Tablets 10 mg Anafranil Tablets 25 mg (Alfresa Pharma Corporation)	Change Change	Clomipramine hydrochloride	Drugs with a new additional indication and a new dosage for the treatment of cataplexy associated with narcolepsy. [Public knowledge-based application after PAFSC's preliminary assessment]
3-1	Nov. 22, 2013	41	Topina Tablets 25 mg Topina Tablets 50 mg Topina Tablets 100 mg (Kyowa Hakko Kirin Co., Ltd.)	Change Change Change	Topiramate	Drugs with a new additional pediatric dosage. These drugs are indicated for use as an adjunctive therapy with other antiepileptic drugs to treat partial seizures (including secondary generalized seizures) in patients with epilepsy who have not responded sufficiently to other antiepileptic drugs.
3-1	Dec. 20, 2013	42	Concerta Tablets 18 mg Concerta Tablets 27 mg (Janssen Pharmaceutical K.K.)	Change Change	Methylphenidate hydrochloride	Drugs with a new additional indication and a new dosage for the treatment of attention-deficit/hyperactivity disorder (AD/HD) in adults.
3-1	Jan. 17, 2014	43	Topina Fine Granules 10% (Kyowa Hakko Kirin Co., Ltd.)	Approval	Topiramate	A drug with a new additional pediatric dosage in an additional dosage form. The drug is indicated for use as an adjunctive therapy with other antiepileptic drugs to treat partial seizures (including secondary generalized seizures) in patients with epilepsy who have not responded sufficiently to other antiepileptic drugs.
3-1	Jan. 17, 2014	44	Concerta Tablets 36 mg (Janssen Pharmaceutical K.K.)	Approval	Methylphenidate hydrochloride	A drug with a new indication and a new dosage in an additional dosage form indicated for the treatment of attention deficit/hyperactivity disorder (AD/HD) in adults.

Review Category	Approval Date	No.	Brand Name (Applicant Company)	New Approval/ Partial Change	Active Ingredient(s) (underlined: new active ingredient)	Notes
3-2	Jun. 14, 2013	46	Precedex Intravenous Solution 200 μg "Hospira" (Hospira Japan Co., Ltd.) Precedex Intravenous Solution 200 μg "Maruishi" (Maruishi Pharmaceutical Co., Ltd.)	Change Change	Dexmedetomidine hydrochloride	Drugs with a new additional indication and a new dosage for sedation of non-intubated patients during surgical and other procedures under local anesthesia.
3-2	Jun. 14, 2013	47	Tramal Capsules 25 mg Tramal Capsules 50 mg (Nippon Shinyaku Co., Ltd.)	Change Change	Tramadol hydrochloride	Drugs with a new additional indication for analgesia in patients with chronic non-cancer pain which cannot be managed by treatments with non-opioid analgesics.
3-2	Jun. 14, 2013	48	Penles Tape 18 mg (Nitto Denko Corporation)	Change	Lidocaine	A drug with a new additional indication and a new dosage for the relief of pain during skin laser radiation therapy.
3-2	Jun. 28, 2013	49	E-fen Buccal Tablets 50 μg E-fen Buccal Tablets 100 μg E-fen Buccal Tablets 200 μg E-fen Buccal Tablets 400 μg E-fen Buccal Tablets 600 μg E-fen Buccal Tablets 800 μg (Teikoku Seiyaku Co., Ltd.)	Approval Approval Approval Approval Approval Approval	Fentanyl citrate	Drugs with a new dosage in a new dosage form for the analgesia of breakthrough pain in patients with cancer receiving a potent opioid analgesic at a fixed time.
3-2	Aug. 20, 2013	50	Lucentis Solution for Intravitreal Injection 2.3 mg/0.23 mL (Novartis Pharma K.K.)	Change	Ranibizumab (genetical recombination)	A drug with new additional indications and a new dosage for the treatment of macular edema following retinal vein occlusion and choroidal neovascularisasion in pathologic myopia.
3-2	Sep. 20, 2013	51	Tapcom Combination Ophthalmic Solution (Santen Pharmaceutical Co., Ltd.)	Approval	(1) Tafluprost (2) Timolol maleate	A new combination drug indicated for the treatment of glaucoma and ocular hypertension.
3-2	Sep. 20, 2013	52	Abstral Sublingual Tablet 100 μg Abstral Sublingual Tablet 200 μg Abstral Sublingual Tablet 400 μg (Kyowa Hakko Kirin Co., Ltd.)	Approval Approval Approval	Fentanyl citrate	Drugs with a new dosage in a new dosage form indicated for analgesia of breakthrough pain in patients with cancer receiving a potent opioid analgesic at fixed time.
3-2	Sep. 20, 2013	53	Azorga Combination Ophthalmic Suspension (Alcon Japan Ltd.)	Approval	(1) Brinzolamide (2) Timolol maleate	A new combination drug indicated for the treatment of glaucoma and ocular hypertension in patients who have not responded sufficiently to other glaucoma drugs.
3-2	Nov. 22, 2013	54	Eylea Intravitreal Injection 40 mg/mL Eylea Intravitreal Injection Kit 40 mg/mL (Bayer Yakuhin, Ltd.)	Change Change	Aflibercept (genetical recombination)	Drugs with a new additional indication and a new dosage for the treatment of macular edema following central retinal vein occlusion.
3-2	Dec. 20, 2013	55	Dormicum Injection 10 mg (Astellas Pharma Inc.)	Change	Midazolam	A drug with a new additional indication and a new dosage for sedation during surgeries and other procedures in the field of dentistry and oral surgery.
3-2	Dec. 20, 2013	56	OneDuro Patch 0.84 mg OneDuro Patch 1.7 mg OneDuro Patch 3.4 mg OneDuro Patch 5 mg OneDuro Patch 6.7 mg (Janssen Pharmaceutical K.K.)	Change Change Change Change Change	Fentanyl	Drugs with a new additional indication for analgesia in moderate to severe chronic pain which cannot be managed by treatments with non-opioid analgesics and weak opioid analgesics (for use only in patients who switch from an opioid analgesic).
3-2	Feb. 21, 2014	57	Lucentis solution for intravitreal injection 2.3 mg/0.23 mL (Novartis Pharma K.K.)	Change	Ranibizumab (genetical recombination)	A drug with a new additional indication for the treatment of diabetic macular edema.
3-2	Mar. 24, 2014	58	Tapenta Tablets 25 mg Tapenta Tablets 50 mg Tapenta Tablets 100 mg (Janssen Pharmaceutical K.K.)	Approval Approval Approval	Tapentadol hydrochloride	Drugs with a new active ingredient indicated for management of moderate to severe pain in various types of cancer.
4	Aug. 20, 2013	59	Cubicin IV 350 mg (MSD K.K.)	Change	Daptomycin	A drug with a new dosage indicated for the treatment of sepsis, infective endocarditis, deep skin infection, secondary infection of trauma, burn and surgical wound, and secondary infection of erosion and ulcer caused by daptomycin-sensitive methicillin-resistant *Staphylococcus aureus* (MRSA)
4	Aug. 20, 2013	60	Synagis for Intramuscular Injection 50 mg Synagis for Intramuscular Injection 100 mg Synagis for Intramuscular Solution 50 mg Synagis for Intramuscular Solution 100 mg (Abbvie G.K.)	Change Change Change Change	Palivizumab (genetical recombination)	Drugs with new indications for the suppression of development of serious lower respiratory tract disease caused by RS viral infection in newborns, infants, and children aged 24 months or less with immunodeficiency and Down syndrome. [Priority review]
4	Sep. 13, 2013	61	Gentacin Injection 10 Gentacin Injection 40 Gentacin Injection 60 (MSD K.K.)	Change Change Change	Gentamicin sulfate	Drugs with a new dosage indicated for the treatment of sepsis, secondary infection of trauma, burn, and surgical wound, pneumonia, cystitis, pyelonephritis, peritonitis, otitis media caused by following applicable microorganisms: Gentamicin-sensitive *Staphylococcus, Escherichia coli, Klebsiella, Enterobacter, Serratia, Proteus, Morganella morganii, Providencia, Pseudomonas aeruginosa*

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4	Dec. 20, 2013	63	Inavir Dry Powder Inhaler 20 mg (Daiichi Sankyo Company, Limited)	Change	Laninamivir octanoate hydrate	A drug with a new additional indication and a new dosage for prophylaxis of influenza A or B virus infections.
4	Dec. 20, 2013	64	Meropen for Intravenous Drip Infusion Vial 0.25 g Meropen for Intravenous Drip Infusion Vial 0.5 g Meropen for Intravenous Drip Infusion Kit 0.5 g (Dainippon Sumitomo Pharma Co., Ltd.)	Change Change Change	Meropenem hydrate	Drugs with a new dosage (the daily dose has been changed) in patients with purulent meningitis.
4	Feb. 21, 2014	65	Streptomycin Sulfate 1 g "Meiji" for Injection (Meiji Seika Pharma Co., Ltd.)	Change	Streptomycin sulfate	A drug with a new additional indication and new dosage for the treatment of non-tuberculous mycobacterial infection including mycobacterium avium complex (MAC) caused by streptomycin-sensitive *mycobacterium* as its applicable microorganism. [Public knowledge-based application after PAFSC's preliminary assessment]
4	Feb. 21, 2014	66	Dalacin S Injection 300 mg Dalacin S Injection 600 mg (Pfizer Japan Inc.)	Change Change	Clindamycin phosphate	Drugs with a new additional indication for cellulitis around the jaw bone and jaw inflammation. [Public knowledge-based application after PAFSC's preliminary assessment]
4	Mar. 24, 2014	67	Avigan Tablet 200 mg (Toyama Chemical Co., Ltd.)	Approval	Favipiravir	A drug with a new active ingredient indicated for novel or re-emerging influenza virus infections (for use only in patients who have not responded or not responded sufficiently to other anti-influenza virus drugs). [Priority review]
4	Mar. 24, 2014	68	Sumithrin Lotion 5% (Kracie Pharma, Ltd.)	Approval	Phenothrin	A drug with a new indication and a new dosage for the treatment of scabies. [Priority review]
4	Mar. 24, 2014	69	Tenozet Tablets 300 mg (GlaxoSmithKline K.K.)	Approval	Tenofovir disoproxil fumarate	A drug with a new active ingredient indicated for the growth inhibition of hepatitis B virus in patients with chronic hepatitis B who show liver dysfunction accompanied by proliferation of the virus. [Priority review]
5	May 16, 2013	70	Lunabell Tablets LD (Nobelpharma Co., Ltd.)	Change	Norethisterone/ ethinylestradiol	A drug with a revised indication from "dysmenorrhea associated with endometriosis; functional dysmenorrhea" to "dysmenorrhea."
5	Jun. 28, 2013	71	Lunabell Tablets ULD (Nobelpharma Co., Ltd.)	Approval	Norethisterone/ ethinylestradiol	A drug with a new indication and a new dosage in an additional dosage form indicated for the treatment of dysmenorrhea.
5	Sep. 20, 2013	72	(1) Reguneal HCa 1.5 Peritoneal Dialysis Solution Reguneal HCa 2.5 Peritoneal Dialysis Solution Reguneal HCa 4.25 Peritoneal Dialysis Solution (2) Reguneal LCa 1.5 Peritoneal Dialysis Solution Reguneal LCa 2.5 Peritoneal Dialysis Solution Reguneal LCa 4.25 Peritoneal Dialysis Solution (Baxter Limited)	 Approval Approval Approval Approval Approval Approval	N/A for this combination drug	Combination prescription drugs with similar formulations indicated for the treatment of (1) peritoneal dialysis in patients with chronic renal failure (used when the peritoneal dialysis is not sufficiently effective to improve hypermagnesemia), (2) peritoneal dialysis in patients with chronic renal failure (used when the peritoneal dialysis is not sufficiently effective to improve hypermagnesemia and when hypercalcaemia may occur due to the treatment with calcium preparation or active vitamin D preparation).
5	Jan. 17, 2014	73	Zalutia 2.5 mg Tablets Zalutia 5 mg Tablets (Eli Lilly Japan K.K.)	Approval Approval	Tadalafil	Drugs with a new indication and a new dosage in a new additional dosage form indicated for the treatment of dysuria associated with benign prostatic hypertrophy.
5	Feb. 21, 2014	74	Estrana Tape 0.72 mg (Hisamitsu Pharmaceutical Co., Inc.)	Change	Estradiol	A drug with a new additional indication and new dosages for the treatment of hypoestrogenism caused by hypogonadism, gonadectomy or primary ovarian insufficiency. [Public knowledge-based application after PAFSC's preliminary assessment]
5	Mar. 24, 2014	75	Racol-NF Semisolid for Enteral Use (EN Otsuka Pharmaceutical Co., Ltd.)	Approval	N/A for this combination drug	A combination prescription drug with similar formulations indicated for tube feeding for especially patients with long-term oral feeding difficulties. It also generally can be used for nutrient retention for postoperative patients.
5	Mar. 24, 2014	76	Enevo Liquid for Enteral Use (Abbott Japan Co., Ltd.)	Approval	N/A for this combination drug	A combination prescription drug with similar formulations indicated for tube feeding for especially patients with long-term oral feeding difficulties. It also generally can be used for nutrient retention for postoperative patients.
6-1	Jun. 14, 2013	77	Prograf Capsules 0.5 mg Prograf Capsules 1 mg (Astellas Pharma Inc.)	Change Change	Tacrolimus hydrate	Drugs with a new additional indication and new dosage for the treatment of interstitial pneumonia associated with polymyositis/dermatomyositis. [Orphan drug]

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6-1	Jun. 28, 2013	78	Orencia SC 125 mg Syringe 1 mL (Bristol-Myers K.K.)	Approval	Abatacept (genetical recombination)	A drug with a new route of administration and a new dosage in a new dosage form indicated for the treatment of rheumatoid arthritis in patients who have not responded sufficiently to conventional treatments.
6-1	Sep. 20, 2013	81	Flutiform 50 Aerosol 56 puffs Flutiform 125 Aerosol 56 puffs Flutiform 50 Aerosol 120 puffs Flutiform 125 Aerosol 120 puffs (Kyorin Pharmaceutical Co., Ltd.)	Approval Approval Approval Approval	(1) Fluticasone propionate (2) Formoterol fumarate hydrate	New combination drugs indicated for the treatment of bronchial asthma (when a combination treatment of an inhaled steroid and a long-acting beta-2 agonist is needed).
6-1	Sep. 20, 2013	82	Alesion Ophthalmic Solutoin 0.05% (Santen Pharmaceutical Co., Ltd.)	Approval	Epinastine hydrochloride	A drug with a new route of administration indicated for the treatment of allergic conjunctivitis.
6-1	Sep. 20, 2013	83	Relvar 100 Ellipta 14 doses Relvar 100 Ellipta 30 doses Relvar 200 Ellipta 14 doses Relvar 200 Ellipta 30 doses (GlaxoSmithKline K.K.)	Approval Approval Approval Approval	(1) Vilanterol trifenatate (2) Fluticasone furoate	New combination drugs with a new active ingredient indicated for the treatment of bronchial asthma (when a combination treatment of an inhaled steroid and a long-acting beta-2 agonist is needed).
6-1	Sep. 20, 2013	84	Ultibro Inhalation Capsules (Novartis Pharma K.K.)	Approval	(1) Indacaterol maleate (2) Glycopyrronium bromide	A new combination drug indicated for the relief of symptoms secondary to airway obstructive disorder in chronic obstructive pulmonary disease (chronic bronchitis, emphysema) (when a combination treatment of an inhaled long-acting anticholinergic and a long-acting beta-2 agonist is needed).
6-1	Jan. 17, 2014	85	Allegra 5% Dry Syrup (Sanofi K.K.)	Approval	Fexofenadine hydrochloride	A drug with a new additional pediatric (6 months of age and older and less than 7 years of age) dosage in an additional dosage form of dry syrup. This drug is indicated for the treatment of allergic rhinitis, urticaria, and itching associated with skin diseases (eczema/dermatitis, pruritus cutaneous, atopic dermatitis).
6-1	Jan. 17, 2014	86	Cedartolen Sublingual Drop-Japanese Cedar Polllen 200 JAU/mL bottle Cedartolen Sublingual Drop-Japanese Cedar Polllen 2,000 JAU/mL bottle Cedartolen Sublingual Drop-Japanese Cedar Polllen 2,000 JAU/mL pack (Torii Pharmaceutical Co., Ltd.)	Approval Approval Approval	Standardized Japanese cedar pollen extract original solution 10,000 JAU/mL	Drugs with a new route of administration indicated for the treatment of Japanese cedar pollinosis. (Allergen immunotherapy).
6-1	Jan. 17, 2014	87	Xyzal Syrup 0.05% (GlaxoSmithKline K.K.)	Approval	Levocetirizine hydrochloride	A drug with a new additional pediatric (6 months of age and older and less than 7 years of age) dosage in an additional dosage form of dry syrup. This drug is indicated for the treatment of allergic rhinitis, urticaria and itching associated with skin disease. (eczema/dermatitis and pruritus cutaneous)
6-1	Mar. 17, 2014	88	Allermist 27.5 μg 56 metered Nasal Spray (GlaxoSmithKline K.K.)	Change	Fluticasone furoate	A drug with a new additional pediatric dosage indicated for the treatment of allergic rhinitis.
6-1	Mar. 24, 2014	89	Respia Injection or oral solution 60 mg (Nobelpharma Co., Ltd.)	Approval	Anhydrous caffeine	A drug with a new route of administration indicated for the treatment of primary apnea (apnea of prematurity) in immature or low birth weight infants. [Orphan drug]
6-2	Jun. 28, 2013	90	Topiloric Tablets 20 mg Topiloric Tablets 40 mg Topiloric Tablets 60 mg (Fujiyakuhin Co., Ltd.) Uriadec Tab. 20 mg Uriadec Tab. 40 mg Uriadec Tab. 60 mg (Sanwa Kagaku Kenkyusho Co., Ltd.)	Approval Approval Approval Approval Approval Approval	Topiroxostat	Drugs with a new active ingredient indicated for the treatment of gout and hyperuricemia.
6-2	Jun. 28, 2013	91	Lyxumia 300 μg solution for injection (Sanofi K.K.)	Approval	Lixisenatide	A drug with a new active ingredient indicated for the treatment of type 2 diabetes mellitus (for use only in patients who have not responded sufficiently to either treatment (1) or (2): (1) Use of sulfonylureas (including combination with biguanides) in addition to diet and exercise therapies; (2) Use of long-acting soluble insulin or intermediate-acting insulin preparations (including combination with sulfonylureas) in addition to diet and exercise therapies.
6-2	Jun. 28, 2013	92	Bonviva IV Injection 1 mg Syringe (Chugai Pharmaceutical Co., Ltd.)	Approval	Ibandronate sodium hydrate	A drug with a new active ingredient indicated for the treatment of osteoporosis.
6-2	Sep. 13, 2013	93	Glufast Tab. 5 mg Glufast Tab. 10 mg (Kissei Pharmaceutical Co., Ltd.)	Change Change	Mitiglinide calcium hydrate	Drugs with a new indication for the treatment of type 2 diabetes mellitus.
6-2	Dec. 20, 2013	94	Tenelia Tablets 20 mg (Mitsubishi Tanabe Pharma Corporation)	Change	Teneligliptin hydrobromide hydrate	A drug with a revised indication for the treatment of type 2 diabetes mellitus.
6-2	Jan. 17, 2014	95	Suglat Tablets 25 mg Suglat Tablets 50 mg (Astellas Pharma Inc.)	Approval Approval	Ipragliflozin L-proline	Drugs with a new active ingredient indicated for the treatment of type 2 diabetes mellitus.

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6-2	Mar. 24, 2014	97	Forxiga Tablets 5 mg Forxiga Tablets 10 mg (Bristol-Myers K.K.)	Approval Approval	Dapagliflozin propylene glycolate hydrate	Drugs with a new active ingredient indicated for the treatment of type 2 diabetes mellitus.
6-2	Mar. 24, 2014	98	Lusefi Tab. 2.5 mg Lusefi Tab. 5 mg (Taisho Pharmaceutical Co., Ltd.)	Approval Approval	Luseogliflozin hydrate	Drugs with a new active ingredient indicated for the treatment of type 2 diabetes mellitus.
6-2	Mar. 24, 2014	99	Deberza Tablets 20 mg (Kowa Company, Ltd.) Apleway 20 mg Tablets (Sanofi K.K.)	Approval Approval	Tofogliflozin hydrate	Drugs with a new active ingredient indicated for the treatment of type 2 diabetes mellitus.
Radio-pharmaceuticals	Sep. 20, 2013	100	DaTscan Intravenous Injection (Nihon Medi-Physics Co., Ltd.)	Approval	Ioflupane (123I)	A drug with a new active ingredient indicated for dopamine transporter scintigraphy in the diagnoses of Parkinson's syndrome and dementia with lewy bodies.
Oncology drugs	Jun. 14, 2013	101	Avastin 100 mg/4 mL Intravenous Infusion Avastin 400 mg/16 mL Intravenous Infusion (Chugai Pharmaceutical Co., Ltd.)	Change Change	Bevacizumab (genetical recombination)	Drugs with a new additional indication and a new dosage for the treatment of malignant glioma. [Orphan drug]
Oncology drugs	Jun. 14, 2013	102	Tarceva Tablet 25 mg Tarceva Tablet 100 mg Tarceva Tablet 150 mg (Chugai Pharmaceutical Co., Ltd.)	Change Change Change	Erlotinib hydrochloride	Drugs with a new additional indication and a new dosage for the treatment of unresectable advanced or recurrent non-small cell lung cancer with *EGFR* gene mutation in patients who have not been treated with chemotherapy.
Oncology drugs	Jun. 14, 2013	103	Herceptin Intravenous Infusion 60 Herceptin Intravenous Infusion 150 (Chugai Pharmaceutical Co., Ltd.)	Change Change	Trastuzumab (genetical recombination)	Drugs with a new dosage for the treatment of breast cancer with HER2 overexpression. [Public knowledge-based application after PAFSC's preliminary assessment]
Oncology drugs	Jun. 14, 2013	104	Hycamtin for Injection 1.1 mg (Nippon Kayaku Co., Ltd.)	Change	Nogitecan hydrochloride	A drug with a new additional indication and a new dosage for the treatment of pediatric malignant solid tumors. [Public knowledge-based application after PAFSC's preliminary assessment]
Oncology drugs	Jun. 28, 2013	105	Perjeta Intravenous Infusion 420 mg/14 mL (Chugai Pharmaceutical Co., Ltd.)	Approval	Pertuzumab (genetical recombination)	A drug with a new active ingredient indicated for the treatment of unresectable or recurrent HER2-positive breast cancer.
Oncology drugs	Aug. 20, 2013	106	Stivarga Tablets 40 mg (Bayer Yakuhin, Ltd.)	Change	Regorafenib hydrate	A drug with a new additional indication for the treatment of gastrointestinal stromal tumor which has progressed after cancer chemotherapy. [Priority review]
Oncology drugs	Sep. 20, 2013	107	Unitalc Intrapleural 4 g (Nobelpharma Co., Ltd.)	Approval	Sterile talc	A drug with a new active ingredient indicated for the suppression of recurrence of malignant pleural effusions.
Oncology drugs	Sep. 20, 2013	108	Kadcyla Intravenous Infusion 100 mg Kadcyla Intravenous Infusion 160 mg (Chugai Pharmaceutical Co., Ltd.)	Approval Approval	Trastuzumab emtansine (genetical recombination)	Drugs with a new active ingredient indicated for the treatment of unresectable or recurrent HER2-positive breast cancer. [Priority review]
Oncology drugs	Sep. 20, 2013	109	Laserphyrin 100 mg for Injection (Meiji Seika Pharma Co., Ltd.)	Change	Talaporfin sodium	A drug with a new additional indication and a new dosage for the treatment of primary malignant brain tumor (only for the case where surgical excision of tumor is performed). [Orphan drug]
Oncology drugs	Nov. 22, 2013	110	Avastin 100 mg/4 mL Intravenous Infusion Avastin 400 mg/16 mL Intravenous Infusion (Chugai Pharmaceutical Co., Ltd.)	Change Change	Bevacizumab (genetical recombination)	Drugs with a new additional indication for the treatment of ovarian cancer.
Oncology drugs	Nov. 22, 2013	111	Farmorubicin for Injection 10 mg Farmorubicin for Injection 50 mg (Pfizer Japan Inc.)	Change Change	Epirubicin hydrochloride	Drugs with a new additional dosage indicated for transcatheter arterial chemo-embolization (TACE) in hepatocellular carcinoma. [Public knowledge-based application]
Oncology drugs	Dec. 20, 2013	112	Elplat I.V. Infusion Solution 50 mg Elplat I.V. Infusion Solution 100 mg Elplat I.V. Infusion Solution 200 mg (Yakult Honsha Co., Ltd.)	Change Change Change	Oxaliplatin	Drugs with a new additional indication and a new dosage for the treatment of unresectable pancreatic cancer. [Priority review], [Expedited review]
Oncology drugs	Dec. 20, 2013	113	Campto 40 mg for I.V. Infusion Campto 100 mg for I.V. Infusion (Yakult Honsha Co., Ltd.)	Change Change	Irinotecan hydrochloride hydrate	Drugs with a new additional indication and a new dosage for the treatment of unresectable pancreatic cancer. [Priority review], [Expedited review]
Oncology drugs	Dec. 20, 2013	114	Topotecin Intravenous Drip Infusion 40 mg Topotecin Intravenous Drip Infusion 100 mg (Daiichi Sankyo Company, Limited)	Change Change	Irinotecan hydrochloride hydrate	Drugs with a new additional indication and a new dosage for the treatment of unresectable pancreatic cancer. [Priority review], [Expedited review]
Oncology drugs	Dec. 20, 2013	115	Isovorin Injection 25 mg Isovorin Injection 100 mg (Pfizer Japan Inc.)	Change Change	Levofolinate calcium	Drugs with a new additional indication and a new dosage for the treatment of unresectable pancreatic cancer. [Priority review], [Expedited review]

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Oncology drugs	Dec. 20, 2013	117	5-FU Injection 250 mg 5-FU Injection 1000 mg (Kyowa Hakko Kirin Co., Ltd.)	Change Change	Fluorouracil	Drugs with a new additional indication and a new dosage for the treatment of unresectable pancreatic cancer. [Priority review], [Expedited review]
Oncology drugs	Jan. 17, 2014	118	Giotrif Tablets 20 mg Giotrif Tablets 30 mg Giotrif Tablets 40 mg Giotrif Tablets 50 mg (Nippon Boehringer Ingelheim Co., Ltd.)	Approval Approval Approval Approval	Afatinib maleate	Drugs with a new active ingredient indicated for the treatment of unresectable advanced or recurrent non-small cell lung cancer with EGFR gene mutation.
Oncology drugs	Jan. 17, 2014	119	Adcetris for Intravenous Drip Infusion 50 mg (Takeda Pharmaceutical Company Limited)	Approval	Brentuximab vedotin (genetical recombination)	A drug with a new active ingredient indicated for the treatment of relapsed or refractory CD30-positive Hodgkin's lymphoma and anaplastic large-cell lymphoma. [Orphan drug]
Oncology drugs	Mar. 17, 2014	120	Zoladex LA 10.8 mg depot (AstraZeneca K.K.)	Change	Goserelin acetate	A drug with a new additional indication for the treatment of premenopausal breast cancer.
Oncology drugs	Mar. 17, 2014	121	Afinitor Tablets 2.5 mg Afinitor Tablets 5 mg (Novartis Pharma K.K.)	Change Change	Everolimus	Drugs with a new additional indication and a new dosage for the treatment of unresectable or recurrent breast cancer.
Oncology drugs	Mar. 17, 2014	122	Votrient Tablets 200 mg (GlaxoSmithKline K.K.)	Change	Pazopanib hydrochloride	A drug with a new additional indication for the treatment of unresectable or metastatic renal cell carcinoma.
Oncology drugs	Mar. 17, 2014	123	Poteligeo Injection 20 mg (Kyowa Hakko Kirin Co., Ltd.)	Change	Mogamulizumab (genetical recombination)	A drug with new additional indications for the treatment of relapsed or refractory CCR4-positive peripheral T-cell lymphoma and relapsed or refractory CCR4-positive cutaneous T-cell lymphoma. [Orphan drug]
Oncology drugs	Mar. 24, 2014	124	Lonsurf Combination Tablet T15 Lonsurf Combination Tablet T20 (Taiho Pharmaceutical Co., Ltd.)	Approval Approval	Trifluridine/tipiracil hydrochloride	New combination drugs with a new active ingredient indicated for the treatment of unresectable advanced or recurrent colorectal cancer (for use only if refractory or intolerant to standard therapies).
Oncology drugs	Mar. 24, 2014	125	Xtandi Capsules 40 mg (Astellas Pharma Inc.)	Approval	Enzalutamide	A drug with a new active ingredient indicated for the treatment of castration-resistant prostate cancer. [Priority review]
(1) Oncology drugs (2) 6-1	Jun. 14, 2013	126	Rituxan Injection 10 mg/mL (Zenyaku Kogyo Co., Ltd.)	Change	Rituximab (genetical recombination)	A drug with new additional indications and a new dosage for the treatment of (1) CD 20-positive B-cell lymphoproliferative disorders in immunocompromised patients and (2) Wegener's granulomatosis and microscopic polyangiitis. [Public knowledge-based application after PAFSC's preliminary assessment]
AIDS drugs	Mar. 24, 2014	127	Tivicay Tablets 50 mg (ViiV Healthcare K.K.)	Approval	Dolutegravir sodium	A drug with a new active ingredient indicated for the treatment of HIV infection. [Orphan drug]
Vaccines	Apr. 26, 2013	128	Cell Culture-derived Influenza Vaccine (prototype) "Baxter" (Baxter Limited) Cell Culture-derived Influenza Vaccine (prototype) "Takeda" 5 mL (Takeda Pharmaceutical Company Limited)	Approval Approval	Cell culture-derived influenza vaccines (prototype)	Drugs with a new active ingredient indicated for the prevention of pandemic influenza. [Orphan drug]
Vaccines	Jun. 18, 2013	129	Prevenar 13 Suspension Liquid for Injection (Pfizer Japan Inc.)	Approval	Pneumococcal 13-valent conjugate vaccine adsorbed (mutated diphtheria CRM_{197} conjugate)	A drug with a new active ingredient indicated for the prophylaxis of pneumococcal invasive infections (serotypes 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F).
Vaccines	Jun. 18, 2013	130	Cell Culture-derived Influenza Vaccine H5N1 "Baxter" (Baxter Limited) Cell Culture-derived Influenza Vaccine H5N1 "Takeda" 5 mL (Takeda Pharmaceutical Company Limited)	Approval Approval	Cell culture-derived influenza vaccine (H5N1)	Drugs with a new active ingredient indicated for the prevention of pandemic influenza (H5N1). [Orphan drug]
Vaccines	Mar. 17, 2014	131	Heptavax-II (MSD K.K.) Bimmugen Bimmugen Injection 0.25 mL Bimmugen Injection 0.5 mL (Kaketsuken [The Chemo-Sero-Therapeutic Research Institute])	Change Change Change Change	Recombinant adsorbed hepatitis B vaccine (prepared from yeast)	Drugs with a revised dosage indicated for the prevention of perinatal hepatitis B virus infection (concomitant use with anti-Hepatitis B surface [HBs] human immunoglobulin). [Public knowledge-based application after PAFSC's preliminary assessment]
Vaccines	Mar. 24, 2014	132	Cell Culture-derived Influenza Emulsion HA Vaccine H5N1 for Intramuscular Injection "Kaketsuken" (Kaketsuken [The Chemo-Sero-Therapeutic Research Institute])	Approval	Cell culture-derived influenza emulsion HA vaccine (H5N1)	A drug with a new active ingredient indicated for the prevention of pandemic influenza (H5N1). [Orphan drug]

Review Category	Approval Date	No.	Brand Name (Applicant Company)	New Approval/ Partial Change	Active Ingredient(s) (underlined: new active ingredient)	Notes
Blood products	May 16, 2013	134	NovoSeven HI for Intravenous Injection 1 mg NovoSeven HI for Intravenous Injection 2 mg NovoSeven HI for Intravenous Injection 5 mg (Novo Nordisk Pharma Ltd.)	Change Change Change	Eptacog alfa (activated) (genetical recombination)	Drugs with a new dosage to add single-dose administration for the prevention of bleeding in patients with congenital hemophilia who have inhibitors against blood coagulation factor VIII or IX. [Public knowledge-based application after PAFSC's preliminary assessment]
Blood products	Sep. 13, 2013	135	Fibrogammin P I.V. Injection (CSL Behring K.K.)	Change	Lyophilized human blood coagulation factor XIII concentrate	A drug with a new additional indication for the treatment of bleeding tendency caused by acquired blood coagulation factor XIII deficiency. [Public knowledge-based application after PAFSC's preliminary assessment]
Blood products	Sep. 27, 2013	136	Hizentra 20% S.C. Injection 1 g/5 mL Hizentra 20% S.C. Injection 2 g/10 mL Hizentra 20% S.C. Injection 4 g/20 mL (CSL Behring K.K.)	Approval Approval Approval	pH4-treated normal human immunoglobulin (subcutaneous injection)	Drugs with a new active ingredient indicated for the treatment of agammaglobulinemia or hypogammaglobulinemia.
Blood products	Jan. 17, 2014	137	NovoEight i.v.injection 250 NovoEight i.v.injection 500 NovoEight i.v.injection 1000 NovoEight i.v.injection 1500 NovoEight i.v.injection 2000 NovoEight i.v.injection 3000 (Novo Nordisk Pharma Ltd.)	Approval Approval Approval Approval Approval Approval	Turoctocog alpha (genetical recombination)	Drugs with a new active ingredient indicated for inhibition of bleeding tendency in patients with blood coagulation factor VIII deficiency.
Bio-CMC	Mar. 24, 2014	138	Filgrastim BS Inj.75 μg Syringe “Sandoz” Filgrastim BS Inj.150 μg Syringe “Sandoz” Filgrastim BS Inj.300 μg Syringe “Sandoz” (Sandoz K.K.)	Approval Approval Approval	Filgrastim (genetical recombination) [Filgrastim biosimilar 3]	Follow-on biologics indicated for mobilization of hematopoietic stem cell to peripheral blood, promotion of increase in neutrophil count at the time of hematopoietic stem cell transplantation, and the treatment of neutropenia caused by cancer chemotherapy, neutropenia which affects the treatment of human immunodeficiency virus (HIV) infection, neutropenia associated with myelodysplastic syndrome, neutropenia associated with aplastic anemia and congenital/idiopathic neutropenia.

Table2. Products Approved in FY 2013: New Medical Devices

Review Category	Approval Date	Approval Date in US Clinical Study Results: Domestic/Foreign	No.	Brand Name (Applicant Company)	New Approval /Partial Change	Classification Generic Name	Notes
1	May 21, 2013 Total review time: 193 days Regulatory review time: 77 days	- (About these changes) No clinical study results	1	Baerveldt Glaucoma Implant (AMO Japan K.K.)	Change	Medical products 4 Intraocular drain	An artificial aqueous drainage device implanted to decrease intraocular pressure in patients with refractory glaucoma who have not responded to conventional therapy. It drains aqueous humor from the anterior or posterior chamber to the episclera to decrease intraocular pressure. Application for a partial change to add raw material to be used in the elbow of pars plana insertion type. (A partial change during the reexamination period)
1	Sep. 20, 2013 Total review time: 245 days Regulatory review time: 161 days	- Foreign clinical study results	2	MED-EL EAS Hearing Implant System (MED-EL Elektro-Medizinische Geräte GmbH)	Approval	Medical products 4 Cochlear implant system	A cochlear implant system for perceiving information such as supporting hearing by acoustic stimulation to the low-frequencies and electric stimulation to the high-frequencies in patients with ski-slope hearing loss, in which there is good hearing for lower frequencies who have not responded sufficiently to wearing hearing aids. This product consists of an audio processor (an audio signal processing device) and an implant (an electrode and a stimulator). Of the sound signals picked up by the microphone embedded the audio processor, the high-frequency sounds are perceived by electric stimulation generated from the electrode in the same way as an existing cochlear implant, while the low-frequency sounds are amplified to be perceived by acoustic stimulation through the ear canal. A clinical study was conducted to evaluate the efficacy and safety of this product in patients with ski-slope hearing loss. [Priority review]
1	Nov. 5, 2013 Total review time: 228 days Regulatory review time: 74 days	- (About these changes) No clinical study results	3	Alcon Ex-PRESS Glaucoma Filtration Device (Alcon Japan Ltd.)	Change	Medical products 4 Intraocular drain	A stainless-steel glaucoma filtration device intended to create an aqueous humor outflow tract between the anterior chamber and extraocular segment and to lower the intraocular pressure by puncture and placement from the limbus into the anterior chamber under the scleral flap with this device. An application for a partial change to change the Ex-PRESS delivery system (EDS) to the improved ESD in which an Ex-PRESS body hardly fall off from the EDS wire during transport. (A partial change during the reexamination period)
1	Dec. 20, 2013 Total review time: 255 days Regulatory review time: 81 days	- Clinical evaluation report	4	HOYA CTR (HOYA Corporation)	Approval	Medical products 4 Ophthalmic intracapsular ring	A blue C-shaped polymethyl methacrylate open ring used for patients whose cataract surgery is expected to carry risks associated with its completion and to be difficult to perform due to a brittleness or rupture of Zinn's Zonule. The ring, inserted into a capsule of crystalline lens, holds the capsule during surgery by making the subluxated capsule produce an extension from the inside. Shape of the ring is a single or a multiple circle. The multiple-circle ring has one or two sewing hooks which is used for anchoring to the sclera by suture thread. The hook is designed to come out from the anterior capsule and a suture thread which passes through the hook is anchored to the sclera. A clinical evaluation report was submitted to confirm that efficacy and safety of this device are equivalent to foreign similar devices, based on domestic and overseas long-term usage histories of the foreign similar devices of which indication and operative procedure had already been established. [Priority review]
1	Mar. 28, 2014 Total review time: 583 days Regulatory review time: 237 days	Nov. 12, 1993 Clinical evaluation report	5	Ahmed Glaucoma Valve (Japan Focus Company, Ltd.)	Approval	Medical products 4 Intraocular drain	An artificial aqueous drainage device implanted to decrease intraocular pressure in patients with refractory glaucoma who have not responded to conventional therapy. It drains aqueous humor from the inside of the eye to decrease intraocular pressure. It consists of a silicone plate and tube, and a polypropylene valve system with silicone membrane sheet. The components include only an anterior chamber insertion type. A major differences from the original product “Baerveldt Glaucoma Implant (Approval No. 22300BZX00370000)” are that this product is smaller and has a valve system. A clinical evaluation report summarizing the results of literature search on overseas clinical studies and experience of this product was submitted to evaluate its safety and efficacy in decreasing intraocular pressure.

Review Category	Approval Date	Approval Date in US Clinical Study Results: Domestic/Foreign	No.	Brand Name (Applicant Company)	New Approval /Partial Change	Classification Generic Name	Notes
3-1	May 1, 2013 Total review time: 418 days Regulatory review time: 116 days	Nov. 7, 2012 Domestic and foreign clinical study results	6	SMART CONTROL Stent (Johnson & Johnson K.K.)	Approval	Instrument & apparatus 7 Stent for iliac artery	A device that is identical to the approved product Smart Stent for Iliac Artery (Approval No.21700BZY00247000). A stent system consisting of a self-expanding nickel-titanium alloy stent used for bail-out treatment (for acute or impending occlusion caused by failure in intervention therapy) and a delivery system to deliver the stent to the site of the lesion, for the treatment of stenosis or occlusion of the vessels in the superficial femoral artery region in addition to the treatment of iliac artery which is the applicable scope of the approved product. A clinical study was conducted to evaluate the efficacy and safety of this product for bail-out treatment. (The original product is in a reexamination period)
3-1	May 1, 2013 Total review time: 418 days Regulatory review time: 116 days	Nov. 7, 2012 Domestic and foreign clinical study results	7	SMART stent (Johnson & Johnson K.K.)	Approval	Instrument & apparatus 7 Stent for blood vessel	A stent system consisting of a self-expanding nickel-titanium alloy stent used for bail-out treatment (for acute or impending occlusion caused by failure in intervention therapy) and a delivery system to deliver the stent to the site of the lesion, for the treatment of stenosis or occlusion of the vessels in the superficial femoral artery region. A clinical study was conducted to evaluate the efficacy and safety of this product for bail-out treatment. (The original product is in a reexamination period)
'3-1	Jun. 26, 2013 Total review time: 425 days Regulatory review time: 329 days	Feb. 17, 2012 Domestic and foreign clinical study results	8	Resolute Integrity SV Coronary Stent System (Medtronic Japan Co., Ltd.)	Approval	Instrument & apparatus 7 Coronary stent	A stent system for percutaneous coronary stent placement consisting of a stent to be inserted and placed at the site of a lesion to maintain the vascular lumen and a delivery catheter used to deliver the stent to the site of the lesion. The stent is coated with zotarolimus with a cytostatic effect to topically inhibit neointimal proliferation that is thought to be a cause of in-stent restenosis. A clinical study was conducted to evaluate the efficacy and safety of this product. (The original product is in a reexamination period)
3-1	Jun. 19, 2013 Total review time: 182 days Regulatory review time: 156 days	- (About these changes) No clinical study results	9	Promus Element Plus Stent System (Boston Scientific Japan K.K.)	Change	Instrument & apparatus 7 Coronary stent	A stent system for percutaneous coronary stent placement consisting of a stent to be inserted and placed at the site of a lesion to maintain the vascular lumen and a delivery catheter used to deliver the stent to the site of the lesion. The stent is coated with everolimus with an immunosuppression to topically inhibit neointimal proliferation that is thought to be a cause of in-stent restenosis. Application for a partial change to alter the product specification of the kinetic drug release of everolimus. (A partial change during the reexamination period)
3-1	Jul. 23, 2013 Total review time: 400 days Regulatory review time: 250 days	- Domestic clinical study results	10	SeQuent Please Drug Eluting Balloon Catheter (Nipro Corporation)	Approval	Instrument & apparatus 51 Balloon-dilating catheter for coronary angioplasty	The first balloon-dilating catheter for coronary angioplasty with a paclitaxel-coated balloon in Japan to inhibit restenosis during revascularization for restenotic lesion in coronary artery stent. A clinical study was conducted to evaluate the efficacy and safety of this product for coronary in-stent restenosis.
3-1	Dec. 25, 2013 Total review time: 187 days Regulatory review time: 144 days	- Domestic clinical study results	11	Misago (Terumo Corporation)	Change	Instrument & apparatus 7 Stent for blood vessel	A stent system consisting of a self-expanding nickel-titanium alloy stent used for bail-out treatment (for acute or impending occlusion caused by failure in percutaneous angioplasty) and a delivery system to deliver the stent to the site of the lesion, for the treatment of symptomatic arterial diseases in the superficial femoral artery region. An application for a partial change to add longer stents (120 mm and 150 mm) than the approved ones. A domestic clinical study was conducted to evaluate the efficacy and safety of additional lengths of stents. (A partial change during the reexamination period)

Review Category	Approval Date	Approval Date in US Clinical Study Results: Domestic/Foreign	No.	Brand Name (Applicant Company)	New Approval /Partial Change	Classification Generic Name	Notes
3-2	Apr. 12, 2013 Total review time: 848 days Regulatory review time: 356 days	Dec. 16, 2002 Foreign clinical study results	12	DC Bead (Eisai Co., Ltd.)	Approval	Instrument & apparatus 51 Prosthetic material for embolization in vessels of the central circulation system	A hydrophilic microsphere (spherical particulate) composed of polyvinyl alcohol polymer with a bridged structure. This product is used in transcatheter arterial embolization for patients with hepatocellular carcinoma. A clinical study was conducted to evaluate the efficacy and safety of the transcatheter arterial chemoembolization using this product for patients with unresectable hepatocellular carcinoma.
3-2	May 1, 2013 Total review time: 254 days Regulatory review time: 203 days	· Reperfusion catheter Type 2b, type 3b: Nov. 23, 2011 · Separator Flex (Nitinol) type 1-4: May 21, 2010 Type 2b: Nov. 23, 2011 No clinical study results	13	Penumbra System (Medico's Hirata Inc.)	Change	Instrument & apparatus 51 Emboli-removal catheter in the central circulatory system	An emboli-removal catheter in the central circulatory system is used to suck and remove a thrombus in patients with acute-phase cerebral infarction in combination with Penumbra Aspiration Pump (Approval No. 22300BZX00268000). Application for a partial change to add a separator of Nitinol type, a type of reperfusion catheter and a size of aspiration tube. (A partial change during the reexamination period)
3-2	Jun. 21, 2013 Total review time: 478 days Regulatory review time: 287 days	· Hypervascular tumor and arteriovenous malformation: Apr. 26, 2000 · Uterine myoma: Nov. 22, 2002 Domestic and foreign clinical study results	14	Embosphere (Nippon Kayaku Co., Ltd.)	Approval	Instrument & apparatus 51 Prosthetic material for embolization in vessels of the central circulation system	Embosphere is a microbead for arterial embolization. It is hydrophilic, non-absorbable, and biocompatible spherical particles, which are impregnated and coated with porcine-derived gelatin to acrylic copolymers. A clinical study was conducted to evaluate the efficacy and safety of this product for patients with hypervascular tumor and arteriovenous malformation.
'3-2	Jun. 21, 2013 Total review time: 357 days Regulatory review time: 189 days	Nov. 7, 2006 Domestic clinical study results	15	Hepasphere (Nippon Kayaku Co., Ltd.)	Approval	Instrument & apparatus 51 Prosthetic material for embolization in vessels of the central circulation system	Hepasphere is a microbead for arterial embolization. It is biocompatible, hydrophilic, non-bioabsorbable, swellable, compressible, and deformable spherical particles composed of vinyl alcohol/sodium acrylate copolymers. A clinical study was conducted to evaluate the efficacy and safety of this product for patients with hypervascular tumor and arteriovenous malformation.
'3-2	Jun. 21, 2013 Total review time: 455 days Regulatory review time: 264 days	— Domestic and foreign clinical study results	16	Sapien XT (Edwards Lifescience Corporation)	Approval	Instrument & apparatus 7 Transcatheter bovine pericardial valve	A prosthetic heart valve (balloon expandable bovine pericardial valve) system is used for transcatheter valve implantation for patients with severe symptomatic aortic stenosis attributed to sclerosis and degeneration of the cusp of native aortic valve, for whom surgery cannot be performed and receiving the treatment with this product is considered the best treatment. A clinical study was conducted to evaluate the efficacy and safety of this product and to ensure the feasibility of the procedure.
3-2	Jul. 2, 2013 Total review time: 48 days Regulatory review time: 27 days	- No clinical study results	17	Neuroform Stent (Stryker Japan K.K.)	Change	Instrument & apparatus 51 Prosthetic material for embolization in vessels of the central circulation system	An intracranial artery stent (for treatment of cerebral aneurysm) used to prevent coil migration in coil embolization for wide-necked cerebral aneurysm. An application for partial changes for addition of a manufacturing site. (A partial change during the reexamination period)
3-2	Jul. 5, 2013 Total review time: 371 days Regulatory review time: 259 days	- Clinical evaluation report	18	Codman Enterprise VRD (Johnson & Johnson K.K.)	Change	Instrument & apparatus 51 Prosthetic material for embolization in vessels of the central circulation system	A prosthetic material for embolization in vessels of the central circulation system to prevent the embolic coils from protrude and/or dropout into the parent artery during coil embolization. An application for partial changes to add the jailing technique that is widely used in clinical practice and to add a no-tip type without a distal marker located at the tip of delivery wire. A clinical evaluation report was submitted to evaluate the efficacy and safety of the jailing technique using this device. (A partial change during the reexamination period)

Review Category	Approval Date	Approval Date in US Clinical Study Results: Domestic/Foreign	No.	Brand Name (Applicant Company)	New Approval /Partial Change	Classification Generic Name	Notes
3-2	Jul. 5, 2013 Total review time: 72 days Regulatory review time: 51 days	- No clinical study results	19	DC Bead (Eisai Co., Ltd.)	Change	Instrument & apparatus 51 Prosthetic material for embolization in vessels of the central circulation system	A hydrophilic microsphere (spherical particulate) composed of polyvinyl alcohol polymer with a bridged structure. This product is used in transcatheter arterial embolization for patients with hepatocellular carcinoma. An application for partial changes for addition of a manufacturing site. (A partial change during the reexamination period)
3-2	Nov. 22, 2013 Total review time: 434 days Regulatory review time: 145 days	Aug. 3, 2005 Domestic clinical study results	20	Wingspan stent (Stryker Japan K.K.)	Approval	Instrument & apparatus 7 Cerebral artery stent	A self-expanding cerebral artery stent used in patients who have a dissection of the vessel or acute or impending occlusion caused by failure in percutaneous angioplasty for intracranial arterial stenosis with balloon angioplasty catheter or who require the re-treatment with no other effective treatment option. A domestic clinical study was conducted in patients with drug-resistant transient ischemic attack or cerebral apoplexy caused by intracranial artery stenosis to evaluate the safety and performance under domestic medical environments. [Priority review]
3-2	Dec. 20, 2013 Total review time: 424 days Regulatory review time: 294 days	Mar. 2, 2012 Foreign clinical study results	21	Solitaire FR Revascularization Device (Covidien Japan, Inc.)	Approval	Instrument & apparatus 51 Emboli-removal catheter in the central circulatory system	A multi-cell retriever intended to restore blood flow by removing thrombus for patients in acute phase of ischemic cerebral infarction who are ineligible for intravenous t-PA or who failed to restore blood flow with intravenous t-PA therapy. A clinical study was conducted to evaluate that safety and efficacy of this device substantially equal to the existing approved devices.
3-2	Mar. 28, 2014 Total review time: 456 days Regulatory review time: 175 days	Type I: Aug. 3, 2012, Type II: Oct. 31, 2012 Foreign clinical study results	22	Trevo Pro Clot Retriever (Stryker Japan K.K.)	Approval	Instrument & apparatus 51 Emboli-removal catheter in the central circulatory system	An emboli-removal catheter in the central circulatory system intended to restore blood flow by removing thrombus for patients with acute-phase cerebral infarction (generally, within 8 hours of symptom onset) who are ineligible for intravenous tissue plasminogen activator (t-PA) or who failed to restore blood flow with intravenous t-PA therapy. A clinical study was conducted to evaluate that safety and efficacy of this device substantially equal the existing approved device, “Merci retriever” (Approval No. 22200BZX00596000).
4	Apr. 12, 2013 Total review time: 308 days Regulatory review time: 212 days	Mar. 27, 2009 Clinical evaluation report	23	Activa RC (Medtronic Japan Co., Ltd.)	Change	Instrument & apparatus 12 Electrical brain stimulation device for tremor	Activa RC is an implantable electrical stimulation device used to reduce tremor associated with Parkinson's disease, essential tremor, etc. that are adequately controlled with medication. The device stimulates the deep brain (thalamus, subthalamic nucleus or internal globus pallidus), unilaterally or bilaterally. A partial change was applied for additional indications to treat for movement disorder caused by Parkinson's disease and dystonia that are not adequately controlled with medication. A clinical evaluation report summarizing results of foreign clinical studies and literatures, etc. was submitted for evaluating the efficacy and safety of this product for Parkinson's disease and dystonia.
4	Jun. 7, 2013 Total review time: 557 days Regulatory review time: 161 days	– Clinical evaluation report	24	Tendril MRI (St. Jude Medical Japan Co., Ltd.)	Approval	Instrument & apparatus 7 Implantable defibrillator/pacemaker lead	An implantable defibrillator/pacemaker lead used for long-term the heart rhythm regulation by cardiac stimulation in combination with an implantable cardiac pacemaker, etc. The patients implanted with the device can undergo an MRI scan under specific conditions. A clinical evaluation report summarizing the results of the foreign clinical studies of this product was submitted to evaluate the safety of this device in MRI scans. (The original product is in a reexamination period)

Review Category	Approval Date	Approval Date in US Clinical Study Results: Domestic/Foreign	No.	Brand Name (Applicant Company)	New Approval /Partial Change	Classification Generic Name	Notes
4	Jun. 7, 2013 Total review time: 557 days Regulatory review time: 161 days	– Clinical evaluation report	25	Accent MRI (St. Jude Medical Japan Co., Ltd.)	Approval	Instrument & apparatus 7 Implantable cardiac pacemaker	An implantable cardiac pacemaker to regulate the heart rhythm by cardiac stimulation for a long term. The patients implanted with the device can undergo an MRI scan under specific conditions. A clinical evaluation report summarizing the results of the foreign clinical studies of this product was submitted to evaluate the safety of this device in MRI scans. (The original product is in a reexamination period)
4	Jun. 7, 2013 Total review time: 557 days Regulatory review time: 161 days	– Clinical evaluation report	26	Accent MRI RF (St. Jude Medical Japan Co., Ltd.)	Approval	Instrument & apparatus 7 Implantable cardiac pacemaker	An implantable cardiac pacemaker to regulate the heart rhythm by cardiac stimulation for a long term. The patients implanted with the device can undergo an MRI scan under specific conditions. A clinical evaluation report summarizing the results of the foreign clinical studies of this product was submitted to evaluate the safety of this device in MRI scans. (The original product is in a reexamination period)
4	Jun. 7, 2013 Total review time: 74 days Regulatory review time: 73 days	– No clinical study results	27	Nuance MRI (St. Jude Medical Japan Co., Ltd.)	Approval	Instrument & apparatus 7 Implantable cardiac pacemaker	Application for addition of brand name to "Accent MRI" (Approval No. 22500BZX00241000). (The original product is in a reexamination period)
4	Jun. 7, 2013 Total review time: 74 days Regulatory review time: 73 days	– No clinical study results	28	Nuance MRI RF (St. Jude Medical Japan Co., Ltd.)	Approval	Instrument & apparatus 7 Implantable cardiac pacemaker	Application for addition of brand name to "Accent MRI RF" (Approval No. 22500BZX00242000). (The original product is in a reexamination period)
4	Jun. 7, 2013 Total review time: 74 days Regulatory review time: 73 days	– No clinical study results	29	Tendril MRI J (St. Jude Medical Japan Co., Ltd.)	Approval	Instrument & apparatus 7 Implantable defibrillator/pacemaker lead	Application for addition of brand name to "Tendril MRI" (Approval No. 22500BZX00240000). (The original product is in a reexamination period)
4	Jun. 24, 2013 Total review time: 222 days Regulatory review time: 211 days	– Clinical evaluation report	30	Solia JT (Biotronik Japan, Inc.)	Approval	Instrument & apparatus 7 Endocardial implantable pacemaker lead	An endocardial implantable pacemaker lead connected with an implantable cardiac pacemaker. The patients implanted with the device can conditionally undergo an MRI scan. This device was newly applied as a pacemaker lead which is compatible with MRI. A clinical evaluation report was submitted to evaluate the safety of this device in MRI scans. (The original product is in a reexamination period)
4	Jun. 28, 2013 Total review time: 59 days Regulatory review time: 47 days	– No clinical study results	31	DuralHeart Left Ventricular Assist System (Terumo Corporation)	Change	Instrument & apparatus 7 Implantable ventricular assist device	An implantable ventricular assist device system to be used to improve the blood circulation until heart transplant is performed in patients who have severe cardiac failure for which cardiac transplantation is indicated, show continuous decompensation in spite of drug therapy or circulation assist techniques, such as an external ventricular assist system, and for whom it is considered difficult to survive without heart transplant. It was revealed after the approval that the electrostatic discharge resistance is not sufficient when using a protect cover (supportive tool that ensures the connection of the power supply to the controller and prevents unintended disconnection); it may cause the occurrence of anomalies. Application for a partial change that the diameter of the speaker hole of the protect cover is expanded and non-conductive coating is included on the surface of the protect cover in order to improve resistance to electrostatic discharge and secure electromagnetic compatibility of the system. (A partial change during the reexamination period) [Orphan device]

Review Category	Approval Date	Approval Date in US Clinical Study Results: Domestic/Foreign	No.	Brand Name (Applicant Company)	New Approval /Partial Change	Classification Generic Name	Notes
4	Jul. 2, 2013 Total review time: 449 days Regulatory review time: 276 days	- Clinical evaluation report	32	Lumax 740 ICD Pro (Biotronik Japan, Inc.)	Approval	Instrument & apparatus 12 Automatic implantable defibrillator	An automatic implantable defibrillator intended for the treatment of ventricular tachycardia or ventricular fibrillation. The patients implanted with the device can conditionally undergo an MRI scan. A clinical evaluation report was submitted to evaluate the safety of this device in MRI scans. (The original product is in a reexamination period)
4	Jul. 2, 2013 Total review time: 449 days Regulatory review time: 276 days	- Clinical evaluation report	33	Linox Smart Pro S (Biotronik Japan, Inc.)	Approval	Instrument & apparatus 7 Implantable defibrillator/ pacemaker lead	An implantable defibrillator/pacemaker lead. The patients implanted with the device can conditionally undergo an MRI scan. A clinical evaluation report was submitted to evaluate the safety of this device in MRI scans. (The original product is in a reexamination period)
4	Jul. 2, 2013 Total review time: 449 days Regulatory review time: 276 days	- Clinical evaluation report	34	Linox Smart Pro SD (Biotronik Japan, Inc.)	Approval	Instrument & apparatus 7 Implantable defibrillator/ pacemaker lead	An implantable defibrillator/pacemaker lead. The patients implanted with the device can conditionally undergo an MRI scan. A clinical evaluation report was submitted to evaluate the safety of this device in MRI scans. (The original product is in a reexamination period)
4	Jul. 2, 2013 Total review time: 449 days Regulatory review time: 276 days	- Clinical evaluation report	35	Linox Smart Pro S DX (Biotronik Japan, Inc.)	Approval	Instrument & apparatus 7 Implantable defibrillator/ pacemaker lead	An implantable defibrillator/pacemaker lead. The patients implanted with the device can conditionally undergo an MRI scan. A clinical evaluation report was submitted to evaluate the safety of this device in MRI scans. (The original product is in a reexamination period)
4	Jul. 2, 2013 Total review time: 364 days Regulatory review time: 239 days	- Clinical evaluation report	36	Lumax 740 CRT-D Pro (Biotronik Japan, Inc.)	Approval	Instrument & apparatus 7 Implantable biventricular pacing pulse generator with defibrillator function	An implantable biventricular pacing pulse generator with a defibrillator function intended for the treatment of ventricular tachycardia. The patients implanted with the device can conditionally undergo an MRI scan. A clinical evaluation report was submitted to evaluate the safety of this device in MRI scans. (The original product is in a reexamination period)
4	Jul. 2, 2013 Total review time: 364 days Regulatory review time: 239 days	- Clinical evaluation report	37	Corox Pro OTW BP (Biotronik Japan, Inc.)	Approval	Instrument & apparatus 7 Implantable defibrillator/ pacemaker lead	An implantable defibrillator/pacemaker lead. The patients implanted with the device can conditionally undergo an MRI scan. A clinical evaluation report was submitted to evaluate the safety of this device in MRI scans. (The original product is in a reexamination period)
4	Jul. 2, 2013 Total review time: 197 days Regulatory review time: 177 days	- Clinical evaluation report	38	Ilest 7 ICD Pro (Biotronik Japan, Inc.)	Approval	Instrument & apparatus 12 Automatic implantable defibrillator	An automatic implantable defibrillator intended for the treatment of ventricular tachycardia or ventricular fibrillation. This product was developed based on the approved product “Lumax 740 ICD” (Approval No.22400BZX00162000). The major improvements from the approved product include downsizing of the product, a newly added automatic threshold monitoring function in the right atrium, and MRI compatibility under specific conditions. A clinical evaluation report was submitted to evaluate the safety of this device in MRI scans. (The original product is in a reexamination period)

Review Category	Approval Date	Approval Date in US Clinical Study Results: Domestic/Foreign	No.	Brand Name (Applicant Company)	New Approval /Partial Change	Classification Generic Name	Notes
4	Jul. 2, 2013 Total review time: 189 days Regulatory review time: 171 days	- Clinical evaluation report	39	Ilest 7 CRT-D Pro (Biotronik Japan, Inc.)	Approval	Instrument & apparatus 7 Implantable biventricular pacing pulse generator with defibrillator function	An Implantable biventricular pacing pulse generator with a defibrillator function intended for the treatment of ventricular tachycardia. This product was developed based on the approved product “Lumax 740 CRT-D” (Approval No.22400BZX00161000). The major improvements from the approved product include downsizing of the product, a newly added automatic threshold monitoring function in the right atrium, and MRI compatibility under specific conditions. A clinical evaluation report was submitted to evaluate the safety of this device in MRI scans. (The original product is in a reexamination period)
4	Jul. 2, 2013 Total review time: 189 days Regulatory review time: 171 days	- Clinical evaluation report	40	Ilest 7 ICD DF4 Pro (Biotronik Japan, Inc.)	Approval	Instrument & apparatus 12 Automatic implantable defibrillator	An automatic implantable defibrillator intended for the treatment of ventricular tachycardia or ventricular fibrillation. This product was developed based on the approved product “Lumax 740 ICD” (Approval No.22400BZX00162000). The major improvements from the approved product include downsizing of the product, a newly added automatic threshold monitoring function in the right atrium, MRI compatibility under specific conditions, and an equipped DF4 connector port. A clinical evaluation report was submitted to evaluate the safety of this device in MRI scans. (The original product is in a reexamination period)
4	Jul. 2, 2013 Total review time: 189 days Regulatory review time: 171 days	- Clinical evaluation report	41	Linox Smart Pro DF4 SD (Biotronik Japan, Inc.)	Approval	Instrument & apparatus 7 Implantable defibrillator/ pacemaker lead	An implantable defibrillator/pacemaker lead. This product was developed based on the company's approved product “Linox Smart SD” (Approval No.22200BZX00751000). The major modifications from the approved product include a change to the DF4 connector port and the MRI compatibility under specific conditions. A clinical evaluation report was submitted to evaluate the safety of this device in MRI scans. (The original product is in a reexamination period)
4	Jul. 2, 2013 Total review time: 81 days Regulatory review time: 79 days	- No clinical study results	42	Protego Pro SD (Biotronik Japan, Inc.)	Approval	Instrument & apparatus 7 Implantable defibrillator/ pacemaker lead	An implantable defibrillator/pacemaker lead. The patients implanted with the device can conditionally undergo an MRI scan. An application for additional brand name for “Linox Smart Pro DF4 SD”. (The original product is in a reexamination period)
4	Jul. 18, 2013 Total review time: 211 days Regulatory review time: 137 days	- No clinical study results	43	DuraHeart Left Ventricular Assist System (Terumo Corporation)	Change	Instrument & apparatus 7 Implantable ventricular assist device	An implantable ventricular assist device system to be used to improve the blood circulation until heart transplant is performed in patients who have severe cardiac failure for which cardiac transplantation is indicated, show continuous decompensation in spite of drug therapy or circulation assist techniques, such as an external ventricular assist system, and for whom it is considered difficult to survive without heart transplant. After the approval, multiple events due to failure to maintain normal rotation mode of the pump (magnetic suspension) were reported in Japan and overseas. A detailed investigation confirmed that some wires in the percutaneous cable were disconnected, which occurred in the connector area close to a pump. This application for partial change to extend a strain relief of the cable as a measure against the failure due to the fracture of the percutaneous cable. (A partial change during the reexamination period) [Orphan device]
4	Jul. 23, 2013 Total review time: 287 days Regulatory review time: 177 days	Aug. 17, 2009 Foreign clinical study results	44	LifeVest Wearable Defibrillator (ZOLL Lifecor Corporation)	Approval	Instrument & apparatus 12 Wearable defibrillator	The first wearable defibrillator in Japan to monitor and analyze electrocardiograms of the patients wearing this device continuously, and to deliver electric shock for defibrillation automatically if ventricular tachycardia or ventricular fibrillation requiring defibrillation is detected. A clinical study was conducted to evaluate the success rate of defibrillation for arrhythmia which requires defibrillation and the risk of inappropriate electric shock delivery due to false detection of arrhythmia. [Priority review]

Review Category	Approval Date	Approval Date in US Clinical Study Results: Domestic/Foreign	No.	Brand Name (Applicant Company)	New Approval /Partial Change	Classification Generic Name	Notes
4	Aug. 7, 2013 Total review time: 156 days Regulatory review time: 147 days	- No clinical study results	45	Implantable Ventricular Assist System EVAHEART (Sun Medical Technology Research Corp.)	Change	Instrument & apparatus 7 Implantable ventricular assist device	An implantable ventricular assist device used to improve circulation until heart transplantation in patients with severe heart failure for whom heart transplantation is indicated. An application for partial changes to alter the cannula (alterations in its surface processing and shape) in hope of inhibition of wedge thrombus formation to reduce the risk of cerebral infarction, which has been frequently reported in ongoing cases in the clinical trials and post-marketing surveillance. (A partial change during the reexamination period) [Orphan device]
4	Aug. 7, 2013 Total review time: 131 days Regulatory review time: 113 days	Jan. 26, 2011 Clinical evaluation report	46	Activa SC (Medtronic Japan Co., Ltd.)	Change	Instrument & apparatus 12 Electrical brain stimulation device for tremor	Activa SC is an implantable electrical stimulation device used for deep brain stimulation to improve various symptoms associated with movement disorders by delivering electrical stimulus to the deep brain (thalamus, subthalamic nucleus, or internal globus pallidus). This device has already been approved for use in reduction of tremors associated with Parkinson's disease, essential tremor, etc. that are not controlled with medication. A partial change has been approved for additional indications to treat movement disorder caused by Parkinson's disease and dystonia that are not adequately controlled with medication. A clinical evaluation report summarizing results of foreign clinical studies and published literatures, etc. was submitted for evaluating the efficacy and safety of this product for Parkinson's disease and dystonia. (The original product is in a reexamination period)
4	Aug. 27, 2013 Total review time: 419 days Regulatory review time: 192 days	- Clinical evaluation report	47	Evia HF-T Pro (Biotronik Japan, Inc.)	Approval	Instrument & apparatus 7 Implantable biventricular pacing pulse generator without defibrillator function	An implantable biventricular pacing pulse generator without a defibrillator function intended for the treatment of bradycardia. The patients implanted with the device can conditionally undergo an MRI scan. A clinical evaluation report was submitted to evaluate the safety of this device in MRI scans. (The original product is in a reexamination period)
4	Sep. 6, 2013 Total review time: 205 days Regulatory review time: 51 days	Oct. 12, 2010 No clinical study results	48	Thermogard System (ZOLL Circulation, Inc.)	Change	Instrument & apparatus 12 Central venous placement temperature management system	A temperature management device to regulate the body temperature by heat exchange with the blood within a blood vessel through a central venous catheter balloon in which a perfusion fluid (physiological saline) circulates in patients who need fever control. An application for partial change to change raw materials of a coating agent for a central venous catheter having a perfusion balloon. (A partial change during the reexamination period)
4	Sep. 6, 2013 Total review time: 162 days Regulatory review time: 151 days	- No clinical study results	49	Evia T Series Pro (Biotronik Japan, Inc.)	Change	Instrument & apparatus 7 Implantable cardiac pacemaker	An implantable cardiac pacemaker connected with electrodes placed within the heart. The patients implanted with the device can conditionally undergo an MRI scan. An application for a partial change to change conditions for MRI compatibility. (A partial change during the reexamination period)
4	Sep. 6, 2013 Total review time: 162 days Regulatory review time: 151 days	- No clinical study results	50	Evia Series Pro (Biotronik Japan, Inc.)	Change	Instrument & apparatus 7 Implantable cardiac pacemaker	An implantable cardiac pacemaker connected with electrodes placed within the heart. The patients implanted with the device can conditionally undergo an MRI scan. An application for a partial change to change conditions for MRI compatibility. (A partial change during the reexamination period)

Review Category	Approval Date	Approval Date in US Clinical Study Results: Domestic/Foreign	No.	Brand Name (Applicant Company)	New Approval /Partial Change	Classification Generic Name	Notes
4	Sep. 6, 2013 Total review time: 162 days Regulatory review time: 151 days	- No clinical study results	51	Solia T (Biotronik Japan, Inc.)	Change	Instrument & apparatus 7 Endocardial implantable pacemaker leads	An endocardial implantable pacemaker lead connected with an implantable cardiac pacemaker. The patients implanted with the device can conditionally undergo an MRI scan. An application for a partial change to change conditions for MRI compatibility. (A partial change during the reexamination period)
4	Sep. 6, 2013 Total review time: 162 days Regulatory review time: 151 days	- No clinical study results	52	Solia S (Biotronik Japan, Inc.)	Change	Instrument & apparatus 7 Endocardial implantable pacemaker leads	An endocardial implantable pacemaker lead connected with an implantable cardiac pacemaker. The patients implanted with the device can conditionally undergo an MRI scan. An application for a partial change to change conditions for MRI compatibility. (A partial change during the reexamination period)
4	Sep. 17, 2013 Total review time: 116 days Regulatory review time: 59 days	Aug. 24, 2012 No clinical study results	53	Activa RC (Medtronic Japan Co., Ltd.)	Change	Instrument & apparatus 12 Electrical brain stimulation device for tremor	Activa RC is a rechargeable and implantable electrical stimulation device used for deep brain stimulation to improve various symptoms associated with movement disorders by delivering electrical stimulus to the deep brain (thalamus, subthalamic nucleus, or internal globus pallidus). A partial change has been approved for addition of type of a stimulator with no coating applied on its shield case. (A partial change during the reexamination period)
4	Sep. 18, 2013 Total review time: 71 days Regulatory review time: 61 days	- No clinical study results	54	Corox Pro OTW BP (Biotronik Japan, Inc.)	Change	Instrument & apparatus 7 Implantable defibrillator/ pacemaker lead	An implantable defibrillator/pacemaker lead. The patients implanted with the device can conditionally undergo an MRI scan. An application for a partial change to change conditions for MRI compatibility. (A partial change during the reexamination period)
4	Sep. 18, 2013 Total review time: 71 days Regulatory review time: 61 days	- No clinical study results	55	Linox Smart Pro S (Biotronik Japan, Inc.)	Change	Instrument & apparatus 7 Implantable defibrillator/ pacemaker lead	An implantable defibrillator/pacemaker lead. The patients implanted with the device can conditionally undergo an MRI scan. An application for a partial change to change conditions for MRI compatibility. (A partial change during the reexamination period)
4	Sep. 18, 2013 Total review time: 71 days Regulatory review time: 61 days	- No clinical study results	56	Linox Smart Pro SD (Biotronik Japan, Inc.)	Change	Instrument & apparatus 7 Implantable defibrillator/ pacemaker lead	An implantable defibrillator/pacemaker lead. The patients implanted with the device can conditionally undergo an MRI scan. An application for a partial change to change conditions for MRI compatibility. (A partial change during the reexamination period)
4	Sep. 18, 2013 Total review time: 71 days Regulatory review time: 61 days	- No clinical study results	57	Linox Smart Pro S DX (Biotronik Japan, Inc.)	Change	Instrument & apparatus 7 Implantable defibrillator/ pacemaker lead	An implantable defibrillator/pacemaker lead. The patients implanted with the device can conditionally undergo an MRI scan. An application for a partial change to change conditions for MRI compatibility. (A partial change during the reexamination period)

Review Category	Approval Date	Approval Date in US Clinical Study Results: Domestic/Foreign	No.	Brand Name (Applicant Company)	New Approval /Partial Change	Classification Generic Name	Notes
4	Sep. 18, 2013 Total review time: 70 days Regulatory review time: 66 days	- No clinical study results	58	Ilest 7 CRT-D Pro (Biotronik Japan, Inc.)	Change	Instrument & apparatus 7 Implantable biventricular pacing pulse generator with defibrillator function	An implantable biventricular pacing pulse generator with a defibrillator function (CRT-D) intended for the treatment of ventricular tachycardia. The patients implanted with the device can conditionally undergo an MRI scan. An application for a partial change to change conditions for MRI compatibility. (A partial change during the reexamination period)
4	Sep. 18, 2013 Total review time: 70 days Regulatory review time: 60 days	- No clinical study results	59	Linox Smart Pro DF4 SD (Biotronik Japan, Inc.)	Change	Instrument & apparatus 7 Implantable defibrillator/ pacemaker lead	An implantable defibrillator/pacemaker lead. The patients implanted with the device can conditionally undergo an MRI scan. An application for a partial change to change conditions for MRI compatibility. (A partial change during the reexamination period)
4	Sep. 18, 2013 Total review time: 70 days Regulatory review time: 60 days	- No clinical study results	60	Protego Pro SD (Biotronik Japan, Inc.)	Change	Instrument & apparatus 7 Implantable defibrillator/ pacemaker lead	An implantable defibrillator/pacemaker lead. The patients implanted with the device can conditionally undergo an MRI scan. An application for a partial change to change conditions for MRI compatibility. (A partial change during the reexamination period)
4	Sep. 18, 2013 Total review time: 70 days Regulatory review time: 66 days	- No clinical study results	61	Ilest 7 ICD DF4 Pro (Biotronik Japan, Inc.)	Change	Instrument & apparatus 12 Automatic implantable defibrillator	An automatic implantable defibrillator (ICD) intended for the treatment of ventricular tachycardia or ventricular fibrillation. The patients implanted with the device can conditionally undergo an MRI scan. An application for a partial change to change conditions for MRI compatibility. (A partial change during the reexamination period)
4	Sep. 18, 2013 Total review time: 70 days Regulatory review time: 66 days	- No clinical study results	62	Ilest 7 ICD Pro (Biotronik Japan, Inc.)	Change	Instrument & apparatus 12 Automatic implantable defibrillator	An automatic implantable defibrillator (ICD) intended for the treatment of ventricular tachycardia or ventricular fibrillation. The patients implanted with the device can conditionally undergo an MRI scan. An application for a partial change to change conditions for MRI compatibility. (A partial change during the reexamination period)
4	Sep. 18, 2013 Total review time: 20 days Regulatory review time: 20 days	Aug. 24, 2012 No clinical study results	63	Activa SC (Medtronic Japan Co., Ltd.)	Change	Instrument & apparatus 12 Electrical brain stimulation device for tremor	Activa SC is an implantable electrical stimulation device used for deep brain stimulation to improve various symptoms associated with movement disorders by delivering electrical stimulus to the deep brain (thalamus, subthalamic nucleus, or internal globus pallidus). A partial change has been approved for addition of type of a stimulator with no coating applied on its shield case. (A partial change during the reexamination period)
4	Sep. 20, 2013 Total review time: 266 days Regulatory review time: 95 days	- Domestic clinical study results	64	PD Laser BT (Panasonic Healthcare Co., Ltd.)	Approval	Instrument & apparatus 31 PDT semiconductor laser	A laser irradiation device used for photodynamic therapy. This product is used with “Laserphyrin 100mg for Injection” (Approved No. 21500AMZ0050900) as a photosensitizer for which target illness is resection of primary malignant brain tumor. A clinical trial was conducted to confirm the efficacy and safety of photodynamic therapy for primary malignant brain tumor using this device and the concomitant drug. [Orphan medical device]
4	Sep. 30, 2013 Total review time: 536 days Regulatory review time: 389 days	- Foreign clinical study results	65	Libra Single 8 Neurostimulator (St. Jude Medical Japan Co., Ltd.)	Approval	Instrument & apparatus 12 Electrical brain stimulation device for tremor	A deep brain stimulation device is indicated for patients with essential tremor, various symptoms of Parkinson's disease or dystonia that have not responded sufficiently to drug therapy. This product is used for alleviation of essential tremor, movement disorders associated with Parkinson’s disease, and dystonia symptoms. A clinical study was conducted to evaluate the efficacy and safety of this product for Parkinson’s disease and dystonia. (The original product is in a reexamination period)

Review Category	Approval Date	Approval Date in US Clinical Study Results: Domestic/Foreign	No.	Brand Name (Applicant Company)	New Approval /Partial Change	Classification Generic Name	Notes
4	Sep. 30, 2013 Total review time: 536 days Regulatory review time: 385 days	- Foreign clinical study results	66	Brio Dual 8 Neurostimulator (St. Jude Medical Japan Co., Ltd.)	Approval	Instrument & apparatus 12 Electrical brain stimulation device for tremor	A deep brain stimulation device is indicated for patients with essential tremor, various symptoms of Parkinson's disease or dystonia that have not responded sufficiently to drug therapy. This product is used for alleviation of essential tremor, movement disorders associated with Parkinson's disease, and dystonia symptoms. A main body of implantable stimulator is rechargeable. A clinical study was conducted to evaluate the efficacy and safety of this product for Parkinson's disease and dystonia. (The original product is in a reexamination period)
4	Oct. 30, 2013 Total review time: 48 days Regulatory review time: 42 days	- No clinical study results	67	Evia HF-T Pro (Biotronik Japan, Inc.)	Change	Instrument & apparatus 7 Implantable biventricular pacing pulse generator without defibrillator function	An implantable biventricular pacing pulse generator without a defibrillator function used to improve symptoms of cardiac failure. The patients implanted with the device can conditionally undergo an MRI scan. An application for a partial change to change conditions for MRI compatibility. (A partial change during the reexamination period)
4	Oct. 30, 2013 Total review time: 124 days Regulatory review time: 112 days	- No clinical study results	68	Solia JT (Biotronik Japan, Inc.)	Change	Instrument & apparatus 7 Endocardial implantable pacemaker leads	An endocardial implantable pacemaker lead connected with an implantable cardiac pacemaker. The patients implanted with the device can conditionally undergo an MRI scan. An application for a partial change to change conditions for MRI compatibility. (A partial change during the reexamination period)
4	Nov. 22, 2013 Total review time: 1390 days Regulatory review time: 301 days	- Domestic and foreign clinical study results	69	Jarvik 2000 Implantable Ventricular Assist Device (Century Medical, Inc.)	Approval	Instrument & apparatus 7 Implantable ventricular assist device	An axial-flow implantable ventricular assist device system to be used to improve the blood circulation until heart transplant is performed in patients who have severe cardiac failure for which heart transplant is indicated, show continuous decompensation in spite of drug therapy or circulation assist techniques, such as an external ventricular assist system, and for whom it is considered difficult to survive without heart transplant. A clinical study was conducted in the U.S. to evaluate the efficacy and safety of this product, and a domestic clinical study was conducted to evaluate the efficacy and safety in Japan where healthcare environments are different from those in the U.S. [Orphan device]
4	Nov. 29, 2013 Total review time: 410 days Regulatory review time: 74 days	- Clinical evaluation report	70	Ingeino MRI (Boston Scientific Japan K.K.)	Approval	Instrument & apparatus 7 Implantable cardiac pacemaker	An implantable cardiac pacemaker connected with electrodes placed within the heart. The patients implanted with the device can conditionally undergo MRI scans. A clinical evaluation report was submitted to evaluate the safety of this device in MRI scans. (The original product is in a reexamination period)
4	Nov. 29, 2013 Total review time: 99 days Regulatory review time: 60 days	- (About these changes) Clinical evaluation report	71	Fineline Ⅱ PU (Boston Scientific Japan K.K.)	Change	Instrument & apparatus 7 Endocardial implantable pacemaker leads	An endocardial implantable pacemaker lead to regulate the heart rhythm by long-term cardiac stimulation, which is used in conjunction with an implantable cardiac pacemaker. An application for a partial change to enable patients with the device to conditionally undergo MRI scans. A clinical evaluation report was submitted to evaluate the safety of this device in MRI scans. (A partial change during the reexamination period)
4	Nov. 29, 2013 Total review time: 99 days Regulatory review time: 60 days	- (About these changes) Clinical evaluation report	72	Fineline Ⅱ EZ PU (Boston Scientific Japan K.K.)	Change	Instrument & apparatus 7 Endocardial implantable pacemaker leads	An endocardial implantable pacemaker lead to regulate the heart rhythm by long-term cardiac stimulation, which is used in conjunction with an implantable cardiac pacemaker. An application for a partial change to enable patients with the device to conditionally undergo MRI scans. A clinical evaluation report was submitted to evaluate the safety of this device in MRI scans. (A partial change during the reexamination period)

Review Category	Approval Date	Approval Date in US Clinical Study Results: Domestic/Foreign	No.	Brand Name (Applicant Company)	New Approval /Partial Change	Classification Generic Name	Notes
4	Nov. 29, 2013 Total review time: 99 days Regulatory review time: 60 days	- (About these changes) Clinical evaluation report	73	Fineline Ⅱ Sterox (Boston Scientific Japan K.K.)	Change	Instrument & apparatus 7 Endocardial implantable pacemaker leads	An endocardial implantable pacemaker lead to regulate the heart rhythm by long-term cardiac stimulation, which is used in conjunction with an implantable cardiac pacemaker. An application for a partial change to enable patients with the device to conditionally undergo MRI scans. A clinical evaluation report was submitted to evaluate the safety of this device in MRI scans. (A partial change during the reexamination period)
4	Nov. 29, 2013 Total review time: 99 days Regulatory review time: 60 days	- (About these changes) Clinical evaluation report	74	Fineline Ⅱ Sterox EZ (Boston Scientific Japan K.K.)	Change	Instrument & apparatus 7 Endocardial implantable pacemaker leads	An endocardial implantable pacemaker lead to regulate the heart rhythm by long-term cardiac stimulation, which is used in conjunction with an implantable cardiac pacemaker. An application for a partial change to enable patients with the device to conditionally undergo MRI scans. A clinical evaluation report was submitted to evaluate the safety of this device in MRI scans. (A partial change during the reexamination period)
4	Feb. 19, 2014 Total review time: 300 days Regulatory review time: 185 days	Dec. 17, 2010 Foreign clinical study results	75	Freezor MAX Cryoablation Catheter (Medtronic Japan Co., Ltd.)	Approval	Instrument & apparatus 51 Cardiovascular ablation catheter	A long, flexible, steerable catheter is used as an adjunctive device in the endocardial treatment of paroxysmal atrial fibrillation. This product is to be used in conjunction with “Arctic Front Advance Cardiac Cryoablation Catheter” (simultaneously submitted). It is used for gap cryoablation to complete electrical isolation of the pulmonary veins, cryoablation of focal trigger sites, or creation of an ablation line between the inferior vena cava and the tricuspid valve. A clinical study was conducted to evaluate the efficacy and safety of this product when it is applied for patients with drug-resistant recurrent symptomatic paroxysmal atrial fibrillation. [Priority review]
4	Feb. 19, 2014 Total review time: 300 days Regulatory review time: 166 days	Dec. 10, 2010 Foreign clinical study results	76	Medtronic CryoConsole (Medtronic Japan Co., Ltd.)	Approval	Instrument & apparatus 31 Versatile cryosurgical unit	A cryosurgical unit to be used for the treatment of arrhythmia. The device is for the exclusive use of Medtronic cryoablation catheters. A clinical study was conducted to evaluate the efficacy and safety of this product when it is applied for patients with drug-resistant recurrent symptomatic paroxysmal atrial fibrillation. [Priority review]
4	Feb. 19, 2014 Total review time: 300 days Regulatory review time: 204 days	Apr. 12, 2012 Foreign clinical study results	77	Arctic Front Advance Cryoablation Catheter (Medtronic Japan Co., Ltd.)	Approval	Instrument & apparatus 51 Cardiovascular ablation catheter	A balloon catheter used for cardiac cryoablation to treat drug-resistant recurrent symptomatic paroxysmal atrial fibrillation. A clinical study was conducted to evaluate the efficacy and safety of this product when it is applied for patients with drug-resistant recurrent symptomatic paroxysmal atrial fibrillation. [Priority review]
4	Feb. 28, 2014 Total review time: 851 days Regulatory review time: 685 days	- Domestic clinical study results	78	Coopdech i-Cool (Daiken Medical Co., Ltd.)	Approval	Instrument & apparatus 12 Temperature management system	A system used to lower the brain temperature by bringing a cuff in which temperature-controlled physiological saline circulates into contact with parts of pharyngeal and esophagus of the patients who require therapeutic hypothermia following cardiac arrest. A domestic clinical study was conducted to confirm that brain temperature becomes lower early in therapeutic hypothermia by cooling pharyngeal with this device, that it does not worsen outcomes in the patients significantly, and that the risks are acceptable.
4	Feb. 28, 2014 Total review time: 77 days Regulatory review time: 15 days	Jan. 17, 2014 (Approval of application corresponding to the present partial change) No clinical study results	79	Thermogard System (ZOLL Circulation, Inc.)	Change	Instrument & apparatus 12 Central venous placement temperature management system	A temperature management device to regulate the body temperature by heat exchange with the blood within a blood vessel through a central venous catheterballoon in which a perfusion fluid (physiological saline) circulates in patients who need fever control. An application for a partial change to change the manufacturing site. (A partial change during the reexamination period)

Review Category	Approval Date	Approval Date in US Clinical Study Results: Domestic/Foreign	No.	Brand Name (Applicant Company)	New Approval /Partial Change	Classification Generic Name	Notes
4	Mar. 26, 2014 Total review time: 272 days Regulatory review time: 183 days	Feb. 1, 2001 Clinical evaluation report	80	Nykanen RF Wire (Japan Lifeline Co., Ltd.)	Approval	Instrument & apparatus 51 Cardiovascular ablation catheter	A wire used for puncture of atrial septum or membranous atresia of pulmonary artery in patients with severe congenital heart diseases by delivering radiofrequency energy. A clinical evaluation report based on published literatures in foreign countries was submitted without conducting a domestic or foreign clinical study. [Priority review]
4	Mar. 26, 2014 Total review time: 91 days Regulatory review time: 71 days	Jan. 15, 2013 No clinical study results	81	Medtronic Advisa MRI (Medtronic Japan Co., Ltd.)	Change	Instrument & apparatus 7 Implantable cardiac pacemaker	An implantable cardiac pacemaker connected with electrodes placed within the heart. The patients implanted with the device can conditionally undergo an MRI scan. An application for a partial change to change the conditions of usable MRI devices. (A partial change during the reexamination period)
4	Mar. 26, 2014 Total review time: 90 days Regulatory review time: 68 days	- Clinical evaluation report	82	Protego Pro S (Biotronik Japan, Inc.)	Approval	Instrument & apparatus 7 Implantable defibrillator/ pacemaker lead	An implantable electrode lead with a screw-shaped tip having a quadrupolar connector (DF4-Standard). It is used for the treatment of ventricular tachycardia, with being connected to ICD or CRT-D. This lead, having one defibrillation electrode, was developed based on the main body of “Protego Pro SD (Approval No. 22500BZX00295A01).” The patients with the device can conditionally undergo an MRI scan. A clinical evaluation report was submitted to evaluate the safety of this device in MRI scans. (The original product is in a reexamination period)
5	Apr. 12, 2013 Total review time: 197 days Regulatory review time: 97 days	−(No application for this indication) Clinical evaluation report	83	Histoacryl (B. Braun Aesculap Japan Co., Ltd.)	Approval	Instrument & apparatus 51 Prosthetic material for embolization in vessels	An n-butyl-2-cyanoacrylate is injected for endoscopic vascular embolization for gastric varices. This product has been already used in and out of Japan as material for endoscopic vascular embolization. Based on the current situation, a clinical evaluation report was submitted to evaluate the efficacy and safety of this product. [Priority review]
5	Jun. 21, 2013 Total review time: 396 days Regulatory review time: 192 days	− Domestic clinical study results	84	Magnetic Stimulator TMU-1100 (Nihon Kohden Corporation)	Approval	Instrument & apparatus 12 Magnetic stimulation device for treatment of urinary incontinence	A magnetic stimulation device to improve symptoms of overactive bladder with urinary incontinence. This product is used for adult female patients with overactive bladder who are not responsive to or cannot use therapeutic agents for urinary incontinence. Pulse current flowing in a stimulation coil under the sealing surface of a chair-shaped stimulation unit generates magnetic energy through the upper portion of the sealing surface. The variable magnetic fields induce eddy currents in the body of the patient who is seated on the stimulation unit. The eddy currents primarily stimulate the nerves in the pelvic floor area of the patient. A clinical study was conducted to evaluate the efficacy and safety of this product in female patients with overactive bladder with urinary incontinence.
5	Jul. 5, 2013 Total review time: 43 days Regulatory review time: 12 days	- No clinical study results	85	CryoSeal CS-1 (Asahi Kasei Medical Co.,Ltd.)	Change	Instrument & apparatus 7 Apparatus for blood component separation	A device to be used to prepare a biological tissue adhesive of autologous plasma origin in a sterilized closed circuit for patients whose blood was donated for preserved blood type autotransfusion. An application for a partial change to change the manufacturing sites. (A partial change during the reexamination period)
5	Sep. 20, 2013 Total review time: 386 days Regulatory review time: 126 days	Mar. 14, 2011 Domestic and foreign clinical study results	86	InterStim II Neurostimulator for Sacral Neuromodulation (Medtronic Japan Co., Ltd.)	Approval	Instrument & apparatus 12 Implantable stimulator for bladder and bowel control	An implantable nerve stimulation system to improve fecal incontinence by electrical stimulation to sacral nerves for the patients with fecal incontinence who have not responded or cannot apply to conservative treatment. Clinical studies were conducted to evaluate therapeutic effect of this device for fecal incontinence and the safety during a test stimulation period and an implantation period.

Review Category	Approval Date	Approval Date in US Clinical Study Results: Domestic/Foreign	No.	Brand Name (Applicant Company)	New Approval /Partial Change	Classification Generic Name	Notes
5	Feb. 19, 2014 Total review time: 72 days Regulatory review time: 19 days	- No clinical study results	87	Cryoseal Disposable Kit (Asahi Kasei Medical Co.,Ltd.)	Change	Instrument & apparatus 7 Blood component separation kit	Blood component separation kit to be used to isolate/collect blood components in a sterile state when preparing a biological tissue adhesive from autologous plasma. Patients are to undergo preoperative autologous blood donation. An application for a partial change of approval application for medical device to change manufacturing sites. (A partial change during the reexamination period)
6-1	Sep. 20, 2013 Total review time: 756 days Regulatory review time: 371 days	May 14, 2004 (stem, etc.) Mar. 16, 2005 (baseplate, etc.) Jul. 20, 2006 (baseplate long post, etc.) Clinical evaluation report	88	Aequalis Reversed Shoulder Prosthesis (Tornier S.A.S.)	Approval	Medical products 4 Total shoulder prosthesis	A reversed shoulder prosthesis system in a reversed form of the conventional, anatomically-structured shoulder prosthesis with a spherical glenoid component and a humeral head component that is a concave hemispherical shell. Since there was no similar device in Japan, a clinical evaluation report was submitted to confirm the efficacy and safety of this device equivalent to similar devices based on overseas usage history and publications of this device and the similar devices by taking into account that the indication and operative procedure had already been established by its long-term usage history overseas.
6-1	Oct. 30, 2013 Total review time: 1038 days Regulatory review time: 666 days	Dec. 19, 2005 Clinical evaluation report	89	Trabecular Metal Reverse Shoulder System (Zimmer K.K.)	Approval	Medical products 4 Total shoulder prosthesis	A total shoulder prosthesis having the concept of a reversed shoulder prosthesis system in which the anatomical structure is reversed. It is used for cases of having difficulty in elevetion of a shoulder with an unreconstructible rotator cuff function such as a massive rotator cuff tear. When it can not be used in reversed combination for the reason that a base plate can not be applied during surgery, it can be emergently combined in an anatomical shape. Trabecular metal is applied to portions contacting bone on a humeral stem and a reversed base plate. A clinical evaluation report was submitted to confirm the efficacy and safety of this device is equivalent to the existing approved devices based on overseas usage histories and publications of this device and similar devices. (The original product is in a reexamination period)
6-2	Oct. 11, 2013 Total review time: 416 days Regulatory review time: 112 days	Feb. 20, 2013 Foreign clinical study results	90	Natrelle 410 Breast Implant (Allergan Japan K. K.)	Approval	Medical products 4 Gel-filled artificial breast	A gel-filled artificial breast for restoring or forming the shape of a breast after the insertion into the application site. It is used for breast reconstruction surgery or augmentation mammaplasty. It is improved compared with the approved "Natrelle Breast Implant (Approval No. 22400BZX00354000)".The improvements are that it is designed with an anatomical shape that mirrors a woman's real breast and the gel with increased degree of crosslinking makes the breast harder. A clinical study was conducted to evaluate the performance as an artificial breast and adverse events in breast reconstruction surgery or augmentation mammaplasty. (The original product is in a reexamination period)
Cellular and tissue-based products	Jul. 30, 2013 Total review time: 75 days Regulatory review time: 40 days	- No clinical study results	91	Jace (Japan Tissue Engineering Co., Ltd.)	Change	Instrument & apparatus 7 Human autologous cells and tissue	This is an autologous-cultured epidermis processed from epidermal cells and multiple animal origin-materials for severe burn injury. This application for partial changes to add a new supplier of bovine serum used in the processes of this product and to change the preparation method of culture medium.
Cellular and tissue-based products	Mar. 17, 2014 Total review time: 109 days Regulatory review time: 39 days	- No clinical study results	92	Jace (Japan Tissue Engineering Co., Ltd.)	Change	Instrument & apparatus 7 Human autologous cells and tissue	This is an autologous-cultured epidermis processed from epidermal cells and multiple animal origin-materials for severe burn injury. An application for partial changes to change and add raw materials of this product, and to change storage period of the intermediates.

Review Category	Approval Date	Approval Date in US Clinical Study Results: Domestic/Foreign	No.	Brand Name (Applicant Company)	New Approval /Partial Change	Classification Generic Name	Notes
Specified partial change	Jan. 16, 2014 Total review time: 83 days Regulatory review time: 37 days	Feb. 13, 2014 No clinical study results	93	Promus Element Plus Stent System (Boston Scientific Japan K.K.)	Change	Instrument & apparatus 7 Coronary stent	A stent system used in percutaneous coronary stent placement. The stent is coated with everolimus with immunosuppression. An application for a partial change of approval application for medical device to add everolimus with a different manufacturing number. (A partial change during the reexamination period)
Specified partial change	Mar. 11, 2014 Total review time: 62 days Regulatory review time: 29 days	- No clinical study results	94	Cryoseal Disposable Kit (Asahi Kasei Medical Co.,Ltd.)	Change	Instrument & apparatus 7 Blood component separation kit	Blood component separation kit to be used to isolate/collect blood components in a sterile state when preparing a biological tissue adhesive from autologous plasma. Patients are to undergo preoperative autologous blood donation. An application for a partial change of approval application for medical device to add new raw materials of the components for stabilizing supply of the materials. (A partial change during the reexamination period)

Table3. Products Approved in FY 2013: Improved Medical Devices (with Clinical Data)

Review Category	Approval Date	Date Approved in US Clinical Study Results: Domestic/Foreign	No.	Brand Name (Applicant Company)	New Approval/ Partial Change	Classification Generic Name	Notes
1	Apr. 8, 2013 Total review time: 299 days Regulatory review time: 141 days	Jun. 5, 2012 Foreign clinical study results	1	Biotrue Oneday (B.L.J. Company, Ltd.)	Approval	Instrument & apparatus 72 Single-use colored contact lens for correcting visual acuity	A single use soft contact lens with 78% water content and oxygen permeability (Dk) of 42 composed of nesofilcon A. It is integrally colored light blue and contains an ultraviolet absorber. Because the product has novel raw materials, but not a novel design, a clinical study was conducted to evaluate the efficacy and safety of wearing this product for correction of visual acuity.
1	Aug. 27, 2013 Total review time: 382 days Regulatory review time: 207 days	Apr. 15, 2013 Foreign clinical study results	2	Tecnis Toric 1-Piece (AMO Japan K.K.)	Approval	Instrument & apparatus 72 Posterior chamber lens	A one-piece monofocal posterior chamber lens to be inserted into an aphakic eye after cataract surgery accompanied with corneal astigmatism. The same raw materials as those of “Tecnis one-piece (Approval No. 22000BZX01610000)” are used. A cylindrical frequency was newly added to the front of the lens to correct corneal astigmatism, which is difference from the existing approved product. A clinical study was conducted to evaluate the clinical efficacy and safety of this product with the newly added correcting function of corneal astigmatism.
1	Jan. 14, 2014 Total review time: 491 days Regulatory review time: 141 days	- Domestic clinical study results	3	HOYA iSert Micro Toric (HOYA Corporation)	Approval	Instrument & apparatus 72 Posterior chamber lenses with an injector	A posterior chamber lens with an injector in which a monofocal posterior chamber lens is preloaded to insert it into an aphakic eye with corneal astigmatism after cataract surgery. The raw materials of the lens are the same as those of “HOYA iSert Micro (Approval No. 22200BZX00615000).” A cylindrical power is newly added to one side of the lens to correct corneal astigmatism, which is the difference from the existing approved product. A domestic clinical study was conducted to evaluate the clinical efficacy and safety of this lens with the newly added correcting function of corneal astigmatism.
1	Jan. 15, 2014 Total review time: 292 days Regulatory review time: 227 days	- Domestic clinical study results	4	Alcon Acrysof IQ Restor Toric Single-Piece (Alcon Japan Ltd.)	Approval	Instrument & apparatus 72 Multifocal posterior chamber lens	A multifocal toric intraocular lens to be inserted into an aphakic eye with corneal astigmatism. This product has an aspheric, diffractive, and multifocal structure on the anterior optical surface and a toric structure on the posterior surface. The each optical design is identical to that of the company’s approved product. In addition, the raw material and basic structure of the lens are also identical to those of the company’s approved product. A domestic clinical study was conducted to evaluate that this device corrects corneal astigmatism and provides adequate multifocal function, compared to clinical study results of the approved single-function lenses of multifocal or toric.
1	Mar. 3, 2014 Total review time: 213 days Regulatory review time: 150 days	- Clinical evaluation report	5	ICL KS-AquaPORT (STAAR Japan Inc.)	Approval	Instrument & apparatus 72 Phakic posterior chamber intraocular lens	A one-piece intraocular lens to correct refractive errors. It is designed to be implanted in the posterior chamber of a phakic eye (in front of the human crystalline lens). A through-hole is added to the center of the optical zone of the company’s approved product “ICL (Approval No. 22200BZY00001000),” which makes laser iridotomy, required as a preoperative procedure in the original product, unnecessary. A clinical evaluation report was submitted to evaluate the effects on the change on visual function and corneal endothelial cells, and the presence or absence of increased ocular pressure associated with the absence of laser iridotomy.
2	Jan. 23, 2014 Total review time: 391 days Regulatory review time: 188 days	Jun. 30, 2004 Domestic and foreign clinical study results	6	Straumann Implant (SLActive) TL (Straumann Japan K.K.)	Approval	Medical products 4 Dental implant body	The first dental implant in Japan that enables earlier loading than conventional loading. This device is sealed into vial filled with normal saline to keep hydrophilic nature of titanium until just before use, which accelerates osteointegration. A domestic clinical study on an implant of 4.1mm in diameter was conducted to evaluate its efficacy and safety in early loading compared to in conventional loading. In addition, results of foreign clinical studies on a thinner implant of 3.3mm in diameter were submitted.

Review Category	Approval Date	Date Approved in US Clinical Study Results: Domestic/Foreign	No.	Brand Name (Applicant Company)	New Approval/ Partial Change	Classification Generic Name	Notes
3-1	Jul. 10, 2013 Total review time: 349 days Regulatory review time: 233 days	Dec. 21, 2012 Foreign clinical study results	7	XIENCE Xpedition Drug Eluting Stent (Abbott Vascular Japan Co.,Ltd.)	Approval	Instrument & apparatus 7 Coronary stent	A coronary stent composed of a drug-eluting stent used for treatment of patients with symptomatic ischemic heart diseases who have a new coronary lesion (a lesion length of 32mm or less) with a reference vessel diameter of 2.50-3.75mm and a delivery catheter used to implant a stent to the coronary stenosis site. The device has a different stent delivery system from the company's approved product “XIENCE PRIME Drug Eluting Stent (Approval No. 22400BZX00145000).” A new stent diameter of 3.25mm is added. Results from clinical studies on “XIENCE PRIME Drug Eluting Stent” were submitted to confirm the efficacy and safety of this product.
3-1	Sep. 26, 2013 Total review time: 300 days Regulatory review time: 205 days	Oct. 15, 2009 Clinical evaluation report	8	Hyperform/Hyperglide Occlusion Balloon Catheter (Covidien Japan, Inc.)	Change	Instrument & apparatus 51 Intravascular catheter for embolization of the central circulation system	An intravascular catheter for embolization in the central circulation system used for a temporary interruption of blood flow in percutaneous intravascular surgery or as an adjunct of coil embolization for cerebral aneurysm. An application for a partial change to change the intended use and the operation procedures to enable this product to be used in coil embolization for wide-neck cerebral aneurysm as an assisting balloon, in addition to an indication as an occlusion balloon. A clinical evaluation report was submitted to confirm the efficacy and safety of balloon-assisted coil embolization using this device.
3-1	Dec. 9, 2013 Total review time: 404 days Regulatory review time: 265 days	Feb. 22, 2013 Foreign clinical study results	9	Resolute Integrity Coronary Stent System (Medtronic Japan Co., Ltd.)	Change	Instrument & apparatus 7 Coronary stent	A stent system for percutaneous coronary stent placement consisting of a stent to be inserted and placed at the site of a lesion to maintain the vascular lumen and a delivery catheter used to deliver the stent to the site of the lesion. Application for a partial change to add a product with a stent length of 34mm and 38mm to the existing products for extending the target lesion length from 27mm to 35mm and change the specification of drug content uniformity. A clinical study was conducted to evaluate the efficacy and safety of the product for patients with symptomatic ischemic heart diseases who have a new coronary lesion (a lesion length of 35mm or less).
3-1	Jan. 30, 2014 Total review time: 265 days Regulatory review time: 192 days	- Clinical evaluation report	10	Kaneka Assistant Balloon Catheter NE-N3 (Kaneka Corporation)	Approval	Instrument & apparatus 51 Intravascular catheter for embolization of the central circulation system	A intravascular catheter for embolization in the central circulation system used for a temporary interruption of blood flow in percutaneous intravascular surgery or as an adjunct of coil embolization for cerebral aneurysm. A clinical evaluation report was submitted to confirm the efficacy and safety of balloon-assisted coil embolization using this device.
3-1	Feb. 4, 2014 Total review time: 221 days Regulatory review time: 112 days	Feb. 22, 2012 Foreign clinical study results	11	AbsolutePro Vascular Stent (Abbott Vascular Japan Co.,Ltd.)	Approval	Instrument & apparatus 7 Stent for iliac artery	A self-expanding stent and stent delivery system inserted and placed at the site of new lesions or restenotic lesions of symptomatic atherosclerosis in the iliac artery (common iliac artery and external iliac artery) to secure intravascular lumen. A clinical study was conducted to evaluate that the efficacy and safety of the product are not inferior compared to the results from past clinical studies.
3-1	Feb. 28, 2014 Total review time: 182 days Regulatory review time: 76 days	Jul. 31, 2012 Foreign clinical study results	12	Omnilink Elite Vascular Stent (Abbott Vascular Japan Co.,Ltd.)	Approval	Instrument & apparatus 7 Stent for iliac artery	A balloon-expanding stent and stent delivery system inserted and placed at the site of new lesions or restenotic lesions of symptomatic atherosclerosis in the iliac artery (common iliac artery and external iliac artery) to secure intravascular lumen. A clinical study was conducted to evaluate that the efficacy and safety of the product are not inferior compared to the results from past clinical studies.
3-1	Mar. 26, 2014 Total review time: 363 days Regulatory review time: 129 days	Mar. 19, 2013 Clinical evaluation report	13	Guidezilla Extension Catheter (Boston Scientific Japan K.K.)	Approval	Instrument & apparatus 51 Coronary recanalization catheter	A coronary recanalization catheter to enhance access to the stenotic site of the coronary artery and facilitate placement of interventional devices including a guidewire. A clinical evaluation report was submitted to evaluate that the device has equal efficacy and safety to those of the approved devices.

Review Category	Approval Date	Date Approved in US Clinical Study Results: Domestic/Foreign	No.	Brand Name (Applicant Company)	New Approval/ Partial Change	Classification Generic Name	Notes
3-1	Mar. 28, 2014 Total review time: 361 days Regulatory review time: 147 days	- Clinical evaluation report	14	Nipro Guiding Catheter B (Nipro Corporation)	Approval	Instrument & apparatus 51 Coronary recanalization catheter	A coronary recanalization catheter providing back-up support for insertion of a therapeutic device. It is inserted into the coronary artery when it is difficult for a guidewire or an intravascular therapeutic device to reach a target lesion or pass a lesion in percutaneous transluminal coronary angioplasty. A clinical evaluation report was submitted to evaluate that the device has equal efficacy and safety to those of the approved devices.
3-2	Jul. 19, 2013 Total review time: 618 days Regulatory review time: 389 days	Nov. 9, 2006 Foreign clinical study results	15	Gore Propaten Vascular Graft (W.L. GORE & Associates, Co., Ltd.)	Approval	Instrument & apparatus 7 Artificial blood vessel using heparin	An artificial blood vessel used in vascular replacement, bypass grafting, hemodialysis or other vascular techniques for patients with occlusive diseases or aneurysms or trauma patients who require vascular replacement. It has a basic structure of a stretched polytetrafluoroethylene (PTFE) tube. Heparin bonded covalently to the luminal surface of the graft is expected to produce a local and long-term antithrombotic effect and improve the 1-year patency rate and limb salvage rate after peripheral vascular bypass surgery for patients with peripheral artery occlusive disease. A clinical study was conducted to evaluate its efficacy and safety in above-knee femoropopliteal artery bypass surgery for vascular occlusive diseases.
3-2	Sep. 27, 2013 Total review time: 434 days Regulatory review time: 254 days	Aug. 23, 2011 Foreign clinical study results	16	GORE CTAG Thoracic Endoprosthesis (W.L. GORE & Associates, Co., Ltd.)	Approval	Instrument & apparatus 7 Aortic stent graft	An aortic stent graft system used for endovascular treatment of thoracic aortic aneurysm. The product consists of a stent graft and delivery catheter. The main differences from the approved product “GORE TAG Thoracic Endoprosthesis (Approval No. 22000BZX00185000)” include a shape change of the stent graft (removal of flare parts at both ends of a stent graft), an increase in the stent wire diameter, a change of the apex number of the stent, an addition of a new stent graft size, and a position change of adhesive tape, etc. These changes enhanced compression resistance of the stent graft and followability to an implanted vessel so that the product is applicable to more diversified blood vessel diameters. A clinical study was conducted to evaluate its efficacy and safety in cases with thoracic aortic aneurysm.
3-2	Oct. 11, 2013 Total review time: 178 days Regulatory review time: 148 days	Apr. 16, 2013 Foreign clinical study results	17	ENDURANT II Stent Graft System (Medtronic Japan Co., Ltd.)	Change	Instrument & apparatus 7 Aortic stent graft	An aortic stent graft system used for endovascular treatment of infrarenal abdominal aortic aneurysm. The product consists of a stent graft and delivery system. An application for a partial change to add AUI (aorta uni-iliac) configuration. Results from a clinical study using the first generation product were submitted to evaluate the efficacy and safety of the AUI configuration for infrarenal abdominal aortic aneurysm.
3-2	Dec. 6, 2013 Total review time: 595 days Regulatory review time: 380 days	Dec. 1, 2011 Clinical evaluation report	18	GuideLiner Catheter (Japan Lifeline Co., Ltd.)	Approval	Instrument & apparatus 51 Coronary recanalization catheter	A coronary recanalization catheter providing back-up support for insertion of the therapeutic device. It is inserted into the coronary artery when it is difficult for a guidewire or an intravascular therapeutic device to reach a target lesion or pass a lesion in percutaneous transluminal coronary angioplasty. A clinical evaluation report was submitted to confirm the efficacy and safety when this device is used as a slave catheter.
3-2	Jan. 30, 2014 Total review time: 456 days Regulatory review time: 419 days	- Domestic clinical study results	19	J Graft Open Stent Graft (Japan Lifeline Co., Ltd.)	Approval	Instrument & apparatus 7 Aortic stent graft	An aortic open stent graft used for the treatment of diseases which require aorta replacement from the distal aortic arch to the proximal descending aorta. This product is capable of being fixed securely on the central side in a similar suturing way with a conventional synthetic graft, and is fixed on the peripheral side by the spring force of the stent graft without suture which provide one-stage, low invasive treatment for a widespread lesion. A clinical study was conducted to confirm the efficacy and safety of this device for diseases requiring aorta replacement.

Review Category	Approval Date	Date Approved in US Clinical Study Results: Domestic/Foreign	No.	Brand Name (Applicant Company)	New Approval/ Partial Change	Classification Generic Name	Notes
3-2	Feb. 6, 2014 Total review time: 132 days Regulatory review time: 99 days	- Clinical evaluation report	20	BA Soft Balloon Catheter (Fuji Systems Corporation)	Approval	Instrument & apparatus 51 Intravascular catheter for embolization of the central circulation system	An intravascular catheter for embolization in the central circulation system used for a temporary interruption of blood flow in percutaneous intravascular surgery or as an adjunct of coil embolization for a cerebral aneurysm to prevent a coil body from protruding or being disengaged toward the parent artery. A clinical evaluation report was submitted to confirm the efficacy and safety of balloon-assisted coil embolization using this device.
3-2	Feb. 24, 2014 Total review time: 594 days Regulatory review time: 366 days	OTW System (Jan. 31, 2007) DV System (Sep. 19, 2007) Clinical evaluation report	21	AERO Hybrid Stent for Airway Stenosis (Sugan Co., Ltd.)	Approval	Instrument & apparatus 7 Tracheal stent	A tracheal stent used to secure an airway for tracheal or bronchial stenosis caused by malignant tumors. Since this stent made of nitinol is fully covered with polyurethane film, it has the advantage of both metal stent which can be inserted by rigid or flexible endoscope and silicon stent which has low complication rates in granulation, tumor infiltration and so on. A clinical study report was submitted to confirm the efficacy and safety of this device for tracheal and bronchial stenosis caused by malignant tumors.
3-2	Feb. 28, 2014 Total review time: 1428 days Regulatory review time: 167 days	Aug. 30, 2008 Foreign clinical study results	22	ATS 3f Aortic Bioprosthesis (Century Medical, Inc.)	Approval	Instrument & apparatus 7 Equine pericardial valve	The ATS 3f Aortic Bioprosthesis is used for replacement as an alternative to dysfunctional aortic valve. Its leaflets are made of equine pericardium. This aortic bioprosthetic valve is designed as a tubular structure without a stent, which allows the valve to open and close like a native valve. A clinical study was conducted to confirm the efficacy and safety of this device when it was implanted in patients with aortic stenosis.
3-2	Feb. 28, 2014 Total review time: 730 days Regulatory review time: 270 days	Jan. 7, 2010 Foreign clinical study results	23	Floseal (Baxter Limited)	Approval	Medical products 4 Gelatin-based local absorbable hemostatic material with human thrombin	A local absorbable hemostatic material used in surgical procedures (other than in ophthalmic) as an adjunct to hemostasis when control of bleeding by ligature or conventional procedures is ineffective or impractical. A clinical study was conducted to evaluate its performance and safety for a bleeding area in cardiac, vascular and spine/spinal surgery.
3-2	Mar. 28, 2014 Total review time: 302 days Regulatory review time: 153 days	Sep. 11, 2008 Foreign clinical study results	24	NAV 6 Filter (Abbott Vascular Japan Co.,Ltd.)	Approval	Instrument & apparatus 51 Emboli-capturing catheter in the central circulatory system	A device is used to prevent distal emboli by capture and removal of obstructing materials such as thrombi during carotid artery stent procedure. It is percutenously and temporarily placed in the distal sites from stenotic region in the cervical part of carotid artery. A clinical study was conducted to confirm the effectiveness and safety when this device is used during CAS.
4	Jul. 18, 2013 Total review time: 335 days Regulatory review time: 193 days	Jan. 29, 2013 Global clinical trials	25	Viva CRT-D Series (Medtronic Japan Co., Ltd.)	Approval	Instrument & apparatus 7 Implantable biventricular pacing pulse generator with defibrillator function	An implantable defibrillator with a biventricular pacing function. The device is newly equipped with AdaptivCRT technology developed to automatically control CRT parameters (AV and VV delays) based on patients' conduction and CardioSync Optimization supporting CRT parameter control by measuring patients' electric conduction property at follow-up visits, with which the approved product “Protecta XT CRT-D (Approval No. 22200BZX00913000)” was equipped. There are six models of the products having different shapes of connectors of lead connection parts and different mounting functions. A clinical study was conducted to evaluate the efficacy and safety of the AdaptivCRT function.
4	Aug. 9, 2013 Total review time: 696 days Regulatory review time: 280 days	Aug. 14, 2008 Foreign clinical study results	26	Watch PAT (Philips Respironics GK)	Approval	Instrument & apparatus 21 Sleep evaluation device	A medical device used as an adjunct in evaluation and diagnosis of sleep-disordered breathing events and sleep stages in patients suspected of sleep-disordered breathing. The wrist-worn device records PAT (Peripheral Artery Tonometry) signal (finger plethysmogram), $Sp0_2$, snoring, and body position and motion during sleep. Results from clinical studies on the precedent device equipped with the same software as this device were submitted to examine whether the software of this device can evaluate sleep disorder.

Review Category	Approval Date	Date Approved in US Clinical Study Results: Domestic/Foreign	No.	Brand Name (Applicant Company)	New Approval/ Partial Change	Classification Generic Name	Notes
4	Sep. 12, 2013 Total review time: 265 days Regulatory review time: 172 days	- Global clinical trials	27	Viva Quad CRT-D Series (Medtronic Japan Co., Ltd.)	Approval	Instrument & apparatus 7 Implantable biventricular pacing pulse generator with defibrillator function	An implantable defibrillator with a biventricular pacing function. One of the IS-1 connector ports of the original product “Viva CRT-D Series (Approval No. 22500BZX00320000)” is changed to a IS4 connector port capable of being adopted to a left ventricle (LV) lead that has four independent pacing electrodes. There are three models of the products having different mounting functions. It also has VectorExpress, a support function to be used for selecting a pacing vector, which provides automatic measurement of the capture threshold based on impedance and pulse width of 16 types of LV vector and relative battery life. A clinical study was conducted to evaluate the efficacy and safety of AdaptivCRT technology.
4	Sep. 30, 2013 Total review time: 536 days Regulatory review time: 382 days	- Foreign clinical study results	28	DBS 4 contacts lead (St. Jude Medical Japan Co., Ltd.)	Approval	Instrument & apparatus 12 Electrical brain stimulation device for tremor	An electrode lead placed on the deep brain in deep brain stimulation therapy. It transmits electric stimulus generated from an implanted stimulation device. The product consists of an electrode lead and its accessories. It is used in conjunction with “Libra Single 8 Neurostimulator (Approval No. 22500BZX00450000)” and “Brio Dual 8 Neurostimulator (Approval No. 22500BZX00451000).” A clinical study was conducted to evaluate the efficacy and safety of product in Parkinson’s disease and dystonia.
4	Jan. 28, 2014 Total review time: 1033 days Regulatory review time: 401 days	Sep. 24, 2003 Domestic clinical study results	29	AB5000 Ventricle (Medix Japan, Inc.)	Approval	Instrument & apparatus 7 Single-use external ventricular assist system	An pneumatic ventricular support system that is placed external to the patient. A domestic clinical trial was conducted to evaluate its adaptability to domestic medical circumstances. Results of a post-marketing surveillance submitted to the US FDA were reviewed as reference data.
4	Jan. 28, 2014 Total review time: 944 days Regulatory review time: 314 days	Aug. 1, 2006 Foreign clinical study results	30	Endovenous Closure System (Covidien Japan Inc.)	Approval	Instrument & apparatus 29 Therapeutic electrosurgical device	An electrosurgical device used for the treatment of primary varicose veins of lower extremities. It generates a laser in the veins to obstruct saphenous veins. It thermally coagulates the main saphenous vein to cause vascular obstruction. This device is composed of a generator which generates high-frequency current and a catheter which is connected to the generator. The catheter, to the tip of which a heating coil is attached, is inserted via the skin and lumina to an objective lesion region (the main saphenous vein). The heating coil obstructs a vascular vessel. A clinical study in which it is compared to the domestically approved product “ELVeS Laser (Approval No. 22200BZX00660000)” was conducted to evaluate its clinical efficacy and safety.
4	Feb. 28, 2014 Total review time: 375 days Regulatory review time: 252 days	Apr. 4, 2012 Foreign clinical study results	31	Protecta XT CRT-D (Medtronic Japan Co., Ltd.)	Change	Instrument & apparatus 7 Implantable biventricular pacing pulse generator with defibrillator function	An implantable defibrillator with a biventricular pacing function. An application for a partial change to add NYHA class II (mild) cardiac function to the current indications of class III or IV (moderate or severe) for extending its indication. A clinical study was conducted to confirm the validity of the new indication. In addition, results from evaluations of multiple clinical studies were submitted as a clinical evaluation report.
4	Mar. 7, 2014 Total review time: 345 days Regulatory review time: 167 days	Nov. 17, 2011 Foreign clinical study results	32	INCEPTA Plus CRT-D (Boston Scientific Japan K.K.)	Approval	Instrument & apparatus 7 Implantable biventricular pacing pulse generator with defibrillator function	An implantable defibrillator with a biventricular pacing function. An application to add NYHA class II (mild) cardiac function to the current indications of class III (moderate) or IV (severe). A clinical study was conducted to evaluate the validity of the new indication.
4	Mar. 7, 2014 Total review time: 245 days Regulatory review time: 172 days	- Domestic clinical study results	33	ELVeS Laser 1470 (Integral Corporation)	Approval	Instrument & apparatus 31 Diode laser	A laser treatment device used for varicose veins of lower extremities. It generates a laser in the veins to obstruct saphenous veins. A domestic clinical study was conducted to confirm that this device provides a similar degree of interruption of blood flow to the original product “ELVeS Laser” and that it is less associated with postoperative pains than the original.

Review Category	Approval Date	Date Approved in US Clinical Study Results: Domestic/Foreign	No.	Brand Name (Applicant Company)	New Approval/ Partial Change	Classification Generic Name	Notes
4	Mar. 11, 2014 Total review time: 326 days Regulatory review time: 160 days	Jun. 11, 2001 Clinical evaluation report	34	Subcutaneous Implantable Lead System (Medtronic Japan Co., Ltd.)	Approval	Instrument & apparatus 7 Implantable defibrillator/ pacemaker lead	A subcutaneously implanted lead with a defibrillation coil electrode for ICD and CRT-D. This product is used for patients with a high defibrillation threshold in whom it is difficult for a normal transvenous defibrillation lead to work effectively. A clinical evaluation report summarizing results of foreign clinical studies was submitted to confirm the efficacy and safety of this device.
5	Apr. 17, 2013 Total review time: 279 days Regulatory review time: 240 days	- (About these changes) Clinical evaluation report	35	Dornier Delta II (Dornier Medtech Japan Co., Ltd.)	Change	Instrument & apparatus 12 Extracorporeal lithotripter	An electromagnetic lithotripter used in bloodless treatment by radiating a shock wave from outside the body to a calculus to crush it into small fragments. The product consists of a shock wave generating device, a X-ray device, an ultrasonic device, ECG device, and a treatment table. An application for a partial change to add an indication for pancreatolithiasis to the conventional indication for calculus of the upper urinary tract and biliary calculus with no change of the product itself. A clinical evaluation report summarizing literature cited in three domestic guidelines on treatment of pancreatolithiasis and literature on clinical use of this product.
5	May 21, 2013 Total review time: 294 days Regulatory review time: 142days	- Clinical evaluation report	36	Niti-S Colorectal Stent (Century Medical, Inc.)	Approval	Instrument & apparatus 7 Colonic stent	A biliary stent used to relieve obstructive symptoms before surgery for stricture of the large intestine caused by malignant tumors or for palliation in patients with unresectable malignant tumors or who are not expected to respond to other treatments. A clinical study report, which summarizes literature information using technical success of stent placement, improvement of obstructive symptoms after the placement, and the incidence of adverse events as evaluation items, was submitted to confirm the efficacy and safety of this device when it is used for relief of obstructive symptoms before surgery or palliation.
5	Jun. 5, 2013 Total review time: 125 days Regulatory review time: 114 days	- Domestic clinical study results	37	PEPA Hemodiafilter GDF (Nikkiso Co., Ltd.)	Approval	Instrument & apparatus 7 Hemodiafilter	A hollow fiber membrane hemodiafilter used to remove fluid and uremic substances stored in the body due to uremia. It is indicated for patients whose renal function has been markedly reduced due to chronic or acute renal failure, etc. Because equivalence to the approved haemodiafiltration device was not demonstrated with regard to the semipermeable membrane material, a clinical study was conducted to confirm the efficacy and safety.
5	Jul. 3, 2013 Total review time: 400 days Regulatory review time: 115 days	- Clinical evaluation report	38	Niti-S Comvi Pyloric/Duodenal stent (Century Medical, Inc.)	Approval	Instrument & apparatus 7 Gastroduodenal stent	A gastroduodenal stent for patients with unresectable malignant gastroduodenal stenosis who cannot be managed by palliative surgical therapy and are not expected to achieve improvement with other treatments. The main difference from the approved product “Niti-S Gastroduodenal Stent (Approval No. 22300BZX00428000)” is that this product has a cover made of PTFE. A clinical study report was submitted summarizing results of literature research on clinical data to evaluate the efficacy and safety of this device compared to an uncovered stent.
5	Jul. 11, 2013 Total review time: 296 days Regulatory review time: 172 days	- Domestic clinical study results	39	PillCam COLON 2 Capsule Endoscopy System (Given Imaging K.K.)	Approval	Instrument & apparatus 25 Capsule electronic endoscope system	A capsule electronic endoscope system to take images of colorectal mucosa and provide the images when colonoscopy is required for diagnosis of colonic diseases but it is difficult to be performed. The main difference from the approved product “Given Capsule Endoscopy (Approval No. 22100BZX00363000)” is that this product is used for diagnosis of colonic diseases. A clinical study was conducted to evaluate the sensitivity of this device in subjects who were detected by colonoscopy to have diseases which require endoscopic or surgical therapy.

Review Category	Approval Date	Date Approved in US Clinical Study Results: Domestic/Foreign	No.	Brand Name (Applicant Company)	New Approval/ Partial Change	Classification Generic Name	Notes
5	Sep. 12, 2013 Total review time: 295 days Regulatory review time: 164 days	- Domestic clinical study results	40	Prismaflex ST (Gambro K.K.)	Approval	Instrument & apparatus 7 Slow continuous hemofilter	A slow continuous hemofilter to improve clinical conditions by performing continuous hemodiafiltration. It is used in patients with severe sepsis or septic shock, patients with acute renal failure accompanying diseases or conditions including sepsis, multi organ failure, acute hepatic failure, acute respiratory failure, acute cardiovascular failure, acute pancreatitis, burn injury, traumatic injury, postoperative diseases or patients with chronic renal failure who have unstable circulation dynamics associated with these diseases or conditions. This product is a filter used for slow continuous hemofiltation that is connected to a blood circuit. The main difference from the approved product “Hemofeel SH (Approval No. 21200BZZ00274000)” is that the product is indicated for patients with severe sepsis or septic shock. A clinical study was conducted to evaluate the efficacy and safety of this device in patients with severe sepsis or septic shock.
5	Sep. 12, 2013 Total review time: 295 days Regulatory review time: 164 days	- Domestic clinical study results	41	SepXiris (Gambro K.K.)	Approval	Instrument & apparatus 7 Slow continuous hemofilter	A slow continuous hemofilter to improve clinical conditions by performing continuous hemodiafiltration. It is used in patients with severe sepsis or septic shock, patients with acute renal failure accompanying diseases or conditions including sepsis, multi organ failure, acute hepatic failure, acute respiratory failure, acute cardiovascular failure, acute pancreatitis, burn injury, traumatic injury, postoperative diseases or patients with chronic renal failure who have unstable circulation dynamics associated with the diseases or conditions. The main difference from the approved product “Hemofeel SH (Approval No. 21200BZZ00274000)” is that the product is indicated for patients with severe sepsis or septic shock. A clinical study was conducted to evaluate the efficacy and safety of this device in patients with severe sepsis or septic shock.
5	Jan. 14, 2014 Total review time: 264 days Regulatory review time: 162 days	- Domestic clinical study results	42	Fineflux (Nipro Corporation)	Approval	Instrument & apparatus 7 Hemodiafilter	A hollow fiber membrane hemodiafilter used to remove fluid and uremic substances stored in the body due to uremia. It is indicated for patients whose renal function has been markedly reduced due to chronic or acute renal failure, etc. Cellulose triacetate, which has been conventionally used as a hollow fiber membrane raw material of a hemodialyzer, is adopted as a hollow fiber membrane raw material of the hemodiafilter. A clinical study was conducted to evaluate the efficacy and safety because the raw material of its semipermeable membrane was proved to be not equivalent to that of the approved product.
5	Jan. 28, 2014 Total review time: 152 days Regulatory review time: 113 days	- Clinical evaluation report	43	MucoUp (Seikagaku Corporation)	Change	Medical products 4 Submucosal filling material for endoscope	A submucosal filling material for an endoscope containing the active ingredient sodium hyaluronate. It is injected submucosally during endoscopic mucosal resection or endoscopic submucosal dissection to form a mucosal protrusion and maintain it. This application for a partial change for medical devices is to add an indication for the site of esophageal tumors. A clinical evaluation report summarizing literature information was submitted to evaluate the efficacy and safety when it is used in endoscopic mucosal resection/endoscopic submucosal dissection.
6-1	Jun. 12, 2013 Total review time: 957 days Regulatory review time: 260 days	- Clinical evaluation report	44	Biomet Biolox Delta Ceramic Liner (At the time of approval, Biomet Japan, Inc.; currently, Biomet Japan, LLC)	Approval	Medical products 4 Artificial hip joint, acetabular component	A liner made of zirconia-toughened alumina ceramic composites used in combination with the company’s approved product “Biomet Biolox Delta Ceramic Head (Approval No. 22400BZX00141000).” Because the combination of the company’s liner material and head material was an unprecedented combination, a clinical evaluation report summarizing its efficacy and safety based on foreign use results and published literature was submitted.

Review Category	Approval Date	Date Approved in US Clinical Study Results: Domestic/Foreign	No.	Brand Name (Applicant Company)	New Approval/ Partial Change	Classification Generic Name	Notes
6-1	Sep. 6, 2013 Total review time: 134 days Regulatory review time: 107 days	- Clinical evaluation report	45	Adler BIOLOX delta Ceramic System (Robert Reid Inc.)	Approval	Medical products 4 Total hip prosthesis	A femoral stem-head and an acetabulum-forming liner made of alumina-zirconia ceramics composite used in hip replacement used in combination with the approved products “Alder prosthetic hip joint system (Approval No. 22500BZX00017000),” “HYDRA Femoral Component (Approval No. 22500BZX00018000),” and “BIOLOX delta Ceramic Head (Approval No. 22500BZX00019000).” Because combination of the company’s head and liner made of the raw material was unprecedented, a clinical evaluation report evaluating the incidence of repeat replacements and the incidence of defects based on foreign use results and published literature was submitted.
6-1	Jan. 28, 2014 Total review time: 144 days Regulatory review time: 62 days	- Clinical evaluation report	46	R3 Delta Ceramic Liner (Smith & Nephew Orthopaedics KK)	Approval	Medical products 4 Artificial hip joint, acetabular component	An acetabular liner used for total hip replacement. It is made of zirconia-toughened alumina (BIOLOX delta) for improvement of its brittleness and abrasion property. It was developed to obtain a hip joint bearing with excellent abrasion characteristics and fracture strength by delta on delta in combination with a delta ceramic head made of the same material. A clinical evaluation report was submitted to confirm the performance of the bearing surface with the new material.
6-1	Feb. 13, 2014 Total review time: 539 days Regulatory review time: 159 days	- Domestic clinical study results	47	Zimmer Delta Ceramic Liner (Zimmer K.K.)	Approval	Medical products 4 Artificial hip joint, acetabular component	An acetabular liner used for total hip replacement. It is made of zirconia-toughened alumina (BIOLOX delta) for improvement of its brittleness and abrasion property. It was developed to obtain a hip joint bearing with excellent abrasion characteristics and fracture strength by delta on delta in combination with the company’s artificial caput made of the same material. Domestic clinical study results were submitted to demonstrate that this device with the newly adopted material is not inferior to the approved prosthetic hip joint in the efficacy and safety.
6-2	Aug. 9, 2013 Total review time: 591 days Regulatory review time: 220 days	Mar. 31, 2004 Domestic clinical study results	48	CranioFix Absorbable (B. Braun Aesculap Japan Co., Ltd.)	Approval	Medical products 4 Absorbable cranial fixation clamp	An implantable cranial fixation device composed of two absorbable discs, of which are made of polyester [Poly (L-lactide-co-D, L-lactide) 70:30], and a non-absorbable suture to fix them. It is used to fix a free bone flap during closing of the cranium in a craniotomy. This device has the following points as differences from the approved devices: (1) The device offers a more simple operation of cranial fixation in a shorter time because operation to heat and shape a plate and exclusive tools became unnecessary; (2) It also has no artifact in postoperative MRI or CT images; (3) The absorbable material causes no problems of impeding growth of bones in children or its moving and it is not necessary to be removed at the time of repeat surgery. Clinical studies were conducted to confirm the efficacy and safety of this product with the newly adopted absorbable material.
6-2	Sep. 6, 2013 Total review time: 220 days Regulatory review time: 138 days	Mar. 11, 2009 Domestic clinical study results	49	GRYPHON BR Anchor (Johnson & Johnson K.K.)	Approval	Medical products 4 Absorbable ligament anchor	A suture anchor used to fix soft tissues such as ligaments in a shoulder, foot/ankle, elbow, hip to a bone. The product consists of an absorbable anchor, partially absorbable sutures, and an inserter. The point of improvement is that a complex of glycolic acid-lactic acid polyester and β-tricalcium phosphate which is unprecedented in Japan, is adopted as a raw material of the anchor. A clinical study was conducted to confirm the efficacy and safety of this product with the newly adopted absorbable material.
6-2	Sep. 6, 2013 Total review time: 220 days Regulatory review time: 140 days	Feb. 29, 2012 Domestic clinical study results	50	HEALIX ADVANCE BR Anchor (Johnson & Johnson K.K.)	Approval	Medical products 4 Absorbable ligament anchor	A suture anchor to fix a rotator cuff to a bone. The product consists of an absorbable anchor, partially absorbable sutures, and an inserter. The point of improvement is that a complex of glycolic acid-lactic acid polyester and β-tricalcium phosphate of which a remaining period is shorter than that of a poly-L-lactic acid anchor, is adopted as a raw material. Clinical study results using anchors of the same raw material as that of this product were submitted to confirm that failure caused by the material does not occur.

Review Category	Approval Date	Date Approved in US Clinical Study Results: Domestic/Foreign	No.	Brand Name (Applicant Company)	New Approval/ Partial Change	Classification Generic Name	Notes
6-2	Sep. 6, 2013 Total review time: 190 days Regulatory review time: 103 days	Mar. 31, 2004 Domestic clinical study results	51	MILAGRO Interference Screw (Johnson & Johnson K.K.)	Approval	Medical products 4 Absorbable ligament anchor	An interference screw used to fix soft tissue to a bone. The point of improvement is that a complex of glycolic acid-lactic acid polyester and β-tricalcium phosphate of which a remaining period is shorter than that of a poly-L-lactic acid anchor, is adopted as a raw material. Clinical study results using anchors of the same raw material as that of this product were submitted to confirm that failure caused by the material does not occur.
6-2	Sep. 17, 2013 Total review time: 1040 days Regulatory review time: 529 days	Apr. 3, 2009 Foreign clinical study results	52	Hydrosite Gentle Ag (Smith & Nephew Wound Management KK)	Approval	Medical products 4 Antibacterial wound dressing and protecting material	An antibacterial wound dressing and protecting material containing sulfadiazine silver as an antibacterial ingredient added to the absorption pad layer of the approved product “Hydrosite AD Gentle (Approval No. 22100BZX00942000).” It is used for wounds with exudate fluid which have a high possibility of infection. Foreign clinical study results on a similar product which has a different adhesive agent on a wound contact layer were submitted to confirm if the antibacterial ingredient causes no problems such as protracted wound healing.
6-2	Sep. 17, 2013 Total review time: 1040 days Regulatory review time: 529 days	Apr. 3, 2009 Foreign clinical study results	53	Hydrosite Ag (Smith & Nephew Wound Management KK)	Approval	Medical products 4 Antibacterial wound dressing and protecting material	An antibacterial wound dressing and protecting material containing sulfadiazine silver as an antibacterial ingredient added to the absorption pad layer of the approved product “Hydrosite Plus (Approval No. 22100BZX01097000).” In addition, soft gel is applied to the wound contact surface of the approved product to improve the operability. It is used for wounds with exudate fluid which have a high possibility of infection. Foreign clinical study results on a similar product which has a different adhesive agent on a wound contact layer were submitted to confirm if the antibacterial ingredient causes no problems such as protracted wound healing.
6-2	Sep. 24, 2013 Total review time: 501 days Regulatory review time: 197 days	Aug. 1, 2011 Domestic clinical study results	54	Versajet II (Smith & Nephew Wound Management KK)	Approval	Instrument & apparatus 12 Hydraulic knife	A device to be used for wound debridement (acute wounds, chronic wounds and burn wounds), soft tissue debridement and operative wound cleaning with waterjet. Improvement in connectivity between the hand piece and the console and water resistance of the console was provided to enhance the operability of the approved product “Versajet S (Approval No. 22400BZX00233000)”. A non-clinical study demonstrated the performance equality between both products. A clinical study was conducted to confirm the efficacy and safety of debridement.
6-2	Sep. 27, 2013 Total review time: 1646 days Regulatory review time: 346 days	Jan. 25, 2007 Clinical evaluation report	55	Mepilex Ag (Mölnlycke Health Care K.K.)	Approval	Medical products 4 Antibacterial wound dressing and protecting material	A wound dressing and protecting material used to "protect wound" reaching subcutaneous adipose tissue (except for third degree burns), "maintain a moist environment," "promote healing," and "relieve pain." It is used for wounds with exudate fluid which have a high possibility of infection. The product consists of a silicone gel-coated hydrophilic polyurethane foam containing silver and a vapor-permeable polyurethane film. A clinical evaluation report based on foreign use-results and published literature of this product and similar products was submitted to confirm if silver contained in the product causes no problem such as protracted wound healing.
6-2	Dec. 12, 2013 Total review time: 1081 days Regulatory review time: 256 days	- Clinical evaluation report	56	Laminoplasty Basket Plate Set (Ammtec Inc.)	Approval	Medical products 4 Internal fixation plate	An internal fixation plate used for fixing severed bone parts after spinal decompression for spinal cord compression. It is fixed to the space of vertebral lamina removed in laminoplasty by a screw. In addition, an implanted bone is able to be filled into the basket portion. A clinical evaluation report based on literature research on usual laminoplasty and use results of the approved product used in the surgery was submitted to demonstrate that the fixation performance and safety of this product are equivalent to the approved product.

Review Category	Approval Date	Date Approved in US Clinical Study Results: Domestic/Foreign	No.	Brand Name (Applicant Company)	New Approval/ Partial Change	Classification Generic Name	Notes
6-2	Dec. 25, 2013 Total review time: 288 days Regulatory review time: 75 days	- Clinical evaluation report	57	SonicWeld Rx System (Nippon Martin K.K.)	Approval	Medical products 4 Absorbable plate for internal fixation	A device consisting of a plate and a pin used in a bone junction or reconstruction of cranio-maxillo-facial bone or bone fragment fixation in bone transplantation to cranio-maxillo-facial bone, and an ultrasonic fixator to fix them. The pin and the plate are made of polylactic acid which is absorbed into the body. This product has a characteristic that its ultrasonic fixator generates vibrating energy, which melts and hardens the pin in the bone hole to fix the plate. A clinical evaluation report was submitted to evaluate that the fixation performance and safety with this absorbable material are equivalent to those of similar products.
6-2	Jan. 28, 2014 Total review time: 1065 days Regulatory review time: 123 days	May 6, 2003 Clinical evaluation report	58	Simplex P with Tobramycin (Stryker Japan K.K.)	Approval	Medical products 4 Orthopedic bone cement	The acrylic orthopedic bone cement used to fix a substitution material (artificial bone head, hip joint or knee joint) to an in vivo bone. One gram of tobramycin is sterilely added to the approved product “Surgical Simplex.” It is used in the second stage of a two-stage revision prosthetic joint replacement associated with postoperative infection in a prosthetic joint replacement. A clinical evaluation report was submitted to demonstrate that the added antibacterial agent does not affect the efficacy and safety of the orthopedic bone cement.
6-2	Feb. 28, 2014 Total review time: 273 days Regulatory review time: 94 days	Aug. 3, 2005 Clinical evaluation report	59	Cobalt G-HV Bone Cement (At the time of approval, Biomet Japan, Inc.; currently, Biomet Japan, LLC)	Approval	Medical products 4 Orthopedic bone cement	A device that gentamicin sulfate is added to the company’s approved orthopedic bone cement “Cobalt HV Bone Cement” as an antibacterial agent. It is used in the second stage of a two-stage revision prosthetic joint replacement associated with postoperative infection in a prosthetic joint replacement. A clinical evaluation report was submitted to demonstrate that the added antibacterial agent does not affect the efficacy and safety of the orthopedic bone cement.
6-2	Mar. 19, 2014 Total review time: 2211 days Regulatory review time: 484 days	Jun. 2, 2006 Foreign clinical study results	60	Juvederm Vista Ultra (Allergan Japan KK)	Approval	Medical products 4 Injectable material to a soft tissue using hyaluronic acid	An injectable material into soft-tissue using hyaluronic acid. It is injected into the dermis to correct facial wrinkles and folds. Crosslinked and non-crosslinked hyaluronic acid, non-animal derived, obtained by fermentation of bacteria are mixed and filled into a syringe. Compared to the conventional injectable material using animal-derived collagen, the risk of allergy and infection was reduced. This product has different degrees of gel crosslinking from “Juvederm Vista Ultra Plus,” an application of which was submitted at the same time. This product is a softer injectable material. Foreign clinical study results were submitted to demonstrate its non-inferiority and safety compared to a control injectable material using collagen and safety.
6-2	Mar. 19, 2014 Total review time: 2211 days Regulatory review time: 484 days	Jun. 2, 2006 Foreign clinical study results	61	Juvederm Vista Ultra Plus (Allergan Japan KK)	Approval	Medical products 4 Injectable material to a soft tissue using hyaluronic acid	An injectable material into soft tissue using hyaluronic acid. It is injected into the dermis to correct facial wrinkles and folds. Crosslinked and non-crosslinked hyaluronic acid, non-animal derived, obtained by fermentation of bacteria are mixed and filled into a syringe. Compared to the conventional injectable material using animal-derived collagen, the risk of allergy and infection was reduced. This product has different degrees of gel crosslinking from “Juvederm Vista Ultra,” an application of which was submitted at the same time. This product is a harder injectable material. Foreign clinical study results were submitted to demonstrate its non-inferiority and safety compared to a control injectable material using collagen and safety.
8	Dec. 6, 2013 Total review time: 525 days Regulatory review time: 118 days	- Domestic clinical study results	62	Visceral Fat Meter EW-FA90 (Panasonic Corporation)	Approval	Instrument & apparatus 21 Body constituent analysis instrument	A body component analyzer consisting of an apparatus body, a measuring belt for abdomen, and pads. The cross section area of visceral fat estimated by a unique calculating formula based on abdominal impedance and the measured value of abdominal circumference is displayed on the apparatus body. A clinical study was conducted to evaluate the correlation between the cross section area of visceral fat by CT tomogram of the abdomen and an estimated value by this product and its screening performance (sensitivity and specificity).

Review Category	Approval Date	Date Approved in US Clinical Study Results: Domestic/Foreign	No.	Brand Name (Applicant Company)	New Approval/ Partial Change	Classification Generic Name	Notes
8	Jan. 16, 2014 Total review time: 294 days Regulatory review time: 100 days	- Clinical evaluation report	63	Elmammo, Dedicated PET Scanner for Breast Imaging (Shimadzu Corporation)	Approval	Instrument & apparatus 10 Positron emission tomography device for nuclear medicine diagnosis	A dedicated PET scanner for breast imaging to provide image information of distribution of a positron radioactive drug administered to patients within breasts by detecting exogenously with a gamma radiation detector. A clinical evaluation report was submitted to evaluate the effectiveness of images provided by this product in comparison to those by whole-body PET, contract-enhanced MRI and mammography.

Table 4. Post-marketing Safety Measures Implemented and Revision of PRECAUTIONS for Drugs etc., Directed by MHLW in FY 2013

○ Post-marketing safety measures implemented by MHLW in FY 2013

	Drugs	Medical devices
Directions for revision to precautions in package insert	160	3
Information published in the Pharmaceuticals and Medical Devices Safety Information	40	4

* *Note: Including the issuance of notifications on self-check for medical devices, etc.*

○ Revision of PRECAUTIONS for Drugs Directed by MHLW in FY 2013

Date	Drug name
Apr. 23, 2013	1. Tolvaptan 2. Ambrisentan 3. Tiotropium bromide hydrate 4. Esomeprazole magnesium hydrate 5. Tranexamic acid (oral dosage form) 6. Tranexamic acid (injectable dosage form) 7. Dabigatran etexilate methanesulfonate 8. Nilotinib hydrochloride hydrate 9. Amoxicillin hydrate 10. Potassium clavulanate/Amoxicillin hydrate 11. Clarithromycin 12. Lansoprazole/Amoxicillin hydrate/Clarithromycin 13. Lansoprazole/Amoxicillin hydrate/Clarithromycin 14. Lansoprazole/Amoxicillin hydrate/Metronidazole 15. Terbinafine hydrochloride (oral dosage form) 16. Preparations containing tranexamic acid (OTC)
May 17, 2013	1. Iguratimod 2. Warfarin potassium
Jun. 4, 2013	1. Levetiracetam 2. Loxoprofen sodium hydrate (oral dosage form) 3. Paroxetine hydrochloride hydrate 4. Tolvaptan 5. Sugammadex sodium 6. Tegafur/Gimeracil/Oteracil potassium 7. Nelarabine 8. Carboplatin 9. Ribavirin (capsules) 10. Interferon beta (products for administration in combination with ribavirin) 11. OTC drugs Loxoprofen sodium hydrate (oral dosage form)
Jun. 14, 2013	1. Recombinant adsorbed bivalent human papillomavirus-like particle vaccine (derived from Trichoplusia ni cells) Recombinant adsorbed quadrivalent human papillomavirus-like particle vaccine (yeast origin)
Jul. 9, 2013	1. Paliperidone 2. Tolvaptan 3. Golimumab (genetical recombination) 4. Sulbactam sodium/Ampicillin sodium 5. Sitafloxacin hydrate 6. Peramivir hydrate 7. Itraconazole 8. Albendazole

Date	Drug name
Aug. 6, 2013	1. Isoflurane 2. Desflurane 3. Levodopa Levodopa/Carbidopa hydrate Levodopa/Benserazide hydrochloride 4. Valsartan Valsartan/Amlodipine besilate 5. Valsartan/Hydrochlorothiazide 6. Ganirelix acetate 7. Degarelix acetate 8. Cyanamide 9. Alogliptin benzoate 10. Alogliptin benzoate/Pioglitazone hydrochloride 11. Linagliptin 12. Vildagliptin 13. Diazoxide 14. Thalidomide 15. Orengedokuto (for ethical use) 16. Kamishoyosan (for ethical use) 17. Shin'iseihaito (for ethical use) 18. Orengedokuto (OTC) 19. Kamishoyosan (OTC) 20. Shin'iseihaito (OTC)
Sep. 17, 2013	1. Celecoxib 2. Sertraline hydrochloride 3. Losartan potassium 4. Propylthiouracil 5. Hydroxyethylated starch 70000 Hydroxyethylated starch 70000/Sodium chloride/Potassium chloride/Calcium chloride hydrate/Sodium lactate 6. Hydroxyethylated starch 130000 7. Fondaparinux sodium 8. Zoledronic acid hydrate 9. Erlotinib hydrochloride 10. Bortezomib 11. Minocycline hydrochloride (oral dosage form, injectable dosage form)
Oct. 22, 2013	1. Clobazam 2. Olmesartan medoxomil Olmesartan medoxomil/Azelnidipine 3. Omega-3 fatty acid ethyl ester 4. Apixaban 5. Ethyl icosapentate (for ethical use) 6. Gemcitabine hydrochloride 7. Axitinib 8. Oxaliplatin

Date	Drug name
	9. Cisplatin (non-intra-arterial injection) 10. Bevacizumab (genetical recombination) 11. Regorafenib hydrate 12. Ethyl icosapentate (OTC)
Nov. 26, 2013	1. Donepezil hydrochloride 2. Donepezil hydrochloride 3. Pilsicainide hydrochloride hydrate (oral dosage form) Propafenone hydrochloride Bepridil hydrochloride hydrate 4. Furosemide 5. Beraprost sodium Azithromycin hydrate (tablets for adults, dry syrup for adults, injectable dosage form) Ofloxacin (oral dosage form) Garenoxacin mesilate hydrate Levofloxacin hydrate (injectable dosage form) Telaprevir Famciclovir 6. Bosentan hydrate 7. Clindamycin hydrochloride Clindamycin phosphate (injectable dosage form) 8. Levofloxacin hydrate (oral dosage form) 9. Aciclovir (oral and injectable dosage forms) Valaciclovir hydrochloride
Jan. 7, 2014	1. Sodium valproate 2. Rufinamide 3. Lixisenatide Liraglutide (genetical recombination) Acarbose Anagliptin Alogliptin benzoate Sitagliptin phosphate hydrate Pioglitazone hydrochloride Miglitol Linagliptin 4. Clopidogrel sulfate Clopidogrel sulfate/Aspirin 5. Alogliptin benzoate/Pioglitazone hydrochloride 6. Saxagliptin hydrate 7. Voglibose (products with an indication to treat abnormal glucose tolerance) 8. Voglibose (products without an indication to treat abnormal glucose tolerance) 9. Crizotinib 10. Amphotericin B (liposomal preparation) 11. Atazanavir sulfate
Jan. 17, 2014	1. Drospirenone/Ethinylestradiol betadex

Date	Drug name
Feb. 6, 2014	1. Rivaroxaban
Feb. 18, 2014	1. Mianserin hydrochloride 2. Bixalomer 3. Chlormadinone acetate/Mestranol Norethisterone/Ethinylestradiol (products with an indication to treat dysmenorrhea) Norethisterone/Mestranol Norgestrel/Ethinylestradiol 4. Desogestrel/Ethinylestradiol Norethisterone/Ethinylestradiol (products with an indication for contraception) Levonorgestrel/Ethinylestradiol 5. Felbinac (for ethical use) 6. Minodronic acid hydrate 7. Regorafenib hydrate 8. Yokukansan (for ethical use) 9. Salazosulfapyridine 10. Sulfamethoxazole/Trimethoprim 11. Felbinac-containing products (OTC) 12. Yokukansan (OTC)
Mar. 26, 2014	1. Levetiracetam 2. Ketoprofen (injectable dosage form, suppository) 3. Rotigotine 4. Mirtazapine 5. Ibuprofen piconol 6. Indometacin (dermatologic preparation) Diclofenac sodium (dermatologic preparation) Piroxicam (dermatologic preparation) Flurbiprofen (dermatologic preparation) Loxoprofen sodium hydrate (dermatologic preparation) 7. Ketoprofen (cream, gel, lotion, poultice) 8. Ketoprofen (tape) 9. Potassium citrate/Sodium citrate hydrate 10. Paclitaxel (excluding paclitaxel protein-bound particles for injectable suspension) Nilotinib hydrochloride hydrate

**Note: Detailed information is available at the PMDA's Medical Product Information web page.*

Table 5. Revision of PRECAUTIONS for Medical Devices Directed by MHLW in FY 2013

Date	Title
May 20, 2013	Revision of PRECAUTIONS for Magnetic Resonance Imaging System
Jul. 1, 2013	Revision of PRECAUTIONS for Epicardial Pacing Leads
Sep. 20, 2013	Revision of PRECAUTIONS for Tracheostomy Masks

**Note: Detailed information is available at the PMDA's Medical Product Information web page.*

Table 6. FY 2013 Pharmaceuticals and Medical Devices Safety Information (No.301-311)

Date	No.	Table of Contents
May. 28, 2013	301	1. Precautions in Handling of Reusable Resuscitator 2. Important Safety Information [1] Recombinant Adsorbed Bivalent Human Papillomavirus-like Particle Vaccine (derived from Trichoplusia ni cells) [2] Telaprevir 3. Revision of Precautions (No. 245) (1) Gabapentin (and 19 others) (2) Implantable Cardiac Pacemaker, Biventricular Pacing Pulse Generators without Defibrillator Function List of Products Subject to Early Post-marketing Phase Vigilance
Jun. 26, 2013	302	1. Severe Haemorrhages Associated with Suspected Interaction between Antirheumatic Iguratimod and Warfarin 2. Revision of Precausions for the Effect of Battery Chargers for Electric Cars on Implantable Cardiac Pacemakers 3. Important Safety Information [1] Ambrisentan [2] Tranexamic Acid [3] Iguratimod 4. Revision of Precautions (No. 246) (1) Tolvaptan (and 12 others) (2) Magnetic Resonance Imaging System List of Products Subject to Early Post-marketing Phase Vigilance
Jul. 31, 2013	303	Revision of Pharmaceuticals and Medical Devices Safety Information (No. 303) 1. Tolvaptan and Hepatic Dysfunction 2. Revision of Precautions for Magnetic Resonance Imaging System 3. Important Safety Information [1] Interferon Beta (products for administration in combination with ribavirin) and Ribavirin (capsules) [2] Carboplatin [3] Tegafur/Gimeracil/Oteracil potassium [4] Tolvaptan [5] Paroxetine hydrochloride hydrate [6] Levetiracetam 4. Revision of Precautions (No. 247) Loxoprofen sodium hydrate (oral dosage form) (and 4 others) List of Products Subject to Early Post-marketing Phase Vigilance
Aug. 28, 2013	304	1. Surveillance on Availability, Dissemination, and Utilization of Drug Safety Information in Medical Institutions and Pharmacies 2. Important Safety Information [1] Golimumab (Genetical Recombination) 3. Revision of Precautions (No. 248) Paliperidone (and 5 others) List of Products Subject to Early Post-marketing Phase Vigilance

Date	No.	Table of Contents
Sep. 25, 2013	305	1. Hydroxyethylated Starch-containing Solutions and Renal impairment 2. Project of Japan Drug Information Institute in Pregnancy 3. Important Safety Information [1] Alogliptin benzoate-containing products [2] Valsartan-containing products [3] Vildagliptin [4] Orengedokuto, Kamishoyosan, Shin'iseihaito 4. Revision of Precautions (No. 249) Isoflurane (and 13 others) List of Products Subject to Early Post-marketing Phase Vigilance
Oct. 30, 2013	306	1. Adverse Reactions to Influenza Vaccine in the 2012 Season 2. Important Safety Information [1] Propylthiouracil [2] Bortezomib [3] Minocycline Hydrochloride (oral dosage form, injectable dosage form) [4] Losartan Potassium 3. Revision of Precautions (No. 250) (1) Celecoxib (and 4 others) (2) Tracheostomy Masks (tracheal masks) List of Products Subject to Early Post-marketing Phase Vigilance
Nov. 28, 2013	307	1. Summary of the Relief System for Sufferers from Adverse Drug Reactions and the Cases of Non-payment of Relief Benefits Due to Improper Use of Drugs 2. Important Safety Information [1] Axitinib [2] Bevacizumab (Genetical Recombination) 3. Revision of Precautions (No. 251) Clobazam (and 9 others) List of Products Subject to Early Post-marketing Phase Vigilance
Dec. 26, 2013	308	1. Review of Driving Precautions in Package Inserts of Ethical Drugs 2. Important Safety Information [1] Bosentan Hydrate 3. Revision of Precautions (No. 252) Donepezil Hydrochloride(and 5 others) 4. List of Products Subject to Early Post-marketing Phase Vigilance (Reference) Handling of Fire during Long-term Oxygen Therapy
Jan. 29, 2014	309	1. Precautions for Use of Puncture Site Closure Devices 2. List of Products Subject to Early Post-marketing Phase Vigilance (Reference) Drugs and Medical Devices Safety Information Reporting System

Date	No.	Table of Contents
Feb. 27, 2014	310	1. Thrombosis with YAZ Combination Tablets for Dysmenorrhea 2. Rivaroxaban and Interstitial Pneumonia 3. Direct Patient Reporting System for Adverse Drug Reactions 4. Important Safety Information [1] Atazanavir Sulfate [2] Crizotinib [3] Clopidogrel Sulfate-containing Products [4] Sodium Valproate [5] Drospirenone/Ethinylestradiol Betadex [6] Rivaroxaban 5. Revision of Precautions (No. 253) Rufinamide (and 8 others) List of Products Subject to Early Post-marketing Phase Vigilance
Mar. 26, 2014	311	1. Revised Adverse Reaction Reporting System for Quasi-Drugs and Cosmetics 2. Important Safety Information [1] Salazosulfapyridine [2] Sulfamethoxazole/Trimethoprim [3] Felbinac (for ethical use) [4] Regorafenib Hydrate 3. Revision of Precautions (No. 254) Mianserin Hydrochloride (and 5 others) List of Products Subject to Early Post-marketing Phase Vigilance

**Note: Detailed information is available at the PMDA's Medical Product Information web page.*

Table 7. FY 2013 PMDA Medical Safety Information

No.	Month and year published	Title
37	April 2013	Precautions in Handling of Insulin Injectors
38	May 2013	Improper Assembly of Resuscitator Bags
39	September 2013	Precautions in Handling of Tracheal Masks
40	October 2013	Precautions in Handling of Vaccines
41	January 2014	Precautions in Handling of Epidural Catheters
42	February 2014	Precautions in Handling of Nasogastric Tubes
43	March 2014	Risks in Handling of Gastrostomy Tubes

**Note: Detailed information is available at the PMDA's Medical Product Information web page.*

Table 8. List of User Fees

8-1. List of user fees for reviews etc. of pharmaceuticals, quasi-drugs, and cosmetics based on the Pharmaceutical Affairs Act (Act No. 145, 1960)

(The Cabinet order specifying the following user fees came into effect on April 1, 2009. Please refer to the Table 9-1 that compares the previous user fees with the revised user fees, effective as of April 1, 2014.)

(Yen)

Classification			User fees		
			Review	Inspection	Total
Assessment for manufacturing license of drugs					
New license		On-site		148,100	148,100
				Article 16, Paragraph 1, Item 1 (a)	
		Document		111,500	111,500
				Article 16, Paragraph 1, Item 1 (b)	
Change/addition of classification		On-site		97,400	97,400
				Article 16, Paragraph 1,Item 2 (a)	
		Document		55,300	55,300
				Article 16, Paragraph 1,Item 2 (b)	
Renewal of existing license		On-site		97,400	97,400
				Article 16, Paragraph 1,Item 3 (a)	
		Document		55,300	55,300
				Article 16, Paragraph 1,Item 3 (b)	
Assessment for foreign manufacturers' accreditation of drugs					
New accreditation		On-site		133,300 + travel expenses	133,300 + travel expenses
				Article 16, Paragraph 2, Item 1 (a)	
		Document		58,100	58,100
				Article 16, Paragraph 2, Item 1 (b)	
Change/addition of classification		On-site		64,600 + travel expenses	64,600 + travel expenses
				Article 16, Paragraph 2,Item 2 (a)	
		Document		39,700	39,700
				Article 16, Paragraph 2,, Item 2 (b)	
Renewal of existing accreditation		On-site		64,600 + travel expenses	64,600 + travel expenses
				Article 16, Paragraph 2,Item 3 (a)	
		Document		39,700	39,700
				Article 16, Paragraph 2,Item 3 (b)	
Review for approval of drugs (new approval)					
New drugs (No. 1) (non-orphan drugs)		First application products	23,788,100	6,559,600	30,347,700
			Article 17, Paragraph 1, Item 1 (a)-(1)	Article 17,Paragraph 2, Item 1 (a)	
		Line extension products	2,464,000	1,639,800	4,103,800
			Article 17, Paragraph 1, Item 1 (a)-(3)	Article 17,Paragraph 2, Item 1 (c)	
New drugs (No. 1) (orphan drugs)		First application products	19,934,100	3,286,000	23,220,100
			Article 17, Paragraph 1, Item 1 (a)-(2)	Article 17,Paragraph 2, Item 1 (b)	
		Line extension products	2,061,500	818,100	2,879,600
			Article 17, Paragraph 1, Item 1 (a)-(4)	Article 17,Paragraph 2, Item 1 (d)	
New drugs (No. 2) (non-orphan drugs)		First application products	11,353,100	2,463,200	13,816,300
			Article 17, Paragraph 1, Item 1 (a)-(5)	Article 17,Paragraph 2, Item 1 (e)	
		Line extension products	1,174,300	615,900	1,790,200
			Article 17, Paragraph 1, Item 1 (a)-(6)	Article 17,Paragraph 2, Item 1 (f)	
New drugs (No. 2) (orphan drugs)		First application products	9,345,700	1,232,500	10,578,200
			Article 17, Paragraph 1, Item 1 (a)-(7)	Article 17,Paragraph 2, Item 1 (g)	
		Line extension products	1,004,100	310,100	1,314,200
			Article 17, Paragraph 1, Item 1 (a)-(8)	Article 17,Paragraph 2, Item 1 (h)	
Generic prescription drugs (with inspections)			412,100	214,000	626,100
			Article 17, Paragraph 1, Item 1 (a)-(9)	Article 17,Paragraph 2, Item 1 (i)	
OTC drugs	Switch to OTC status, etc.	First application products	1,291,600		1,291,600
			Article 17, Paragraph 1, Item 1 (a)-(10)		
		Line extension products	1,291,600		1,291,600
			Article 17, Paragraph 1, Item 1 (a)-(10)		
	Others		110,300		110,300
			Article 17, Paragraph 1, Item 1 (a)-(11)		
In vitro diagnostics (without approval standards)			584,100		584,100
			Article 17, Paragraph 1, Item 1 (a)-(14)		
In vitro diagnostics (with approval standards)		Basic	282,900		282,900
			Article 17, Paragraph 1, Item 1 (a)-(13)		
		Addition of series	60,300		60,300
			Article 17, Paragraph 1, Item 1 (a)-(12)		
Quasi-drugs/cosmetics			63,500		63,500
			Article 17, Paragraph 1, Item 1 (b) (c)		
New application for change or replacement of brand name			35,600		35,600
			Article 17, Paragraph 1, Item 1 (e)		

Classification					User fees		
					Review	Inspection	Total
Review for approval of drugs (approval for partial changes to approved matters)							
	New drugs (No. 1) (non-orphan drugs)	Changes in indications, etc.		First application products	10,190,500	2,463,200	12,653,700
					Article 17, Paragraph 1, Item 2 (a)-(1)	Article 17,Paragraph 2, Item 2 (a)	
				Line extension products	1,057,400	615,900	1,673,300
					Article 17, Paragraph 1, Item 2 (a)-(2)	Article 17,Paragraph 2, Item 2 (b)	
		Others			205,100	120,700	325,800
					Article 17, Paragraph 1, Item 2 (a)-(3)	Article 17,Paragraph 2, Item 2 (c)	
	New drugs (No. 1) (orphan drugs)	Changes in indications, etc.		First application products	8,434,300	1,232,500	9,666,800
					Article 17, Paragraph 1, Item 2 (a)-(4)	Article 17,Paragraph 2, Item 2 (d)	
				Line extension products	875,600	310,100	1,185,700
					Article 17, Paragraph 1, Item 2 (a)-(5)	Article 17,Paragraph 2, Item 2 (e)	
		Others			132,700	109,800	242,500
					Article 17, Paragraph 1, Item 2 (a)-(6)	Article 17,Paragraph 2, Item 2 (f)	
	New drugs (No. 2) (non-orphan drugs)	Changes in indications, etc.		First application products	10,190,500	2,463,200	12,653,700
					Article 17, Paragraph 1, Item 2 (a)-(1)	Article 17,Paragraph 2, Item 2 (a)	
				Line extension products	1,057,400	615,900	1,673,300
					Article 17, Paragraph 1, Item 2 (a)-(2)	Article 17,Paragraph 2, Item 2 (b)	
		Others			205,100	120,700	325,800
					Article 17, Paragraph 1, Item 2 (a)-(3)	Article 17,Paragraph 2, Item 2 (c)	
	New drugs (No. 2) (orphan drugs)	Changes in indications, etc.		First application products	8,434,300	1,232,500	9,666,800
					Article 17, Paragraph 1, Item 2 (a)-(4)	Article 17,Paragraph 2, Item 2 (d)	
				Line extension products	875,600	310,100	1,185,700
					Article 17, Paragraph 1, Item 2 (a)-(5)	Article 17,Paragraph 2, Item 2 (e)	
		Others			132,700	109,800	242,500
					Article 17, Paragraph 1, Item 2 (a)-(6)	Article 17,Paragraph 2, Item 2 (f)	
	Generic prescription drugs (with inspections)	Changes in indications, etc.		First application products	10,190,500	2,463,200	12,653,700
					Article 17, Paragraph 1, Item 2 (a)-(1)	Article 17,Paragraph 2, Item 2 (a)	
				Line extension products	1,057,400	615,900	1,673,300
					Article 17, Paragraph 1, Item 2 (a)-(2)	Article 17,Paragraph 2, Item 2 (b)	
		Changes based on guidelines, etc.			35,600		35,600
					Article 17, Paragraph 1, Item 2 (a)-(7)		
		Others			205,100	120,700	325,800
					Article 17, Paragraph 1, Item 2 (a)-(3)	Article 17, Paragraph 2, Item 2 (c)	
	OTC drugs	Switch to OTC status, etc.	Changes in indications, etc.	First application products	10,190,500		10,190,500
					Article 17, Paragraph 1, Item 2 (a)-(1)		
				Line extension products	1,057,400		1,057,400
					Article 17, Paragraph 1, Item 2 (a)-(2)		
		Changes based on guidelines, etc.			35,600		35,600
					Article 17, Paragraph 1, Item 2 (a)-(7)		
		Others			56,400		56,400
					Article 17, Paragraph 1, Item 2 (a)-(8)		
	In vitro diagnostics (without approval standards)				295,800		295,800
					Article 17, Paragraph 1, Item 2 (a)-(11)		
	In vitro diagnostics (with approval standards)			Basic	143,500		143,500
					Article 17, Paragraph 1, Item 2 (a)-(10)		
				Addition of series	31,900		31,900
					Article 17, Paragraph 1, Item 2 (a)-(9)		
	Quasi-drugs/cosmetics				35,600		35,600
					Article 17, Paragraph 1, Item 2 (b) (c)		

Classification					User fees		
					Review	Inspection	Total
GMP inspection of drugs							
Approval, partial change and manufacture for export	New drugs		Domestic			739,800 Article 17, Paragraph 4, Item 1 (b)-(1)	739,800
			Overseas			933,500 + travel expenses Article 17, Paragraph 4, Item 1 (b)-(2)	933,500 + travel expenses
	Biological drugs/Radiopharmaceuticals, etc.		Domestic			666,100 Article 17, Paragraph 4, Item 1 (a)-(1)	666,100
			Overseas			844,400 + travel expenses Article 17, Paragraph 4, Item 1 (a)-(2)	844,400 + travel expenses
	Sterile drugs/Sterile quasi-drugs		Domestic			201,300 Article 17, Paragraph 4, Item 1 (c)-(1)	201,300
			Overseas			229,800 + travel expenses Article 17, Paragraph 4, Item 1 (c)-(2)	229,800 + travel expenses
	Other Drugs/quasi-drugs		Domestic			141,200 Article 17, Paragraph 4, Item 1 (d)-(1)	141,200
			Overseas			155,400 + travel expenses Article 17, Paragraph 4, Item 1 (d)-(2)	155,400 + travel expenses
	Packaging, labeling, storage, external testing, etc.		Domestic			63,800 Article 17, Paragraph 4,Item 2 (a) and Paragraph 5, Item 1 (a)	63,800
			Overseas			84,800 + travel expenses Article 17, Paragraph 4,Item 2 (b) and Paragraph 5, Item 1 (b)	84,800 + travel expenses
Renewal of the above	Biological drugs/ Radiopharmaceuticals, etc.	Basic	Domestic			436,000 Article 17, Paragraph 4, Item 3 (a)-(1)	436,000
			Overseas			554,200 + travel expenses Article 17, Paragraph 4, Item 3 (a)-(2)	554,200 + travel expenses
		Addition of products	Domestic			30,500 Article 17, Paragraph 4, Item 3 (a)-(1)	30,500
			Overseas			30,500 Article 17, Paragraph 4, Item 3 (a)-(2)	30,500
	Sterile drugs/ Sterile quasi-drugs	Basic	Domestic			380,000 Article 17, Paragraph 4, Item 3 (b)-(1)	380,000
			Overseas			480,000 + travel expenses Article 17, Paragraph 4, Item 3 (b)-(2)	480,000 + travel expenses
		Addition of products	Domestic			12,400 Article 17, Paragraph 4, Item 3 (b)-(1)	12,400
			Overseas			12,400 Article 17, Paragraph 4, Item 3 (b)-(2)	12,400
	Other Drugs/ quasi-drugs	Basic	Domestic			336,500 Article 17, Paragraph 4, Item 3 (c)-(1)	336,500
			Overseas			409,400 + travel expenses Article 17, Paragraph 4, Item 3 (c)-(2)	409,400 + travel expenses
		Addition of products	Domestic			9,600 Article 17, Paragraph 4, Item 3 (c)-(1)	9,600
			Overseas			9,600 Article 17, Paragraph 4, Item 3 (c)-(2)	9,600
	Packaging, labeling, storage, external testing, etc.	Basic	Domestic			258,500 Article 17, Paragraph 4, Item 3 (d)-(1) and Paragraph 5, Item 2 (a)	258,500
			Overseas			338,100 + travel expenses Article 17, Paragraph 4, Item 3 (d)-(2) and Paragraph 5, Item 2 (b)	338,100 + travel expenses
		Addition of products	Domestic			6,700 Article 17, Paragraph 4, Item 3 (d)-(1) and Paragraph 5, Item 2 (a)	6,700
			Overseas			6,700 Article 17, Paragraph 4, Item 3 (d)-(2) and Paragraph 5, Item 2 (b)	6,700

Classification				User fees		
				Review	Inspection	Total
GLP inspection of drugs						
	GLP	Domestic			2,062,400	2,062,400
					Article 17, Paragraph 3, Item 1 (a) and Paragraph 9, Item 2 (a)-(1)	
		Overseas			2,282,600 + travel expenses	2,282,600 + travel expenses
					Article 17, Paragraph 3, Item 1 (b) and Paragraph 9, Item 2 (a)-(2)	
GCP inspection of drugs						
	New GCP	First application products	Domestic		2,723,200	2,723,200
					Article 17, Paragraph 3, Item 2 (a)	
			Overseas		3,011,900 + travel expenses	3,011,900 + travel expenses
					Article 17, Paragraph 3, Item 2 (b)	
		Line extension products	Domestic		720,800	720,800
					Article 17, Paragraph 3, Item 2 (c)	
			Overseas		751,800 + travel expenses	751,800 + travel expenses
					Article 17, Paragraph 3, Item 2 (d)	
	GCP inspection of generic drugs		Domestic		645,200	645,200
					Article 17, Paragraph 3, Item 2 (e)	
			Overseas		950,200 + travel expenses	950,200 + travel expenses
					Article 17, Paragraph 3, Item 2 (f)	
Re-examination of drugs						
	Re-examination	First application products		806,600	2,673,700	3,480,300
				Article 17, Paragraph 8, Item 1 (a)	Article 17, Paragraph 9, Item 1 (a)	
		Line extension products		271,500	892,100	1,163,600
				Article 17, Paragraph 8, Item 1 (b)	Article 17, Paragraph 9, Item 1 (b)	
	GPSP	First application products	Domestic		2,193,300	2,193,300
					Article 17, Paragraph 9, Item 2 (b)-(1)	
			Overseas		2,409,600 + travel expenses	2,409,600 + travel expenses
					Article 17, Paragraph 9, Item 2 (b)-(2)	
		Line extension products	Domestic		752,600	752,600
					Article 17, Paragraph 9, Item 2 (b)-(3)	
			Overseas		772,300 + travel expenses	772,300 + travel expenses
					Article 17, Paragraph 9, Item 2 (b)-(4)	

8-2. List of user fees for reviews etc. of medical devices under the Pharmaceutical Affairs Act (Act No. 145, 1960)

(The Cabinet order specifying the following user fees came into effect on April 1, 2009. Please refer to the pages 208-221 that compares the previous user fees with the revised user fees, effective as of April 1, 2014.)

Note: The lower rows in the User fees column indicate the applicable articles of the Cabinet Order on Fees related to the Pharmaceutical Affairs Act. *(Yen)*

Classification				User fees		
				Review	Inspection	Total
Assessment for manufacturing license of medical devices						
	New license		On-site		148,100	148,100
					Article 16, Paragraph 1, Item 1 (a)	
			Document		111,500	111,500
					Article 16, Paragraph 1, Item 1 (b)	
	Change/addition of classification		On-site		97,400	97,400
					Article 16, Paragraph 1, Item 2 (a)	
			Document		55,300	55,300
					Article 16, Paragraph 1, Item 2 (b)	
	Renewal of existing license		On-site		97,400	97,400
					Article 16, Paragraph 1, Item 3 (a)	
			Document		55,300	55,300
					Article 16, Paragraph 1, Item 3 (b)	
Assessment for foreign manufacturers accreditation of medical devices						
	New accreditation		On-site		133,300 + travel expenses	133,300 + travel expenses
					Article 16, Paragraph 2, Item 1 (a)	
			Document		58,100	58,100
					Article 16, Paragraph 2, Item 1 (b)	
	Change/addition of classification		On-site		64,600 + travel expenses	64,600 + travel expenses
					Article 16, Paragraph 2, Item 2 (a)	
			Document		39,700	39,700
					Article 16, Paragraph 2, Item 2 (b)	
	Renewal of existing accreditation		On-site		64,600 + travel expenses	64,600 + travel expenses
					Article 16, Paragraph 2, Item 3 (a)	
			Document		39,700	39,700
					Article 16, Paragraph 2, Item 3 (b)	
Review for approval of medical devices (new approval)						
	Medical devices (with clinical data)	Class IV	New medical devices	8,705,500	664,500	9,370,000
				Article 17, Paragraph 1, Item 1 (d)-(1)	Article 17, Paragraph 2, Item 1 (j)	
			Improved medical devices	6,213,000	664,500	6,877,500
				Article 17, Paragraph 1, Item 1 (d)-(2)	Article 17, Paragraph 2, Item 1 (j)	
		Class III	New medical devices	6,213,000	664,500	6,877,500
				Article 17, Paragraph 1, Item 1 (d)-(3)	Article 17, Paragraph 2, Item 1 (j)	
			Improved medical devices	3,721,200	664,500	4,385,700
				Article 17, Paragraph 1, Item 1 (d)-(4)	Article 17, Paragraph 2, Item 1 (j)	
		Class II	New medical devices	6,213,000	664,500	6,877,500
				Article 17, Paragraph 1, Item 1 (d)-(3)	Article 17, Paragraph 2, Item 1 (j)	
			Improved medical devices	3,721,200	664,500	4,385,700
				Article 17, Paragraph 1, Item 1 (d)-(4)	Article 17, Paragraph 2, Item 1 (j)	
	Medical devices (without approval standards, without clinical data)	Class IV	Improved medical devices	2,355,400	68,500	2,423,900
				Article 17, Paragraph 1, Item 1 (d)-(7)	Article 17, Paragraph 2, Item 1 (l)	
			Generic medical devices	1,767,700	68,500	1,836,200
				Article 17, Paragraph 1, Item 1 (d)-(8)	Article 17, Paragraph 2, Item 1 (l)	
		Class III	Improved medical devices	1,409,900	68,500	1,478,400
				Article 17, Paragraph 1, Item 1 (d)-(9)	Article 17, Paragraph 2, Item 1 (l)	
			Generic medical devices	1,409,900	68,500	1,478,400
				Article 17, Paragraph 1, Item 1 (d)-(9)	Article 17, Paragraph 2, Item 1 (l)	
		Class II	Improved medical devices	1,409,900	68,500	1,478,400
				Article 17, Paragraph 1, Item 1 (d)-(9)	Article 17, Paragraph 2, Item 1 (l)	
			Generic medical devices	1,409,900	68,500	1,478,400
				Article 17, Paragraph 1, Item 1 (d)-(9)	Article 17, Paragraph 2, Item 1 (l)	
	Medical devices (with approval standards, without clinical data)	Class IV		429,200	68,500	497,700
				Article 17, Paragraph 1, Item 1 (d)-(5)	Article 17, Paragraph 2, Item 1 (k)	
		Class III		344,100	68,500	412,600
				Article 17, Paragraph 1, Item 1 (d)-(6)	Article 17, Paragraph 2, Item 1 (k)	
		Class II		344,100	68,500	412,600
				Article 17, Paragraph 1, Item 1 (d)-(6)	Article 17, Paragraph 2, Item 1 (k)	
	Change of brand name			35,600		35,600
				Article 17, Paragraph 1, Item 1 (e)		

Classification				User fees		
				Review	Inspection	Total
Review for approval of medical devices (approval of partial changes to approved matters)						
	Medical devices (with clinical data)	Class IV	New medical devices	4,357,500	664,500	5,022,000
				Article 17, Paragraph 1, Item 2 (d)-(1)	Article 17, Paragraph 2, Item 2 (g)	
			Improved medical devices	3,109,900	664,500	3,774,400
				Article 17, Paragraph 1, Item 2 (d)-(2)	Article 17, Paragraph 2, Item 2 (g)	
		Class III	New medical devices	3,109,900	664,500	3,774,400
				Article 17, Paragraph 1, Item 2 (d)-(3)	Article 17, Paragraph 2, Item 2 (g)	
			Improved medical devices	1,872,400	664,500	2,536,900
				Article 17, Paragraph 1, Item 2 (d)-(4)	Article 17, Paragraph 2, Item 2 (g)	
		Class II	New medical devices	3,109,900	664,500	3,774,400
				Article 17, Paragraph 1, Item 2 (d)-(3)	Article 17, Paragraph 2, Item 2 (g)	
			Improved medical devices	1,872,400	664,500	2,536,900
				Article 17, Paragraph 1, Item 2 (d)-(4)	Article 17, Paragraph 2, Item 2 (g)	
	Medical devices (without approval standards, without clinical data)	Class IV	Improved medical devices	1,181,200	37,100	1,218,300
				Article 17, Paragraph 1, Item 2 (d)-(7)	Article 17, Paragraph 2, Item 2 (i)	
			Generic medical devices	884,200	37,100	921,300
				Article 17, Paragraph 1, Item 2 (d)-(8)	Article 17, Paragraph 2, Item 2 (i)	
		Class III	Improved medical devices	709,500	37,100	746,600
				Article 17, Paragraph 1, Item 2 (d)-(9)	Article 17, Paragraph 2, Item 2 (i)	
			Generic medical devices	709,500	37,100	746,600
				Article 17, Paragraph 1, Item 2 (d)-(9)	Article 17, Paragraph 2, Item 2 (i)	
		Class II	Improved medical devices	709,500	37,100	746,600
				Article 17, Paragraph 1, Item 2 (d)-(9)	Article 17, Paragraph 2, Item 2 (i)	
			Generic medical devices	709,500	37,100	746,600
				Article 17, Paragraph 1, Item 2 (d)-(9)	Article 17, Paragraph 2, Item 2 (i)	
	Medical devices (with approval standards, without clinical data)	Class IV		217,600	37,100	254,700
				Article 17, Paragraph 1, Item 2 (d)-(5)	Article 17, Paragraph 2, Item 2 (h)	
		Class III		173,600	37,100	210,700
				Article 17, Paragraph 1, Item 2 (d)-(6)	Article 17, Paragraph 2, Item 2 (h)	
		Class II		173,600	37,100	210,700
				Article 17, Paragraph 1, Item 2 (d)-(6)	Article 17, Paragraph 2, Item 2 (h)	

Classification					User fees		
					Review	Inspection	Total
QMS inspection of medical devices							
	Approval, partial change and manufacture for export	New medical devices		Domestic		739,800 Article 17, Paragraph 4, Item 1 (b)-(1)	739,800
				Overseas		933,500 + travel expenses Article 17, Paragraph 4, Item 1 (b)-(2)	933,500 + travel expenses
		Biological medical devices, specially controlled medical devices (Class IV), etc.		Domestic		666,100 Article 17, Paragraph 4, Item 1 (a)-(1)	666,100
				Overseas		844,400 + travel expenses Article 17, Paragraph 4, Item 1 (a)-(2)	844,400 + travel expenses
		Sterile medical devices		Domestic		201,300 Article 17, Paragraph 4, Item 1 (c)-(1)	201,300
				Overseas		229,800 + travel expenses Article 17, Paragraph 4, Item 1 (c)-(2)	229,800 + travel expenses
		Other medical devices		Domestic		141,200 Article 17, Paragraph 4, Item 1 (d)-(1)	141,200
				Overseas		155,400 + travel expenses Article 17, Paragraph 4, Item 1 (d)-(2)	155,400 + travel expenses
		Packaging, labeling, storage, external testing, etc.		Domestic		63,800 Article 17, Paragraph 4, Item 2 (a) and Paragraph 5, Item 1 (a)	63,800
				Overseas		84,800 + travel expenses Article 17, Paragraph 4, Item 2 (b) and Paragraph 5, Item 1 (b)	84,800 + travel expenses
	Renewal of the above	Biological medical devices, specially controlled medical devices (Class IV), etc.	Basic	Domestic		436,000 Article 17, Paragraph 4, Item 3 (a)-(1)	436,000
				Overseas		554,200 + travel expenses Article 17, Paragraph 4, Item 3 (a)-(2)	554,200 + travel expenses
			Addition of products	Domestic		30,500 Article 17, Paragraph 4, Item 3 (a)-(1)	30,500
				Overseas		30,500 Article 17, Paragraph 4, Item 3 (a)-(2)	30,500
		Sterile medical devices	Basic	Domestic		380,000 Article 17, Paragraph 4, Item 3 (b)-(1)	380,000
				Overseas		480,000 + travel expenses Article 17, Paragraph 4, Item 3 (b)-(2)	480,000 + travel expenses
			Addition of products	Domestic		12,400 Article 17, Paragraph 4, Item 3 (b)-(1)	12,400
				Overseas		12,400 Article 17, Paragraph 4, Item 3 (b)-(2)	12,400
		Other medical devices	Basic	Domestic		336,500 Article 17, Paragraph 4, Item 3 (c)-(1)	336,500
				Overseas		409,400 + travel expenses Article 17, Paragraph 4, Item 3 (c)-(2)	409,400 + travel expenses
			Addition of products	Domestic		9,600 Article 17, Paragraph 4, Item 3 (c)-(1)	9,600
				Overseas		9,600 Article 17, Paragraph 4, Item 3 (c)-(2)	9,600
		Packaging, labeling, storage, external testing, etc.	Basic	Domestic		258,500 Article 17, Paragraph 4, Item 3 (d)-(1) and Paragraph 5, Item 2 (a)	258,500
				Overseas		338,100 + travel expenses Article 17, Paragraph 4, Item 3 (d)-(2) and Paragraph 5, Item 2 (b)	338,100 + travel expenses
			Addition of products	Domestic		6,700 Article 17, Paragraph 4, Item 3 (d)-(1) and Paragraph 5, Item 2 (a)	6,700
				Overseas		6,700 Article 17, Paragraph 4, Item 3 (d)-(2) and Paragraph 5, Item 2 (b)	6,700

Classification			User fees		
			Review	Inspection	Total
GLP Inspection of medical devices					
	GLP	Domestic		2,062,400	2,062,400
				Article 17, Paragraph 3, Item 1 (a) and Paragraph 9, Item 2 (a)-(1)	
		Overseas		2,282,600 + travel expenses	2,282,600 + travel expenses
				Article 17, Paragraph 3, Item 1 (b) and Paragraph 9, Item 2 (a)-(2)	
GCP inspection of medical devices					
	GCP	Domestic		635,300	635,300
				Article 17, Paragraph 3, Item 3 (a)	
		Overseas		918,400 + travel expenses	918,400 + travel expenses
				Article 17, Paragraph 3, Item 3 (b)	
Re-examination of medical devices					
	New medical devices		502,600	624,600	1,127,200
			Article 17, Paragraph 8, Item 2 (a)	Article 17, Paragraph 9, Item 1 (c)	
	Medical devices other than the new ones		51,600	624,600	676,200
			Article 17, Paragraph 8, Item 2 (b)	Article 17, Paragraph 9, Item 1 (c)	
	GPSP	Domestic		610,700	610,700
				Article 17, Paragraph 9, Item 2 (b)-(5)	
		Overseas		949,000 + travel expenses	949,000 + travel expenses
				Article 17, Paragraph 9, Item 2 (b)-(6)	

8-3. List of user fees under Article 4 of the Administrative Instructions for the Statement of Operating Procedures on Reviews and Related Services of the Pharmaceuticals and Medical Devices Agency

(The Cabinet order specifying the following user fees on April 1, 2012. Please refer to the Table 9-3 that compares the previous user fees with the revised user fees, effective as of February 21, 2014.)

(Yen)

		User fees		Timing of payment
Consultations				
Drugs	Procedural consultation for drugs	per consultation	139,800 yen	Payment by the date of consultation application after arrangement of the consultation date
	Consultation on bioequivalence testing, etc. for drugs	per consultation	556,000 yen	
	Safety consultation for drugs	per consultation	1,782,800 yen	
	Quality consultation for drugs	per consultation	1,478,300 yen	
	Consultation before start of phase I study for drugs (non-orphan drugs)	per consultation	4,239,400 yen	
	Consultation before start of phase I study for drugs (orphan drugs)	per consultation	3,186,100 yen	
	Consultation before start of early phase II study for drugs (non-orphan drugs)	per consultation	1,623,000 yen	
	Consultation before start of early phase II study for drugs (orphan drugs)	per consultation	1,222,500 yen	
	Consultation before start of late phase II study for drugs (non-orphan drugs)	per consultation	3,028,400 yen	
	Consultation before start of late phase II study for drugs (orphan drugs)	per consultation	2,274,200 yen	
	Consultation after completion of phase II study for drugs (non-orphan drugs)	per consultation	6,011,500 yen	
	Consultation after completion of phase II study for drugs (orphan drugs)	per consultation	4,515,700 yen	
	Pre-application consultation for drugs (non-orphan drugs)	per consultation	6,011,400 yen	
	Pre-application consultation for drugs (orphan drugs)	per consultation	4,513,000 yen	
	Consultation on protocols of clinical trials for reevaluation and re-examination of drugs	per consultation	3,320,600 yen	
	Consultation at completion of clinical trials for reevaluation and re-examination of drugs	per consultation	3,319,400 yen	
	Additional consultation for drugs (non-orphan drugs)	per consultation	2,675,600 yen	
	Additional consultation for drugs (orphan drugs)	per consultation	2,010,400 yen	
	Consultation on GLP/GCP compliance for drugs (non-orphan drugs)	per consultation	2,875,500 yen	
	Consultation on GLP/GCP compliance for drugs (orphan drugs)	per consultation	2,157,200 yen	
	Prior assessment consultation for drugs (quality)	per consultation	3,049,300 yen	
	Prior assessment consultation for drugs (non-clinical: toxicity)	per consultation	2,061,100 yen	
	Prior assessment consultation for drugs (non-clinical: pharmacology)	per consultation	2,061,100 yen	
	Prior assessment consultation for drugs (non-clinical: pharmacokinetics)	per consultation	2,061,100 yen	
	Prior assessment consultation for drugs (phase I study)	per consultation	3,484,700 yen	
	Prior assessment consultation for drugs (phase II study)	per consultation	4,497,400 yen	
	Prior assessment consultation for drugs (phase II / III study)	per consultation	6,985,700 yen	
	Consultation on drug product eligibility for priority review	per consultation	823,300 yen	
	Consultation on drug product eligibility for priority review (with pre-application consultation for drugs)	per consultation	168,700 yen	
	Consultation on pharmacogenomics/biomarkers (qualification)	per consultation	3,028,400 yen	
	Consultation on pharmacogenomics/biomarkers (key points of clinical trial protocols)	per consultation	1,111,000 yen	
	Additional consultation on pharmacogenomics/biomarkers (qualification)	per consultation	921,900 yen	
	Additional consultation on pharmacogenomics/biomarkers (key points of clinical trial protocols)	per consultation	403,100 yen	
	Consultation on R&D strategy for drugs	per consultation	1,498,800 yen	
	Consultation on R&D strategy for drugs (universities/research institutions and venture companies meeting requirements specified separately*)	per consultation	149,800 yen	
	Consultations on bioequivalence of generic drugs	per consultation	997,500 yen	
	Quality consultation for generic drugs	per consultation	491,800 yen	
	Pre-application consultation for switch OTC drugs	per consultation	1,501,100 yen	
	Consultation on key points of clinical trial protocols for OTC drugs	per consultation	502,500 yen	
	Consultation on appropriateness of development of new OTC drugs	per consultation	199,100 yen	
	Pre-development consultation for medical devices	per consultation	135,200 yen	
	Safety consultation for medical devices (excluding biological medical devices)	per consultation	822,100 yen	
	Safety consultation for biological medical devices	per consultation	910,100 yen	
	Quality consultation for medical devices (excluding biological medical devices)	per consultation	775,400 yen	
	Quality consultation for biological medical devices	per consultation	921,400 yen	
	Performance testing consultation for medical devices	per consultation	845,900 yen	
	Clinical evaluation consultation for medical devices	per consultation	1,026,600 yen	
	Exploratory clinical trial consultation for medical devices	per consultation	1,105,300 yen	
	Clinical trial consultation for medical devices	per consultation	2,413,000 yen	
	Pre-application consultation for medical devices	per consultation	2,413,000 yen	
	Application procedure consultation for medical devices	per consultation	135,200 yen	
	Additional consultation for medical devices	per consultation	1,130,100 yen	
	Consultation on GLP/GCP compliance for medical devices	per consultation	772,900 yen	

(Yen)

			User fees		Timing of payment
Devices and in vitro diagnostics	Prior assessment consultation for medical devices (quality)		per consultation	2,982,300 yen	Payment by the date of consultation application after arrangement of the consultation date
	Prior assessment consultation for medical devices (non-clinical)		per consultation	2,982,300 yen	
	Prior assessment consultation for medical devices (clinical)		per consultation	4,490,800 yen	
	Consultation on R&D strategy for medical devices		per consultation	849,700 yen	
	Consultation on R&D strategy for medical devices (Universities/research institutions and venture companies meeting requirements specified separately*)		per consultation	84,900 yen	
	Pre-development consultation for in vitro diagnostics		per consultation	139,900 yen	
	Quality consultation for in vitro diagnostics		per consultation	345,500 yen	
	Consultation on conformity with standards for in vitro diagnostics		per consultation	442,800 yen	
	Clinical evaluation consultation for in vitro diagnostics		per consultation	675,400 yen	
	Clinical performance study consultation for in vitro diagnostics		per consultation	1,594,700 yen	
	Pre-application consultation for in vitro diagnostics		per consultation	1,594,700 yen	
	Application procedure consultation for in vitro diagnostics		per consultation	135,200 yen	
	Additional consultation for in vitro diagnostics		per consultation	927,500 yen	
	Prior assessment consultation for in vitro diagnostics (quality)		per consultation	2,982,300 yen	
	Prior assessment consultation for in vitro diagnostics (non-clinical)		per consultation	2,982,300 yen	
	Prior assessment consultation for in vitro diagnostics (clinical)		per consultation	4,490,800 yen	
	Consultation on preparation of documents for gene therapy products		per consultation	223,500 yen	
Simple consultations	Generic drugs		per consultation	21,000 yen	
	OTC drugs		per consultation	21,000 yen	
	Quasi-drugs (including pesticides and rodenticides)		per consultation	21,000 yen	
	Medical devices or in vitro diagnostics		per consultation	34,300 yen	
	Preparation of new drug applications		per consultation	21,000 yen	
	GMP/QMS inspection		per consultation	24,700 yen	
Assessment for designation of priority consultation products					
	Assessment for designation of drugs for priority consultation		per application	818,800 yen	Request to PMDA after advanced payment
	Assessment for designation of medical devices or in vitro diagnostics fo rpriority consultation		per application	818,800 yen	
GLP inspection of test facilities					
	All test items (for drugs and medical devices)		per facility	3,023,800 yen	Request to PMDA after advanced payment
	All test items (for drugs or medical devices)	Domestic	per facility	2,062,400 yen	
		Overseas	per facility	2,282,600 yen + travel expenses	
	Limited test items		per facility	995,200 yen	
	Additional compliance accreditation		per facility	932,600 yen	
Confirmation of certification on drugs, etc.					
	GMP certification on investigational products (with on-site inspection)		per product of one facility	739,800 yen	Request to PMDA after advanced payment
	GMP certification on investigational products (without on-site inspection)		per product of one facility	15,100 yen	
	Certification of drug products		per product	15,100 yen	
	Other certifications		per matter of one product	8,400 yen	
Use of document storage rooms					
			per day per room	3,000 yen	Payment upon invoice sent from PMDA after the end of the period of use

* Universities/research institutions and venture companies meeting requirements specified separately.
All of the following requirements should be met in principle:
For universities/research institutions

- Having not received 90 million yen or more (in the case of drugs) or 50 million yen or more (in the case of medical devices) from the government, to proceed with the research on the seed-stage resource
- Having not received research expenses from a pharmaceutical company/medical device company under a joint research agreement, etc., toward practical application of the seed-stage resource

For venture companies

- Being a small or medium-sized company (with 300 employees or less, or capitalized at 300 million yen or less)
- Any other corporation does not hold 1/2 or more of the total number of shares or investments
- Two or more other corporations do not hold 2/3 or more of the total number of shares or investments
- For the preceding fiscal year, profits of the term have not been reported, or profits of the term have been reported but without operating revenue

List of user fees for reviews etc. of pharmaceuticals, quasi-drugs, and cosmetics based on the Pharmaceutical Affairs Act (Act No. 145, 1960)

Note) The lower rows in the user fees column indicate the applicable articles of the cabinet order on fees related to the Pharmaceutical Affairs Act.

New

(Unit: yen)

Classification		User fees		
		Review	Inspection	Total
Assessment for manufacturing license of drugs				
New license	On-site		152,300	152,300
			Article 16, Paragraph 1, Item 1, a	
	Document		114,700	114,700
			Article 16, Paragraph 1, Item 1, b	
Change/addition of classification	On-site		100,200	100,200
			Article 16, Paragraph 1, Item 2, a	
	Document		56,900	56,900
			Article 16, Paragraph 1, Item 2, b	
Renewal of existing license	On-site		100,200	100,200
			Article 16, Paragraph 1, Item 3, a	
	Document		56,900	56,900
			Article 16, Paragraph 1, Item 3, b	
Assessment for foreign manufacturers' accreditation of drugs				
New accreditation	On-site		137,100 ＋travel expenses	137,100 ＋travel expenses
			Article 16, Paragraph 2, Item 1, a	
	Document		59,700	59,700
			Article 16, Paragraph 2, Item 1, b	
Change/addition of classification	On-site		66,400 ＋travel expenses	66,400 ＋travel expenses
			Article 16, Paragraph 2, Item 2, a	
	Document		40,900	40,900
			Article 16, Paragraph 2, Item 2, b	
Renewal of existing accreditation	On-site		66,400 ＋travel expenses	66,400 ＋travel expenses
			Article 16, Paragraph 2, Item 3, a	
	Document		40,900	40,900
			Article 16, Paragraph 2, Item 3, b	

Old

(Unit: yen)

Classification		User fees		
		Review	Inspection	Total
Assessment for manufacturing license of drugs				
New license	On-site		148,100	148,100
			Article 16, Paragraph 1, Item 1, a	
	Document		111,500	111,500
			Article 16, Paragraph 1, Item 1, b	
Change/addition of classification	On-site		97,400	97,400
			Article 16, Paragraph 1, Item 2, a	
	Document		55,300	55,300
			Article 16, Paragraph 1, Item 2, b	
Renewal of existing license	On-site		97,400	97,400
			Article 16, Paragraph 1, Item 3, a	
	Document		55,300	55,300
			Article 16, Paragraph 1, Item 3, b	
Assessment for foreign manufacturers' accreditation of drugs				
New accreditation	On-site		133,300 ＋travel expenses	133,300 ＋travel expenses
			Article 16, Paragraph 2, Item 1, a	
	Document		58,100	58,100
			Article 16, Paragraph 2, Item 1, b	
Change/addition of classification	On-site		64,600 ＋travel expenses	64,600 ＋travel expenses
			Article 16, Paragraph 2, Item 2, a	
	Document		39,700	39,700
			Article 16, Paragraph 2, Item 2, b	
Renewal of existing accreditation	On-site		64,600 ＋travel expenses	64,600 ＋travel expenses
			Article 16, Paragraph 2, Item 3, a	
	Document		39,700	39,700
			Article 16, Paragraph 2, Item 3, b	

New

(Unit: yen)

Classification			User fees		
			Review	Inspection	Total
Review for approval of drugs (new approval)					
New drugs (No. 1) (non-orphan drugs)		First application products	23,788,100	6,747,000	30,535,100
			Article 17, Paragraph 1, Item 1, a (1)	Article 17, Paragraph 2, Item 1, a	
		Line extension products	2,464,000	1,686,600	4,150,600
			Article 17, Paragraph 1, Item 1, a (3)	Article 17, Paragraph 2, Item 1, c	
New drugs (No. 1) (orphan drugs)		First application products	19,934,100	3,379,900	23,314,000
			Article 17, Paragraph 1, Item 1, a (2)	Article 17, Paragraph 2, Item 1, b	
		Line extension products	2,061,500	841,500	2,903,000
			Article 17, Paragraph 1, Item 1, a (4)	Article 17, Paragraph 2, Item 1, d	
New drugs (No. 2) (non-orphan drugs)		First application products	11,353,100	2,533,600	13,886,700
			Article 17, Paragraph 1, Item 1, a (5)	Article 17, Paragraph 2, Item 1, e	
		Line extension products	1,174,300	633,600	1,807,900
			Article 17, Paragraph 1, Item 1, a (6)	Article 17, Paragraph 2, Item 1, f	
New drugs (No. 2) (orphan drugs)		First application products	9,345,700	1,267,700	10,613,400
			Article 17, Paragraph 1, Item 1, a (7)	Article 17, Paragraph 2, Item 1, g	
		Line extension products	1,004,100	319,000	1,323,100
			Article 17, Paragraph 1, Item 1, a (8)	Article 17, Paragraph 2, Item 1, h	
Generic prescription drugs (with inspections)			412,100	220,100	632,200
			Article 17, Paragraph 1, Item 1, a (9)	Article 17, Paragraph 2, Item 1, i	
OTC drugs	Switch to OTC status, etc.	First application products	1,291,600		1,291,600
			Article 17, Paragraph 1, Item 1, a (10)		
		Line extension products	1,291,600		1,291,600
			Article 17, Paragraph 1, Item 1, a (10)		
	Others		110,300		110,300
			Article 17, Paragraph 1, Item 1, a (11)		
In vitro diagnostics (without approval standards)			584,100		584,100
			Article 17, Paragraph 1, Item 1, a (14)		
In vitro diagnostics (with approval standards)		Basic	282,900		282,900
			Article 17, Paragraph 1, Item 1, a (13)		
		Addition of series	60,300		60,300
			Article 17, Paragraph 1, Item 1, a (12)		
Quasi-drugs/cosmetics			63,500		63,500
			Article 17, Paragraph 1, Item 1, b & c		
New application for change or replacement of brand name			35,600		35,600
			Article 17, Paragraph 1, Item 1, e		

Old

(Unit: yen)

Classification			User fees		
			Review	Inspection	Total
Review for approval of drugs (new approval)					
New drugs (No. 1) (non-orphan drugs)		First application products	23,788,100	6,559,600	30,347,700
			Article 17, Paragraph 1, Item 1, a (1)	Article 17, Paragraph 2, Item 1, a	
		Line extension products	2,464,000	1,639,800	4,103,800
			Article 17, Paragraph 1, Item 1, a (3)	Article 17, Paragraph 2, Item 1, c	
New drugs (No. 1) (orphan drugs)		First application products	19,934,100	3,286,000	23,220,100
			Article 17, Paragraph 1, Item 1, a (2)	Article 17, Paragraph 2, Item 1, b	
		Line extension products	2,061,500	818,100	2,879,600
			Article 17, Paragraph 1, Item 1, a (4)	Article 17, Paragraph 2, Item 1, d	
New drugs (No. 2) (non-orphan drugs)		First application products	11,353,100	2,463,200	13,816,300
			Article 17, Paragraph 1, Item 1, a (5)	Article 17, Paragraph 2, Item 1, e	
		Line extension products	1,174,300	615,900	1,790,200
			Article 17, Paragraph 1, Item 1, a (6)	Article 17, Paragraph 2, Item 1, f	
New drugs (No. 2) (orphan drugs)		First application products	9,345,700	1,232,500	10,578,200
			Article 17, Paragraph 1, Item 1, a (7)	Article 17, Paragraph 2, Item 1, g	
		Line extension products	1,004,100	310,100	1,314,200
			Article 17, Paragraph 1, Item 1, a (8)	Article 17, Paragraph 2, Item 1, h	
Generic prescription drugs (with inspections)			412,100	214,000	626,100
			Article 17, Paragraph 1, Item 1, a (9)	Article 17, Paragraph 2, Item 1, i	
OTC drugs	Switch to OTC status, etc.	First application products	1,291,600		1,291,600
			Article 17, Paragraph 1, Item 1, a (10)		
		Line extension products	1,291,600		1,291,600
			Article 17, Paragraph 1, Item 1, a (10)		
	Others		110,300		110,300
			Article 17, Paragraph 1, Item 1, a (11)		
In vitro diagnostics (without approval standards)			584,100		584,100
			Article 17, Paragraph 1, Item 1, a (14)		
In vitro diagnostics (with approval standards)		Basic	282,900		282,900
			Article 17, Paragraph 1, Item 1, a (13)		
		Addition of series	60,300		60,300
			Article 17, Paragraph 1, Item 1, a (12)		
Quasi-drugs/cosmetics			63,500		63,500
			Article 17, Paragraph 1, Item 1, b & c		
New application for change or replacement of brand name			35,600		35,600
			Article 17, Paragraph 1, Item 1, e		

New

(Unit: yen)

Classification				User fees		
				Review	Inspection	Total
Review for approval of drugs (approval for partial changes to approved matters)						
New drugs (No. 1) (non-orphan drugs)	Changes in indications, etc.		First application products	10,190,500	2,533,600	12,724,100
				Article 17, Paragraph 1, Item 2, a (1)	Article 17, Paragraph 2, Item 2, a	
			Line extension products	1,057,400	633,600	1,691,000
				Article 17, Paragraph 1, Item 2, a (2)	Article 17, Paragraph 2, Item 2, b	
	Others			205,100	124,200	329,300
				Article 17, Paragraph 1, Item 2, a (3)	Article 17, Paragraph 2, Item 2, c	
New drugs (No. 1) (orphan drugs)	Changes in indications, etc.		First application products	8,434,300	1,267,700	9,702,000
				Article 17, Paragraph 1, Item 2, a (4)	Article 17, Paragraph 2, Item 2, d	
			Line extension products	875,600	319,000	1,194,600
				Article 17, Paragraph 1, Item 2, a (5)	Article 17, Paragraph 2, Item 2, e	
	Others			132,700	112,900	245,600
				Article 17, Paragraph 1, Item 2, a (6)	Article 17, Paragraph 2, Item 2, f	
New drugs (No. 2) (non-orphan drugs)	Changes in indications, etc.		First application products	10,190,500	2,533,600	12,724,100
				Article 17, Paragraph 1, Item 2, a (1)	Article 17, Paragraph 2, Item 2, a	
			Line extension products	1,057,400	633,600	1,691,000
				Article 17, Paragraph 1, Item 2, a (2)	Article 17, Paragraph 2, Item 2, b	
	Others			205,100	124,200	329,300
				Article 17, Paragraph 1, Item 2, a (3)	Article 17, Paragraph 2, Item 2, c	
New drugs (No. 2) (orphan drugs)	Changes in indications, etc.		First application products	8,434,300	1,267,700	9,702,000
				Article 17, Paragraph 1, Item 2, a (4)	Article 17, Paragraph 2, Item 2, d	
			Line extension products	875,600	319,000	1,194,600
				Article 17, Paragraph 1, Item 2, a (5)	Article 17, Paragraph 2, Item 2, e	
	Others			132,700	112,900	245,600
				Article 17, Paragraph 1, Item 2, a (6)	Article 17, Paragraph 2, Item 2, f	
Generic prescription drugs (with inspections)	Changes in indications, etc.		First application products	10,190,500	2,533,600	12,724,100
				Article 17, Paragraph 1, Item 2, a (1)	Article 17, Paragraph 2, Item 2, a	
			Line extension products	1,057,400	633,600	1,691,000
				Article 17, Paragraph 1, Item 2, a (2)	Article 17, Paragraph 2, Item 2, b	
	Changes based on guidelines, etc.			35,600		35,600
				Article 17, Paragraph 1, Item 2, a (7)		
	Others			205,100	124,200	329,300
				Article 17, Paragraph 1, Item 2, a (3)	Article 17, Paragraph 2, Item 2, c	
OTC drugs	Switch to OTC status, etc.	Changes in indications, etc.	First application products	10,190,500		10,190,500
				Article 17, Paragraph 1, Item 2, a (1)		
			Line extension products	1,057,400		1,057,400
				Article 17, Paragraph 1, Item 2, a (2)		
	Changes based on guidelines, etc.			35,600		35,600
				Article 17, Paragraph 1, Item 2, a (7)		
	Others			56,400		56,400
				Article 17, Paragraph 1, Item 2, a (8)		
In vitro diagnostics (without approval standards)				295,800		295,800
				Article 17, Paragraph 1, Item 2, a (11)		
In vitro diagnostics (with approval standards)			Basic	143,500		143,500
				Article 17, Paragraph 1, Item 2, a (10)		
			Addition of series	31,900		31,900
				Article 17, Paragraph 1, Item 2, a (9)		
Quasi-drugs/cosmetics				35,600		35,600
				Article 17, Paragraph 1, Item 2, b & c		

Old

(Unit: yen)

Classification				User fees		
				Review	Inspection	Total
Review for approval of drugs (approval for partial changes to approved matters)						
New drugs (No. 1) (non-orphan drugs)	Changes in indications, etc.		First application products	10,190,500	2,463,200	12,653,700
				Article 17, Paragraph 1, Item 2, a (1)	Article 17, Paragraph 2, Item 2, a	
			Line extension products	1,057,400	615,900	1,673,300
				Article 17, Paragraph 1, Item 2, a (2)	Article 17, Paragraph 2, Item 2, b	
	Others			205,100	120,700	325,800
				Article 17, Paragraph 1, Item 2, a (3)	Article 17, Paragraph 2, Item 2, c	
New drugs (No. 1) (orphan drugs)	Changes in indications, etc.		First application products	8,434,300	1,232,500	9,666,800
				Article 17, Paragraph 1, Item 2, a (4)	Article 17, Paragraph 2, Item 2, d	
			Line extension products	875,600	310,100	1,185,700
				Article 17, Paragraph 1, Item 2, a (5)	Article 17, Paragraph 2, Item 2, e	
	Others			132,700	109,800	242,500
				Article 17, Paragraph 1, Item 2, a (6)	Article 17, Paragraph 2, Item 2, f	
New drugs (No. 2) (non-orphan drugs)	Changes in indications, etc.		First application products	10,190,500	2,463,200	12,653,700
				Article 17, Paragraph 1, Item 2, a (1)	Article 17, Paragraph 2, Item 2, a	
			Line extension products	1,057,400	615,900	1,673,300
				Article 17, Paragraph 1, Item 2, a (2)	Article 17, Paragraph 2, Item 2, b	
	Others			205,100	120,700	325,800
				Article 17, Paragraph 1, Item 2, a (3)	Article 17, Paragraph 2, Item 2, c	
New drugs (No. 2) (orphan drugs)	Changes in indications, etc.		First application products	8,434,300	1,232,500	9,666,800
				Article 17, Paragraph 1, Item 2, a (4)	Article 17, Paragraph 2, Item 2, d	
			Line extension products	875,600	310,100	1,185,700
				Article 17, Paragraph 1, Item 2, a (5)	Article 17, Paragraph 2, Item 2, e	
	Others			132,700	109,800	242,500
				Article 17, Paragraph 1, Item 2, a (6)	Article 17, Paragraph 2, Item 2, f	
Generic prescription drugs (with inspections)	Changes in indications, etc.		First application products	10,190,500	2,463,200	12,653,700
				Article 17, Paragraph 1, Item 2, a (1)	Article 17, Paragraph 2, Item 2, a	
			Line extension products	1,057,400	615,900	1,673,300
				Article 17, Paragraph 1, Item 2, a (2)	Article 17, Paragraph 2, Item 2, b	
	Changes based on guidelines, etc.			35,600		35,600
				Article 17, Paragraph 1, Item 2, a (7)		
	Others			205,100	120,700	325,800
				Article 17, Paragraph 1, Item 2, a (3)	Article 17, Paragraph 2, Item 2, c	
OTC drugs	Switch to OTC status, etc.	Changes in indications, etc.	First application products	10,190,500		10,190,500
				Article 17, Paragraph 1, Item 2, a (1)		
			Line extension products	1,057,400		1,057,400
				Article 17, Paragraph 1, Item 2, a (2)		
	Changes based on guidelines, etc.			35,600		35,600
				Article 17, Paragraph 1, Item 2, a (7)		
	Others			56,400		56,400
				Article 17, Paragraph 1, Item 2, a (8)		
In vitro diagnostics (without approval standards)				295,800		295,800
				Article 17, Paragraph 1, Item 2, a (11)		
In vitro diagnostics (with approval standards)			Basic	143,500		143,500
				Article 17, Paragraph 1, Item 2, a (10)		
			Addition of series	31,900		31,900
				Article 17, Paragraph 1, Item 2, a (9)		
Quasi-drugs/cosmetics				35,600		35,600
				Article 17, Paragraph 1, Item 2, b & c		

New

(Unit: yen)

Classification				User fees		
				Review	Inspection	Total
GMP inspection of drugs						
Approval, partial change and manufacture for export	New drugs		Domestic		760,900 Article 17, Paragraph 4, Item 1, b (1)	760,900
			Overseas		960,200 ＋travel expenses Article 17, Paragraph 4, Item 1, b (2)	960,200 ＋travel expenses
	Biological drugs/Radiopharmaceuticals, etc.		Domestic		685,100 Article 17, Paragraph 4, Item 1, a (1)	685,100
			Overseas		868,600 ＋travel expenses Article 17, Paragraph 4, Item 1, a (2)	868,600 ＋travel expenses
	Sterile drugs/Sterile quasi-drugs		Domestic		207,100 Article 17, Paragraph 4, Item 1, c (1)	207,100
			Overseas		236,400 ＋travel expenses Article 17, Paragraph 4, Item 1, c (2)	236,400 ＋travel expenses
	Other drugs/quasi-drugs		Domestic		145,300 Article 17, Paragraph 4, Item 1, d (1)	145,300
			Overseas		159,900 ＋travel expenses Article 17, Paragraph 4, Item 1, d (2)	159,900 ＋travel expenses
	Packaging, labeling, storage, external testing, etc.		Domestic		65,600 Article 17, Paragraph 4, Item 2, a & Paragraph 5, Item 1, a	65,600
			Overseas		87,200 ＋travel expenses Article 17, Paragraph 4, Item 2, b & Paragraph 5, Item 1, b	87,200 ＋travel expenses
Renewal of the above	Biological drugs/Radiopharmaceuticals, etc.	Basic	Domestic		448,500 Article 17, Paragraph 4, Item 3, a (1)	448,500
			Overseas		570,100 ＋travel expenses Article 17, Paragraph 4, Item 3, a (2)	570,100 ＋travel expenses
		Addition of products	Domestic		31,400 Article 17, Paragraph 4, Item 3, a (1)	31,400
			Overseas		31,400 Article 17, Paragraph 4, Item 3, a (2)	31,400
	Sterile drugs/Sterile quasi-drugs	Basic	Domestic		390,900 Article 17, Paragraph 4, Item 3, b (1)	390,900
			Overseas		493,800 ＋travel expenses Article 17, Paragraph 4, Item 3, b (2)	493,800 ＋travel expenses
		Addition of products	Domestic		12,800 Article 17, Paragraph 4, Item 3, b (1)	12,800
			Overseas		12,800 Article 17, Paragraph 4, Item 3, b (2)	12,800
	Other drugs/quasi-drugs	Basic	Domestic		346,100 Article 17, Paragraph 4, Item 3, c (1)	346,100
			Overseas		421,100 ＋travel expenses Article 17, Paragraph 4, Item 3, c (2)	421,100 ＋travel expenses
		Addition of products	Domestic		9,900 Article 17, Paragraph 4, Item 3, c (1)	9,900
			Overseas		9,900 Article 17, Paragraph 4, Item 3, c (2)	9,900
	Packaging, labeling, storage, external testing, etc.	Basic	Domestic		265,900 Article 17, Paragraph 4, Item 3, d (1) & Paragraph 5, Item 2, a	265,900
			Overseas		347,800 ＋travel expenses Article 17, Paragraph 4, Item 3, d (2) & Paragraph 5, Item 2, b	347,800 ＋travel expenses
		Addition of products	Domestic		6,900 Article 17, Paragraph 4, Item 3, d (1) & Paragraph 5, Item 2, a	6,900
			Overseas		6,900 Article 17, Paragraph 4, Item 3, d (2) & Paragraph 5, Item 2, b	6,900

Old

(Unit: yen)

Classification				User fees		
				Review	Inspection	Total
GMP inspection of drugs						
Approval, partial change and manufacture for export	New drugs		Domestic		739,800 Article 17, Paragraph 4, Item 1, b (1)	739,800
			Overseas		933,500 ＋travel expenses Article 17, Paragraph 4, Item 1, b (2)	933,500 ＋travel expenses
	Biological drugs/Radiopharmaceuticals, etc.		Domestic		666,100 Article 17, Paragraph 4, Item 1, a (1)	666,100
			Overseas		844,400 ＋travel expenses Article 17, Paragraph 4, Item 1, a (2)	844,400 ＋travel expenses
	Sterile drugs/Sterile quasi-drugs		Domestic		201,300 Article 17, Paragraph 4, Item 1, c (1)	201,300
			Overseas		229,800 ＋travel expenses Article 17, Paragraph 4, Item 1, c (2)	229,800 ＋travel expenses
	Other drugs/quasi-drugs		Domestic		141,200 Article 17, Paragraph 4, Item 1, d (1)	141,200
			Overseas		155,400 ＋travel expenses Article 17, Paragraph 4, Item 1, d (2)	155,400 ＋travel expenses
	Packaging, labeling, storage, external testing, etc.		Domestic		63,800 Article 17, Paragraph 4, Item 2, a & Paragraph 5, Item 1, a	63,800
			Overseas		84,800 ＋travel expenses Article 17, Paragraph 4, Item 2, b & Paragraph 5, Item 1, b	84,800 ＋travel expenses
Renewal of the above	Biological drugs/Radiopharmaceuticals, etc.	Basic	Domestic		436,000 Article 17, Paragraph 4, Item 3, a (1)	436,000
			Overseas		554,200 ＋travel expenses Article 17, Paragraph 4, Item 3, a (2)	554,200 ＋travel expenses
		Addition of products	Domestic		30,500 Article 17, Paragraph 4, Item 3, a (1)	30,500
			Overseas		30,500 Article 17, Paragraph 4, Item 3, a (2)	30,500
	Sterile drugs/Sterile quasi-drugs	Basic	Domestic		380,000 Article 17, Paragraph 4, Item 3, b (1)	380,000
			Overseas		480,000 ＋travel expenses Article 17, Paragraph 4, Item 3, b (2)	480,000 ＋travel expenses
		Addition of products	Domestic		12,400 Article 17, Paragraph 4, Item 3, b (1)	12,400
			Overseas		12,400 Article 17, Paragraph 4, Item 3, b (2)	12,400
	Other drugs/quasi-drugs	Basic	Domestic		336,500 Article 17, Paragraph 4, Item 3, c (1)	336,500
			Overseas		409,400 ＋travel expenses Article 17, Paragraph 4, Item 3, c (2)	409,400 ＋travel expenses
		Addition of products	Domestic		9,600 Article 17, Paragraph 4, Item 3, c (1)	9,600
			Overseas		9,600 Article 17, Paragraph 4, Item 3, c (2)	9,600
	Packaging, labeling, storage, external testing, etc.	Basic	Domestic		258,500 Article 17, Paragraph 4, Item 3, d (1) & Paragraph 5, Item 2, a	258,500
			Overseas		338,100 ＋travel expenses Article 17, Paragraph 4, Item 3, d (2) & Paragraph 5, Item 2, b	338,100 ＋travel expenses
		Addition of products	Domestic		6,700 Article 17, Paragraph 4, Item 3, d (1) & Paragraph 5, Item 2, a	6,700
			Overseas		6,700 Article 17, Paragraph 4, Item 3, d (2) & Paragraph 5, Item 2, b	6,700

New

(Unit: yen)

Classification			User fees		
			Review	Inspection	Total
GLP inspection of drugs					
GLP	Domestic			2,121,400 Article 17, Paragraph 3, Item 1, a & Paragraph 9, Item 2, a (1)	2,121,400
	Overseas			2,347,900 ＋travel expenses Article 17, Paragraph 3, Item 1, b & Paragraph 9, Item 2, a (2)	2,347,900 ＋travel expenses
GCP inspection of drugs					
New GCP	First application products	Domestic		2,801,000 Article 17, Paragraph 3, Item 2, a	2,801,000
		Overseas		3,098,000 ＋travel expenses Article 17, Paragraph 3, Item 2, b	3,098,000 ＋travel expenses
	Line extension products	Domestic		741,400 Article 17, Paragraph 3, Item 2, c	741,400
		Overseas		773,300 ＋travel expenses Article 17, Paragraph 3, Item 2, d	773,300 ＋travel expenses
GCP inspection of generic drugs		Domestic		663,600 Article 17, Paragraph 3, Item 2, e	663,600
		Overseas		977,400 ＋travel expenses Article 17, Paragraph 3, Item 2, f	977,400 ＋travel expenses
Re-examination of drugs					
Re-examination	First application products		806,600 Article 17, Paragraph 8, Item 1, a	2,750,100 Article 17, Paragraph 9, Item 1, a	3,556,700
	Line extension products		271,500 Article 17, Paragraph 8, Item 1, b	917,600 Article 17, Paragraph 9, Item 1, b	1,189,100
GPSP	First application products	Domestic		2,256,000 Article 17, Paragraph 9, Item 2, b (1)	2,256,000
		Overseas		2,478,500 ＋travel expenses Article 17, Paragraph 9, Item 2, b (2)	2,478,500 ＋travel expenses
	Line extension products	Domestic		774,100 Article 17, Paragraph 9, Item 2, b (3)	774,100
		Overseas		794,400 ＋travel expenses Article 17, Paragraph 9, Item 2, b (4)	794,400 ＋travel expenses

Old

(Unit: yen)

Classification			User fees		
			Review	Inspection	Total
GLP inspection of drugs					
GLP	Domestic			2,062,400 Article 17, Paragraph 3, Item 1, a & Paragraph 9, Item 2, a (1)	2,062,400
	Overseas			2,282,600 ＋travel expenses Article 17, Paragraph 3, Item 1, b & Paragraph 9, Item 2, a (2)	2,282,600 ＋travel expenses
GCP inspection of drugs					
New GCP	First application products	Domestic		2,723,200 Article 17, Paragraph 3, Item 2, a	2,723,200
		Overseas		3,011,900 ＋travel expenses Article 17, Paragraph 3, Item 2, b	3,011,900 ＋travel expenses
	Line extension products	Domestic		720,800 Article 17, Paragraph 3, Item 2, c	720,800
		Overseas		751,800 ＋travel expenses Article 17, Paragraph 3, Item 2, d	751,800 ＋travel expenses
GCP inspection of generic drugs		Domestic		645,200 Article 17, Paragraph 3, Item 2, e	645,200
		Overseas		950,200 ＋travel expenses Article 17, Paragraph 3, Item 2, f	950,200 ＋travel expenses
Re-examination of drugs					
Re-examination	First application products		806,600 Article 17, Paragraph 8, Item 1, a	2,673,700 Article 17, Paragraph 9, Item 1, a	3,480,300
	Line extension products		271,500 Article 17, Paragraph 8, Item 1, b	892,100 Article 17, Paragraph 9, Item 1, b	1,163,600
GPSP	First application products	Domestic		2,193,300 Article 17, Paragraph 9, Item 2, b (1)	2,193,300
		Overseas		2,409,600 ＋travel expenses Article 17, Paragraph 9, Item 2, b (2)	2,409,600 ＋travel expenses
	Line extension products	Domestic		752,600 Article 17, Paragraph 9, Item 2, b (3)	752,600
		Overseas		772,300 ＋travel expenses Article 17, Paragraph 9, Item 2, b (4)	772,300 ＋travel expenses

List of user fees for reviews etc. of medical devices under the Pharmaceutical Affairs Act (Act No. 145, 1960)

Note) The lower rows in the user fees column indicate the applicable articles of the cabinet order

New

(Unit: yen)

Classification			User fees		
			Review	Inspection	Total
Assessment for manufacturing license of medical devices					
New license		On-site		152,300	152,300
				Article 16, Paragraph 1, Item 1, a	
		Document		114,700	114,700
				Article 16, Paragraph 1, Item 1, b	
Change/addition of classification		On-site		100,200	100,200
				Article 16, Paragraph 1, Item 2, a	
		Document		56,900	56,900
				Article 16, Paragraph 1, Item 2, b	
Renewal of existing license		On-site		100,200	100,200
				Article 16, Paragraph 1, Item 3, a	
		Document		56,900	56,900
				Article 16, Paragraph 1, Item 3, b	
Assessment for foreign manufacturers accreditation of medical devices					
New accreditation		On-site		137,100 ＋travel expenses	137,100 ＋travel expenses
				Article 16, Paragraph 2, Item 1, a	
		Document		59,700	59,700
				Article 16, Paragraph 2, Item 1, b	
Change/addition of classification		On-site		66,400 ＋travel expenses	66,400 ＋travel expenses
				Article 16, Paragraph 2, Item 2, a	
		Document		40,900	40,900
				Article 16, Paragraph 2, Item 2, b	
Renewal of existing accreditation		On-site		66,400 ＋travel expenses	66,400 ＋travel expenses
				Article 16, Paragraph 2, Item 3, a	
		Document		40,900	40,900
				Article 16, Paragraph 2, Item 3, b	

Old

(Unit: yen)

Classification			User fees		
			Review	Inspection	Total
Assessment for manufacturing license of medical devices					
New license		On-site		148,100	148,100
				Article 16, Paragraph 1, Item 1, a	
		Document		111,500	111,500
				Article 16, Paragraph 1, Item 1, b	
Change/addition of classification		On-site		97,400	97,400
				Article 16, Paragraph 1, Item 2, a	
		Document		55,300	55,300
				Article 16, Paragraph 1, Item 2, b	
Renewal of existing license		On-site		97,400	97,400
				Article 16, Paragraph 1, Item 3, a	
		Document		55,300	55,300
				Article 16, Paragraph 1, Item 3, b	
Assessment for foreign manufacturers accreditation of medical devices					
New accreditation		On-site		133,300 ＋travel expenses	133,300 ＋travel expenses
				Article 16, Paragraph 2, Item 1, a	
		Document		58,100	58,100
				Article 16, Paragraph 2, Item 1, b	
Change/addition of classification		On-site		64,600 ＋travel expenses	64,600 ＋travel expenses
				Article 16, Paragraph 2, Item 2, a	
		Document		39,700	39,700
				Article 16, Paragraph 2, Item 2, b	
Renewal of existing accreditation		On-site		64,600 ＋travel expenses	64,600 ＋travel expenses
				Article 16, Paragraph 2, Item 3, a	
		Document		39,700	39,700
				Article 16, Paragraph 2, Item 3, b	

New

(Unit: yen)

Classification				User fees		
				Review	Inspection	Total
Review for approval of medical devices (new approval)						
Approval of medical devices (with clinical data)	Class IV	New medical devices		8,705,500	683,500	9,389,000
				Article 17, Paragraph 1, Item 1, d (1)	Article 17, Paragraph 2, Item 1, j	
		Improved medical devices		6,213,000	683,500	6,896,500
				Article 17, Paragraph 1, Item 1, d (2)	Article 17, Paragraph 2, Item 1, j	
	Class III	New medical devices		6,213,000	683,500	6,896,500
				Article 17, Paragraph 1, Item 1, d (3)	Article 17, Paragraph 2, Item 1, j	
		Improved medical devices		3,721,200	683,500	4,404,700
				Article 17, Paragraph 1, Item 1, d (4)	Article 17, Paragraph 2, Item 1, j	
	Class II	New medical devices		6,213,000	683,500	6,896,500
				Article 17, Paragraph 1, Item 1, d (3)	Article 17, Paragraph 2, Item 1, j	
		Improved medical devices		3,721,200	683,500	4,404,700
				Article 17, Paragraph 1, Item 1, d (4)	Article 17, Paragraph 2, Item 1, j	
Approval of medical devices (without approval standards, without clinical data)	Class IV	Improved medical devices		2,355,400	70,500	2,425,900
				Article 17, Paragraph 1, Item 1, d (7)	Article 17, Paragraph 2, Item 1, k	
		Generic medical devices		1,767,700	70,500	1,838,200
				Article 17, Paragraph 1, Item 1, d (8)	Article 17, Paragraph 2, Item 1, k	
	Class III	Improved medical devices		1,409,900	70,500	1,480,400
				Article 17, Paragraph 1, Item 1, d (9)	Article 17, Paragraph 2, Item 1, k	
		Generic medical devices		1,409,900	70,500	1,480,400
				Article 17, Paragraph 1, Item 1, d (9)	Article 17, Paragraph 2, Item 1, k	
	Class II	Improved medical devices		1,409,900	70,500	1,480,400
				Article 17, Paragraph 1, Item 1, d (9)	Article 17, Paragraph 2, Item 1, k	
		Generic medical devices		1,409,900	70,500	1,480,400
				Article 17, Paragraph 1, Item 1, d (9)	Article 17, Paragraph 2, Item 1, k	
Approval of medical devices (with approval standards, without clinical data)	Class IV			429,200	70,500	499,700
				Article 17, Paragraph 1, Item 1, d (5)	Article 17, Paragraph 2, Item 1, k	
	Class III			344,100	70,500	414,600
				Article 17, Paragraph 1, Item 1, d (6)	Article 17, Paragraph 2, Item 1, k	
	Class II			344,100	70,500	414,600
				Article 17, Paragraph 1, Item 1, d (6)	Article 17, Paragraph 2, Item 1, k	
Change of brand name				35,600		35,600
				Article 17, Paragraph 1, Item 1, e		

Old

(Unit: yen)

Classification				User fees		
				Review	Inspection	Total
Review for approval of medical devices (new approval)						
Approval of medical devices (with clinical data)	Class IV	New medical devices		8,705,500	664,500	9,370,000
				Article 17, Paragraph 1, Item 1, d (1)	Article 17, Paragraph 2, Item 1, j	
		Improved medical devices		6,213,000	664,500	6,877,500
				Article 17, Paragraph 1, Item 1, d (2)	Article 17, Paragraph 2, Item 1, j	
	Class III	New medical devices		6,213,000	664,500	6,877,500
				Article 17, Paragraph 1, Item 1, d (3)	Article 17, Paragraph 2, Item 1, j	
		Improved medical devices		3,721,200	664,500	4,385,700
				Article 17, Paragraph 1, Item 1, d (4)	Article 17, Paragraph 2, Item 1, j	
	Class II	New medical devices		6,213,000	664,500	6,877,500
				Article 17, Paragraph 1, Item 1, d (3)	Article 17, Paragraph 2, Item 1, j	
		Improved medical devices		3,721,200	664,500	4,385,700
				Article 17, Paragraph 1, Item 1, d (4)	Article 17, Paragraph 2, Item 1, j	
Approval of medical devices (without approval standards, without clinical data)	Class IV	Improved medical devices		2,355,400	68,500	2,423,900
				Article 17, Paragraph 1, Item 1, d (7)	Article 17, Paragraph 2, Item 1, l	
		Generic medical devices		1,767,700	68,500	1,836,200
				Article 17, Paragraph 1, Item 1, d (8)	Article 17, Paragraph 2, Item 1, l	
	Class III	Improved medical devices		1,409,900	68,500	1,478,400
				Article 17, Paragraph 1, Item 1, d (9)	Article 17, Paragraph 2, Item 1, l	
		Generic medical devices		1,409,900	68,500	1,478,400
				Article 17, Paragraph 1, Item 1, d (9)	Article 17, Paragraph 2, Item 1, l	
	Class II	Improved medical devices		1,409,900	68,500	1,478,400
				Article 17, Paragraph 1, Item 1, d (9)	Article 17, Paragraph 2, Item 1, l	
		Generic medical devices		1,409,900	68,500	1,478,400
				Article 17, Paragraph 1, Item 1, d (9)	Article 17, Paragraph 2, Item 1, l	
Approval of medical devices (with approval standards, without clinical data)	Class IV			429,200	68,500	497,700
				Article 17, Paragraph 1, Item 1, d (5)	Article 17, Paragraph 2, Item 1, k	
	Class III			344,100	68,500	412,600
				Article 17, Paragraph 1, Item 1, d (6)	Article 17, Paragraph 2, Item 1, k	
	Class II			344,100	68,500	412,600
				Article 17, Paragraph 1, Item 1, d (6)	Article 17, Paragraph 2, Item 1, k	
Change of brand name				35,600		35,600
				Article 17, Paragraph 1, Item 1, e		

New

(Unit: yen)

Classification				User fees		
				Review	Inspection	Total
Review for approval of medical devices (new approval)						
Approval of medical devices (with clinical data)	Class IV	New medical devices		8,705,500	664,500	9,370,000
				Article 17, Paragraph 1, Item 1, d (1)	Article 17, Paragraph 2, Item 1, j	
		Improved medical devices		6,213,000	664,500	6,877,500
				Article 17, Paragraph 1, Item 1, d (2)	Article 17, Paragraph 2, Item 1, j	
	Class III	New medical devices		6,213,000	664,500	6,877,500
				Article 17, Paragraph 1, Item 1, d (3)	Article 17, Paragraph 2, Item 1, j	
		Improved medical devices		3,721,200	664,500	4,385,700
				Article 17, Paragraph 1, Item 1, d (4)	Article 17, Paragraph 2, Item 1, j	
	Class II	New medical devices		6,213,000	664,500	6,877,500
				Article 17, Paragraph 1, Item 1, d (3)	Article 17, Paragraph 2, Item 1, j	
		Improved medical devices		3,721,200	664,500	4,385,700
				Article 17, Paragraph 1, Item 1, d (4)	Article 17, Paragraph 2, Item 1, j	
Approval of medical devices (without approval standards, without clinical data)	Class IV	Improved medical devices		2,355,400	68,500	2,423,900
				Article 17, Paragraph 1, Item 1, d (7)	Article 17, Paragraph 2, Item 1, l	
		Generic medical devices		1,767,700	68,500	1,836,200
				Article 17, Paragraph 1, Item 1, d (8)	Article 17, Paragraph 2, Item 1, l	
	Class III	Improved medical devices		1,409,900	68,500	1,478,400
				Article 17, Paragraph 1, Item 1, d (9)	Article 17, Paragraph 2, Item 1, l	
		Generic medical devices		1,409,900	68,500	1,478,400
				Article 17, Paragraph 1, Item 1, d (9)	Article 17, Paragraph 2, Item 1, l	
	Class II	Improved medical devices		1,409,900	68,500	1,478,400
				Article 17, Paragraph 1, Item 1, d (9)	Article 17, Paragraph 2, Item 1, l	
		Generic medical devices		1,409,900	68,500	1,478,400
				Article 17, Paragraph 1, Item 1, d (9)	Article 17, Paragraph 2, Item 1, l	
Approval of medical devices (with approval standards, without clinical data)	Class IV			429,200	68,500	497,700
				Article 17, Paragraph 1, Item 1, d (5)	Article 17, Paragraph 2, Item 1, k	
	Class III			344,100	68,500	412,600
				Article 17, Paragraph 1, Item 1, d (6)	Article 17, Paragraph 2, Item 1, k	
	Class II			344,100	68,500	412,600
				Article 17, Paragraph 1, Item 1, d (6)	Article 17, Paragraph 2, Item 1, k	
Change of brand name				35,600		35,600
				Article 17, Paragraph 1, Item 1, e		

Old

(Unit: yen)

Classification				User fees		
				Review	Inspection	Total
Review for approval of medical devices (approval of partial changes to approved matters)						
Medical devices (with clinical data)	Class IV	New medical devices		4,357,500	664,500	5,022,000
				Article 17, Paragraph 1, Item 2, d (1)	Article 17, Paragraph 2, Item 2, g	
		Improved medical devices		3,109,900	664,500	3,774,400
				Article 17, Paragraph 1, Item 2, d (2)	Article 17, Paragraph 2, Item 2, g	
	Class III	New medical devices		3,109,900	664,500	3,774,400
				Article 17, Paragraph 1, Item 2, d (3)	Article 17, Paragraph 2, Item 2, g	
		Improved medical devices		1,872,400	664,500	2,536,900
				Article 17, Paragraph 1, Item 2, d (4)	Article 17, Paragraph 2, Item 2, g	
	Class II	New medical devices		3,109,900	664,500	3,774,400
				Article 17, Paragraph 1, Item 2, d (3)	Article 17, Paragraph 2, Item 2, g	
		Improved medical devices		1,872,400	664,500	2,536,900
				Article 17, Paragraph 1, Item 2, d (4)	Article 17, Paragraph 2, Item 2, g	
Medical devices (without approval standards, without clinical data)	Class IV	Improved medical devices		1,181,200	37,100	1,218,300
				Article 17, Paragraph 1, Item 2, d (7)	Article 17, Paragraph 2, Item 2, i	
		Generic medical devices		884,200	37,100	921,300
				Article 17, Paragraph 1, Item 2, d (8)	Article 17, Paragraph 2, Item 2, i	
	Class III	Improved medical devices		709,500	37,100	746,600
				Article 17, Paragraph 1, Item 2, d (9)	Article 17, Paragraph 2, Item 2, i	
		Generic medical devices		709,500	37,100	746,600
				Article 17, Paragraph 1, Item 2, d (9)	Article 17, Paragraph 2, Item 2, i	
	Class II	Improved medical devices		709,500	37,100	746,600
				Article 17, Paragraph 1, Item 2, d (9)	Article 17, Paragraph 2, Item 2, i	
		Generic medical devices		709,500	37,100	746,600
				Article 17, Paragraph 1, Item 2, d (9)	Article 17, Paragraph 2, Item 2, i	
Medical devices (with approval standards, without clinical data)	Class IV			217,600	37,100	254,700
				Article 17, Paragraph 1, Item 2, d (5)	Article 17, Paragraph 2, Item 2, h	
	Class III			173,600	37,100	210,700
				Article 17, Paragraph 1, Item 2, d (6)	Article 17, Paragraph 2, Item 2, h	
	Class II			173,600	37,100	210,700
				Article 17, Paragraph 1, Item 2, d (6)	Article 17, Paragraph 2, Item 2, h	

New

(Unit: yen)

Classification					User fees		
					Review	Inspection	Total
QMS inspection of medical devices							
Approval, partial change and manufacture for export		New medical devices		Domestic		760,900 Article 17, Paragraph 4, Item 1, b (1)	760,900
				Overseas		960,200 ＋travel expenses Article 17, Paragraph 4, Item 1, b (2)	960,200 ＋travel expenses
		Biological medical devices, specially controlled medical devices (Class IV), etc.		Domestic		685,100 Article 17, Paragraph 4, Item 1, a (1)	685,100
				Overseas		868,600 ＋travel expenses Article 17, Paragraph 4, Item 1, a (2)	868,600 ＋travel expenses
		Sterile medical devices		Domestic		207,100 Article 17, Paragraph 4, Item 1, c (1)	207,100
				Overseas		236,400 ＋travel expenses Article 17, Paragraph 4, Item 1, c (2)	236,400 ＋travel expenses
		Other medical devices		Domestic		145,300 Article 17, Paragraph 4, Item 1, d (1)	145,300
				Overseas		159,900 ＋travel expenses Article 17, Paragraph 4, Item 1, d (2)	159,900 ＋travel expenses
		Packaging, labeling, storage, external testing, etc.		Domestic		65,600 Article 17, Paragraph 4, Item 2, a & Paragraph 5, Item 1, a	65,600
				Overseas		87,200 ＋travel expenses Article 17, Paragraph 4, Item 2, b & Paragraph 5, Item 1, b	87,200 ＋travel expenses
Renewal of the above		Biological medical devices, specially controlled medical devices (Class IV), etc.	Basic	Domestic		448,500 Article 17, Paragraph 4, Item 3, a (1)	448,500
				Overseas		570,100 ＋travel expenses Article 17, Paragraph 4, Item 3, a (2)	570,100 ＋travel expenses
			Addition of products	Domestic		31,400 Article 17, Paragraph 4, Item 3, a (1)	31,400
				Overseas		31,400 Article 17, Paragraph 4, Item 3, a (2)	31,400
		Sterile medical devices	Basic	Domestic		390,900 Article 17, Paragraph 4, Item 3, b (1)	390,900
				Overseas		493,800 ＋travel expenses Article 17, Paragraph 4, Item 3, b (2)	493,800 ＋travel expenses
			Addition of products	Domestic		12,800 Article 17, Paragraph 4, Item 3, b (1)	12,800
				Overseas		12,800 Article 17, Paragraph 4, Item 3, b (2)	12,800
		Other medical devices	Basic	Domestic		346,100 Article 17, Paragraph 4, Item 3, c (1)	346,100
				Overseas		421,100 ＋travel expenses Article 17, Paragraph 4, Item 3, c (2)	421,100 ＋travel expenses
			Addition of products	Domestic		9,900 Article 17, Paragraph 4, Item 3, c (1)	9,900
				Overseas		9,900 Article 17, Paragraph 4, Item 3, c (2)	9,900
		Packaging, labeling, storage, external testing, etc.	Basic	Domestic		265,900 Article 17, Paragraph 4, Item 3, d (1) & Paragraph 5, Item 2, a	265,900
				Overseas		347,800 ＋travel expenses Article 17, Paragraph 4, Item 3, d (2) & Paragraph 5, Item 2, b	347,800 ＋travel expenses
			Addition of products	Domestic		6,900 Article 17, Paragraph 4, Item 3, d (1) & Paragraph 5, Item 2, a	6,900
				Overseas		6,900 Article 17, Paragraph 4, Item 3, d (2) & Paragraph 5, Item 2, b	6,900

Old

(Unit: yen)

Classification					User fees		
					Review	Inspection	Total
QMS inspection of medical devices							
Approval, partial change and manufacture for export		New medical devices		Domestic		739,800 Article 17, Paragraph 4, Item 1, b (1)	739,800
				Overseas		933,500 ＋travel expenses Article 17, Paragraph 4, Item 1, b (2)	933,500 ＋travel expenses
		Biological medical devices, specially controlled medical devices (Class IV), etc.		Domestic		666,100 Article 17, Paragraph 4, Item 1, a (1)	666,100
				Overseas		844,400 ＋travel expenses Article 17, Paragraph 4, Item 1, a (2)	844,400 ＋travel expenses
		Sterile medical devices		Domestic		201,300 Article 17, Paragraph 4, Item 1, c (1)	201,300
				Overseas		229,800 ＋travel expenses Article 17, Paragraph 4, Item 1, c (2)	229,800 ＋travel expenses
		Other medical devices		Domestic		141,200 Article 17, Paragraph 4, Item 1, d (1)	141,200
				Overseas		155,400 ＋travel expenses Article 17, Paragraph 4, Item 1, d (2)	155,400 ＋travel expenses
		Packaging, labeling, storage, external testing, etc.		Domestic		63,800 Article 17, Paragraph 4, Item 2, a & Paragraph 5, Item 1, a	63,800
				Overseas		84,800 ＋travel expenses Article 17, Paragraph 4, Item 2, b & Paragraph 5, Item 1, b	84,800 ＋travel expenses
Renewal of the above		Biological medical devices, specially controlled medical devices (Class IV), etc.	Basic	Domestic		436,000 Article 17, Paragraph 4, Item 3, a (1)	436,000
				Overseas		554,200 ＋travel expenses Article 17, Paragraph 4, Item 3, a (2)	554,200 ＋travel expenses
			Addition of products	Domestic		30,500 Article 17, Paragraph 4, Item 3, a (1)	30,500
				Overseas		30,500 Article 17, Paragraph 4, Item 3, a (2)	30,500
		Sterile medical devices	Basic	Domestic		380,000 Article 17, Paragraph 4, Item 3, b (1)	380,000
				Overseas		480,000 ＋travel expenses Article 17, Paragraph 4, Item 3, b (2)	480,000 ＋travel expenses
			Addition of products	Domestic		12,400 Article 17, Paragraph 4, Item 3, b (1)	12,400
				Overseas		12,400 Article 17, Paragraph 4, Item 3, b (2)	12,400
		Other medical devices	Basic	Domestic		336,500 Article 17, Paragraph 4, Item 3, c (1)	336,500
				Overseas		409,400 ＋travel expenses Article 17, Paragraph 4, Item 3, c (2)	409,400 ＋travel expenses
			Addition of products	Domestic		9,600 Article 17, Paragraph 4, Item 3, c (1)	9,600
				Overseas		9,600 Article 17, Paragraph 4, Item 3, c (2)	9,600
		Packaging, labeling, storage, external testing, etc.	Basic	Domestic		258,500 Article 17, Paragraph 4, Item 3, d (1) & Paragraph 5, Item 2, a	258,500
				Overseas		338,100 ＋travel expenses Article 17, Paragraph 4, Item 3, d (2) & Paragraph 5, Item 2, b	338,100 ＋travel expenses
			Addition of products	Domestic		6,700 Article 17, Paragraph 4, Item 3, d (1) & Paragraph 5, Item 2, a	6,700
				Overseas		6,700 Article 17, Paragraph 4, Item 3, d (2) & Paragraph 5, Item 2, b	6,700

New

(Unit: yen)

Classification			User fees		
			Review	Inspection	Total
GLP Inspection of medical devices					
	GLP	Domestic		2,121,400 Article 17, Paragraph 3, Item 1, a & Paragraph 9, Item 2, a (1)	2,121,400
		Overseas		2,347,900 ＋travel expenses Article 17, Paragraph 3, Item 1, b & Paragraph 9, Item 2, a (2)	2,347,900 ＋travel expenses
GCP inspection of medical devices					
	GCP	Domestic		653,400 Article 17, Paragraph 3, Item 3, a	653,400
		Overseas		944,700 ＋travel expenses Article 17, Paragraph 3, Item 3, b	944,700 ＋travel expenses
Re-examination of medical devices					
	New medical devices		502,600 Article 17, Paragraph 8, Item 2, a	642,400 Article 17, Paragraph 9, Item 1, c	1,145,000
	Medical devices other than new ones		51,600 Article 17, Paragraph 8, Item 2, b	642,400 Article 17, Paragraph 9, Item 1, c	694,000
	GPSP	Domestic		628,200 Article 17, Paragraph 9, Item 2, b (5)	628,200
		Overseas		976,100 ＋travel expenses Article 17, Paragraph 9, Item 2, b (6)	976,100 ＋travel expenses

Old

(Unit: yen)

Classification			User fees		
			Review	Inspection	Total
GLP Inspection of medical devices					
	GLP	Domestic		2,062,400 Article 17, Paragraph 3, Item 1, a & Paragraph 9, Item 2, a (1)	2,062,400
		Overseas		2,282,600 ＋travel expenses Article 17, Paragraph 3, Item 1, b & Paragraph 9, Item 2, a (2)	2,282,600 ＋travel expenses
GCP inspection of medical devices					
	GCP	Domestic		635,300 Article 17, Paragraph 3, Item 3, a	635,300
		Overseas		918,400 ＋travel expenses Article 17, Paragraph 3, Item 3, b	918,400 ＋travel expenses
Re-examination of medical devices					
	New medical devices		502,600 Article 17, Paragraph 8, Item 2, a	624,600 Article 17, Paragraph 9, Item 1, c	1,127,200
	Medical devices other than new ones		51,600 Article 17, Paragraph 8, Item 2, b	624,600 Article 17, Paragraph 9, Item 1, c	676,200
	GPSP	Domestic		610,700 Article 17, Paragraph 9, Item 2, b (5)	610,700
		Overseas		949,000 ＋travel expenses Article 17, Paragraph 9, Item 2, b (6)	949,000 ＋travel expenses

Related to Article 4 of the Detailed Implementation Rules of PMDA Statement of Operating Classification of User Fees, etc.

New

(Unit: yen)

		User fees		Timing of payment
Consultations				
Drugs	Procedural consultation for drugs	per consultation	143,800	Payment by the date of consultation application after arrangement of the consultation date
	Consultation on bioequivalence testing, etc. for drugs	per consultation	571,900	
	Safety consultation for drugs	per consultation	1,833,700	
	Quality consultation for drugs	per consultation	1,520,500	
	Consultation before start of phase I study for drugs (non-orphan drugs)	per consultation	4,360,500	
	Consultation before start of phase I study for drugs (orphan drugs)	per consultation	3,277,200	
	Consultation before start of early phase II study for drugs (non-orphan drugs)	per consultation	1,669,400	
	Consultation before start of early phase II study for drugs (orphan drugs)	per consultation	1,257,400	
	Consultation before start of late phase II study for drugs (non-orphan drugs)	per consultation	3,114,900	
	Consultation before start of late phase II study for drugs (orphan drugs)	per consultation	2,339,200	
	Consultation after completion of phase II study for drugs (non-orphan drugs)	per consultation	6,183,300	
	Consultation after completion of phase II study for drugs (orphan drugs)	per consultation	4,644,800	
	Pre-application consultation for drugs (non-orphan drugs)	per consultation	6,183,200	
	Pre-application consultation for drugs (orphan drugs)	per consultation	4,642,000	
	Consultation on protocols of clinical trials for reevaluation and re-examination of drugs	per consultation	3,415,500	
	Consultation at completion of clinical trials for reevaluation and re-examination of drugs	per consultation	3,414,200	
	Additional consultation for drugs (non-orphan drugs)	per consultation	2,752,100	
	Additional consultation for drugs (orphan drugs)	per consultation	2,067,900	
	Consultation on GLP/GCP compliance for drugs (non-orphan drugs)	per consultation	2,957,700	
	Consultation on GLP/GCP compliance for drugs (orphan drugs)	per consultation	2,218,900	
	Prior assessment consultation for drugs (quality)	per consultation	3,136,500	
	Prior assessment consultation for drugs (non-clinical: toxicity)	per consultation	2,120,000	
	Prior assessment consultation for drugs (non-clinical: pharmacology)	per consultation	2,120,000	

Old

(Unit: yen)

		User fees		Timing of payment
Consultations				
Drugs	Procedural consultation for drugs	per consultation	139,800	Payment by the date of consultation application after arrangement of the consultation date
	Consultation on bioequivalence testing, etc. for drugs	per consultation	556,000	
	Safety consultation for drugs	per consultation	1,782,800	
	Quality consultation for drugs	per consultation	1,478,300	
	Consultation before start of phase I study for drugs (non-orphan drugs)	per consultation	4,239,400	
	Consultation before start of phase I study for drugs (orphan drugs)	per consultation	3,186,100	
	Consultation before start of early phase II study for drugs (non-orphan drugs)	per consultation	1,623,000	
	Consultation before start of early phase II study for drugs (orphan drugs)	per consultation	1,222,500	
	Consultation before start of late phase II study for drugs (non-orphan drugs)	per consultation	3,028,400	
	Consultation before start of late phase II study for drugs (orphan drugs)	per consultation	2,274,200	
	Consultation after completion of phase II study for drugs (non-orphan drugs)	per consultation	6,011,500	
	Consultation after completion of phase II study for drugs (orphan drugs)	per consultation	4,515,700	
	Pre-application consultation for drugs (non-orphan drugs)	per consultation	6,011,400	
	Pre-application consultation for drugs (orphan drugs)	per consultation	4,513,000	
	Consultation on protocols of clinical trials for reevaluation and re-examination of drugs	per consultation	3,320,600	
	Consultation at completion of clinical trials for reevaluation and re-examination of drugs	per consultation	3,319,400	
	Additional consultation for drugs (non-orphan drugs)	per consultation	2,675,600	
	Additional consultation for drugs (orphan drugs)	per consultation	2,010,400	
	Consultation on GLP/GCP compliance for drugs (non-orphan drugs)	per consultation	2,875,500	
	Consultation on GLP/GCP compliance for drugs (orphan drugs)	per consultation	2,157,200	
	Prior assessment consultation for drugs (quality)	per consultation	3,049,300	
	Prior assessment consultation for drugs (non-clinical: toxicity)	per consultation	2,061,100	
	Prior assessment consultation for drugs (non-clinical: pharmacology)	per consultation	2,061,100	

New

(Unit: yen)

		User fees		Timing of payment
Consultations (continue)				
Drugs	Prior assessment consultation for drugs (non-clinical: pharmacokinetics)	per consultation	2,120,000	Payment by the date of consultation application after arrangement of the consultation date
	Prior assessment consultation for drugs (phase I study)	per consultation	3,584,300	
	Prior assessment consultation for drugs (phase II study)	per consultation	4,625,900	
	Prior assessment consultation for drugs (phase II/III study)	per consultation	7,185,300	
	Consultation on drug product eligibility for priority review	per consultation	846,800	
	Consultation on drug product eligibility for priority review (with pre-application consultation for drugs)	per consultation	173,500	
	Consultation on pharmacogenomics/biomarkers (qualification)	per consultation	3,114,900	
	Consultation on pharmacogenomics/biomarkers (key points of clinical trial protocols)	per consultation	1,142,800	
	Additional consultation on pharmacogenomics/biomarkers (qualification)	per consultation	948,300	
	Additional consultation on pharmacogenomics/biomarkers (key points of clinical trial protocols)	per consultation	414,600	
	Consultation on R&D strategy for drugs	per consultation	1,541,600	
	Consultation on R&D strategy for drugs (universities/research institutes and venture companies meeting requirements specified separately*)	per consultation	154,100	
	Consultations on bioequivalence of generic drugs	per consultation	1,026,000	
	Quality consultation for generic drugs	per consultation	505,800	
	Pre-application consultation for switch OTC drugs	per consultation	1,544,000	
	Consultation on key points of clinical trial protocols for OTC drugs	per consultation	516,800	
	Consultation on appropriateness of development of new OTC drugs	per consultation	204,800	
Devices and in vitro diagnostics	Pre-development consultation for medical devices	per consultation	139,100	
	Safety consultation for medical devices (excluding biological medical devices)	per consultation	845,600	
	Safety consultation for biological medical devices	per consultation	936,200	
	Quality consultation for medical devices (excluding biological medical devices)	per consultation	797,500	
	Quality consultation for biological medical devices	per consultation	947,700	
	Performance testing consultation for medical devices	per consultation	870,100	
	Clinical evaluation consultation for medical devices	per consultation	1,055,900	
	Exploratory clinical trial consultation for medical devices	per consultation	1,136,900	
	Clinical trial consultation for medical devices	per consultation	2,482,000	
	Pre-application consultation for medical devices	per consultation	2,482,000	
	Application procedure consultation for medical devices	per consultation	139,100	

Old

(Unit: yen)

		User fees		Timing of payment
Consultations (continue)				
Drugs	Prior assessment consultation for drugs (non-clinical: pharmacokinetics)	per consultation	2,061,100	Payment by the date of consultation application after arrangement of the consultation date
	Prior assessment consultation for drugs (phase I study)	per consultation	3,484,700	
	Prior assessment consultation for drugs (phase II study)	per consultation	4,497,400	
	Prior assessment consultation for drugs (phase II/III study)	per consultation	6,985,700	
	Consultation on drug product eligibility for priority review	per consultation	823,300	
	Consultation on drug product eligibility for priority review (with pre-application consultation for drugs)	per consultation	168,700	
	Consultation on pharmacogenomics/biomarkers (qualification)	per consultation	3,028,400	
	Consultation on pharmacogenomics/biomarkers (key points of clinical trial protocols)	per consultation	1,111,000	
	Additional consultation on pharmacogenomics/biomarkers (qualification)	per consultation	921,900	
	Additional consultation on pharmacogenomics/biomarkers (key points of clinical trial protocols)	per consultation	403,100	
	Consultation on R&D strategy for drugs	per consultation	1,498,800	
	Consultation on R&D strategy for drugs (universities/research institutes and venture companies meeting requirements specified separately*)	per consultation	149,800	
	Consultations on bioequivalence of generic drugs	per consultation	997,500	
	Quality consultation for generic drugs	per consultation	491,800	
	Pre-application consultation for switch OTC drugs	per consultation	1,501,100 yen	
	Consultation on key points of clinical trial protocols for OTC drugs	per consultation	502,500 yen	
	Consultation on appropriateness of development of new OTC drugs	per consultation	199,100 yen	
Devices and in vitro diagnostics	Pre-development consultation for medical devices	per consultation	135,200	
	Safety consultation for medical devices (excluding biological medical devices)	per consultation	822,100	
	Safety consultation for biological medical devices	per consultation	910,100	
	Quality consultation for medical devices (excluding biological medical devices)	per consultation	775,400	
	Quality consultation for biological medical devices	per consultation	921,400	
	Performance testing consultation for medical devices	per consultation	845,900	
	Clinical evaluation consultation for medical devices	per consultation	1,026,600	
	Exploratory clinical trial consultation for medical devices	per consultation	1,105,300	
	Clinical trial consultation for medical devices	per consultation	2,413,000	
	Pre-application consultation for medical devices	per consultation	2,413,000	
	Application procedure consultation for medical devices	per consultation	135,200	

New

(Unit: yen)

			User fees	Timing of payment
Consultations (continue)				
Devices and in vitro diagnostics	Additional consultation for medical devices	per consultation	1,162,400	Payment by the date of consultation application after arrangement of the consultation date
	Consultation on GLP/GCP compliance for medical devices	per consultation	795,000	
	Prior assessment consultation for medical devices (quality)	per consultation	3,067,600	
	Prior assessment consultation for medical devices (non-clinical)	per consultation	3,067,600	
	Prior assessment consultation for medical devices (clinical)	per consultation	4,619,100	
	Consultation on R&D strategy for medical devices	per consultation	874,000	
	Consultation on R&D strategy for medical devices (universities/research institutes and venture companies meeting requirements specified separately*)	per consultation	87,400	
	Pre-development consultation for in vitro diagnostics	per consultation	143,900	
	Quality consultation for in vitro diagnostics	per consultation	355,400	
	Consultation on conformity with standards for in vitro diagnostics	per consultation	455,400	
	Clinical evaluation consultation for in vitro diagnostics	per consultation	694,700	
	Clinical performance study consultation for in vitro diagnostics	per consultation	1,640,300	
	Pre-application consultation for in vitro diagnostics	per consultation	1,640,300	
	Application procedure consultation for in vitro diagnostics	per consultation	139,100	
	Additional consultation for in vitro diagnostics	per consultation	954,100	
	Prior assessment consultation for in vitro diagnostics (quality)	per consultation	3,067,600	
	Prior assessment consultation for in vitro diagnostics (non-clinical)	per consultation	3,067,600	
	Prior assessment consultation for in vitro diagnostics (clinical)	per consultation	4,619,100	
	Consultation on preparation of documents for gene therapy products	per consultation	229,900	
Simple consultations	Generic drugs	per consultation	21,600	
	OTC drugs	per consultation	21,600	
	Quasi-drugs (including pesticides and rodenticides)	per consultation	21,600	
	Medical devices or in vitro diagnostics	per consultation	35,300	
	Preparation of new drug applications	per consultation	21,600	
	GMP/QMS inspection	per consultation	25,400	

	User fees	Timing of payment
Assessment for designation of priority consultation products		
Assessment for designation of drugs for priority consultation	per application 842,200	Request to PMDA after advanced payment
Assessment for designation of medical devices or in vitro diagnostics for priority consultation	per application 842,200	

			User fees	Timing of payment
GLP inspection of test facilities				
All test items (for drugs and medical devices)		per facility	3,110,300	Request to PMDA after advanced payment
All test items (for drugs or medical devices)	Domestic	per facility	2,121,400	
	Overseas	per facility	2,347,900 + travel expenses	
Limited test items		per facility	1,023,600	
Additional compliance accreditation		per facility	959,300	

Old

(Unit: yen)

			User fees	Timing of payment
Consultations (continue)				
Devices and in vitro diagnostics	Additional consultation for medical devices	per consultation	1,130,100	Payment by the date of consultation application after arrangement of the consultation date
	Consultation on GLP/GCP compliance for medical devices	per consultation	772,900	
	Prior assessment consultation for medical devices (quality)	per consultation	2,982,300	
	Prior assessment consultation for medical devices (non-clinical)	per consultation	2,982,300	
	Prior assessment consultation for medical devices (clinical)	per consultation	4,490,800	
	Consultation on R&D strategy for medical devices	per consultation	849,700	
	Consultation on R&D strategy for medical devices (universities/research institutes and venture companies meeting requirements specified separately*)	per consultation	84,900	
	Pre-development consultation for in vitro diagnostics	per consultation	139,900	
	Quality consultation for in vitro diagnostics	per consultation	345,500	
	Consultation on conformity with standards for in vitro diagnostics	per consultation	442,800	
	Clinical evaluation consultation for in vitro diagnostics	per consultation	675,400	
	Clinical performance study consultation for in vitro diagnostics	per consultation	1,594,700	
	Pre-application consultation for in vitro diagnostics	per consultation	1,594,700	
	Application procedure consultation for in vitro diagnostics	per consultation	135,200	
	Additional consultation for in vitro diagnostics	per consultation	927,500	
	Prior assessment consultation for in vitro diagnostics (quality)	per consultation	2,982,300	
	Prior assessment consultation for in vitro diagnostics (non-clinical)	per consultation	2,982,300	
	Prior assessment consultation for in vitro diagnostics (clinical)	per consultation	4,490,800	
	Consultation on preparation of documents for gene therapy products	per consultation	223,500	
Simple consultations	Generic drugs	per consultation	21,000	
	OTC drugs	per consultation	21,000	
	Quasi-drugs (including pesticides and rodenticides)	per consultation	21,000	
	Medical devices or in vitro diagnostics	per consultation	34,300	
	Preparation of new drug applications	per consultation	21,000	
	GMP/QMS inspection	per consultation	24,700	

	User fees	Timing of payment
Assessment for designation of priority consultation products		
Assessment for designation of drugs for priority consultation	per application 818,800	Request to PMDA after advanced payment
Assessment for designation of medical devices or in vitro diagnostics for priority consultation	per application 818,800	

			User fees	Timing of payment
GLP inspection of test facilities				
All test items (for drugs and medical devices)		per facility	3,023,800	Request to PMDA after advanced payment
All test items (for drugs or medical devices)	Domestic	per facility	2,062,400	
	Overseas	per facility	2,282,600 + travel expenses	
Limited test items		per facility	995,200	
Additional compliance accreditation		per facility	932,600	

New				Old			
(Unit: yen)				(Unit: yen)			
Confirmation of certification on drugs, etc.				Confirmation of certification on drugs, etc.			
GMP certification on investigational products (with on-site inspection)	per product of one facility	760,900	Request to PMDA after advanced payment	GMP certification on investigational products (with on-site inspection)	per product of one facility	739,800	Request to PMDA after advanced payment
GMP certification on investigational products (without on-site inspection)	per product of one facility	15,500		GMP certification on investigational products (without on-site inspection)	per product of one facility	15,100	
Certification of drug products	per product	15,500		Certification of drug products	per product	15,100	
Other certifications (including certification of GMP/QMS)	per matter of one product	8,700		Other certifications (including certification of GMP/QMS)	per matter of one product	8,400	
Use of document storage rooms				Use of document storage rooms			
	per day per room	3,000	Payment upon invoice sent from PMDA after the end of the period of use		per day per room	3,000	Payment upon invoice sent from PMDA after the end of the period of use

* Universities/research institutes and venture companies meeting requirements specified separately

All of the following requirements should be met in principle.

For universities/research institutes

- Having not received 90 million yen or more (in the case of drugs) or 50 million yen or more (in the case of medical devices) from the government, to proceed with the research on the seed-stage resource.
- Having not received research expenses from a pharmaceutical company/medical device company under a joint research agreement, etc., toward practical application of the seed-stage resource.

For venture companies

- Being a small or medium-sized company (with 300 employees or less, or capitalized at 300 million yen or less).
- Any other corporation does not hold 1/2 or more of the total number of shares or investments.
- Two or more other corporations do not hold 2/3 or more of the total number of shares or investments.
- For the preceding fiscal year, profits of the term have not been reported, or profits of the term have been reported but without operating revenue.

Table 9. Planned Financial Statements for the Mid-Term Plan (FY 2009-2013)

Budgets Attachment 1

Budgets for Mid-term Plan (FY2009-FY2013)

(Unit:million yen)

Classification	Amount of money						
	Adverse drug reactions relief account	Infection relief account	Review account	Specified relief account	Commission and loan account	Commission payment account	Total
Income							
Administrative subsidies			2,717				2,717
Governmental subsidies	843	89	2,443				3,375
Contributions	20,410	3,160	12,144	20,255			55,969
User fees			49,448				49,448
Commissioned operations			242		7,140	3,521	10,903
Management income	1,843	266					2,108
Miscellaneous income	7	1	180	0	6	6	200
Total	23,103	3,514	67,174	20,256	7,146	3,527	124,720
Expenditure							
Operating expenses	14,788	520	57,107	24,429	7,079	3,481	107,404
Personnel expenses	1,142	125	26,005	88	186	118	27,665
Administrative expenses	13,646	395	31,102	24,341	6,893	3,363	79,740
General administrative expenses	664	74	13,011	19	68	45	13,881
Personnel expenses	288		3,149		19	9	3,465
Non-personnel expenses	376	74	9,862	19	49	36	10,416
Total	15,452	594	70,119	24,448	7,146	3,527	121,286

[Note]
In principle, all figures have been rounded off; therefore, individual totals shown may not coincide with the actual totals.

Income and Expenditure Plan for the Mid-term Plan (FY 2009 - FY 2013)

(Unit:million yen)

Classification	Amount of money						
	Adverse drug reactions relief account	Infection relief account	Review account	Specified relief account	Commission and loan account	Commission payment account	Total
Expenditure	24,497	780	67,313	24,470	7,147	3,525	127,732
Ordinary expenses	24,497	780	67,313	24,470	7,147	3,525	127,732
Operating expenses	14,623	489	53,782	24,429	7,073	3,456	103,851
Relief benefits	11,619	180					11,799
Operating expenses for health and welfare	171						171
Operating expenses for reviews			20,594				20,594
Operating expenses for safety measures			7,395				7,395
Specified relief benefits				24,080			24,080
Benefits (healthcare allowances, etc.)					6,802		6,802
Benefits (special allowances, etc.)						1,317	1,317
Operating expenses for research and study						1,919	1,919
Administrative expenses	1,696	185		261	86	101	2,329
Personnel expenses	1,136	124	25,792	88	186	118	27,444
General administrative expenses	599	65	10,986	20	69	46	11,786
Personnel expenses	287		3,152		19	9	3,467
Non-personnel expenses	311	65	7,834	20	51	37	8,319
Depreciation expenses	270	46	2,540	21	0	18	2,894
Provision for liability reserve	9,002	175					9,177
Miscellaneous losses	5	5	5		5	5	25
Income	23,103	3,516	67,303	24,470	7,145	3,526	129,064
Ordinary income	23,103	3,516	67,303	24,470	7,145	3,526	129,064
Governmental subsidies	843	89	2,443				3,375
Contributions	20,410	3,160	12,144				35,714
User fees			49,448				49,448
Commissioned operations			242		7,140	3,521	10,903
Other governmental grants				184			184
Administrative subsidies			2,717				2,717
Reversal of asset offset subsidies	1			21			22
Reversal of asset offset administrative subsidies			283				283
Reversal of asset offset gifts received			2				2
Financial income (no operating income)	1,849	268	2				2,119
Gain on reversal of specified relief fund deposit received				24,264			24,264
Miscellaneous income	0	0	22		5	5	32
Net income (△ net loss)	△ 1,394	2,737	△ 10	0	△ 2	1	1,331
Reversal of appropriated surplus							-
Gross income (△ gross loss)	△ 1,394	2,737	△ 10	0	△ 2	1	1,331

[Note 1] Administrative subsidies are assumed to be the financial resource for retirement allowances for staff members in charge of operations financed by administrative subsidies under the review account.
However, this excludes the amount arranged through administrative subsidies as retirement allowances equivalent to tenure, as provided for in Article 8-2 of the supplementary provisions in the Act for Pharmaceuticals and Medical Devices Agency.

[Note 2] In principle, all figures have been rounded off; therefore, individual totals shown may not coincide with the actual totals.

Cash Flows Plan for the Mid-term Plan (FY 2009 - FY 2013)

(Unit:million yen)

Classification	Amount of money						
	Adverse drug reactions relief account	Infection relief account	Review account	Specified relief account	Commission and loan account	Commission payment account	Total
Cash Outflows							
Cash outflows from operating activities	15,423	557	65,157	24,450	7,178	3,520	116,286
Relief benefits	11,564	178					11,743
Operating expenses for health and welfare	171						171
Operating expenses for reviews			20,739				20,739
Operating expenses for safety measures			7,468				7,468
Specified relief benefits				24,080			24,080
Benefits (healthcare allowances, etc.)					6,827		6,827
Benefits (special allowances, etc.)						1,317	1,317
Operating expenses for research and study						1,919	1,919
Administrative expenses	1,986	193		264	105	119	2,668
General administrative expenses	303	64	8,792	19	49	36	9,264
Personnel expenses	1,398	122	28,159	86	197	128	30,091
Cash outflows from investing activities	11,547	2,536	4,975			20	19,078
Payments for purchases of investment in securities	11,320	2,500	676				14,496
Payments for purchases of intangible fixed assets	154	25	2,749			20	2,948
Payments of deposit money and guarantee money	74	11	1,549				1,634
Cash outflows from financial activities							-
Amount carried forward to the next mid-term plan period	3,840	668	2,496	287	39	137	7,466
Total	30,810	3,761	72,628	24,737	7,217	3,677	142,830
Cash Inflows							
Cash inflows from operating activities	23,354	3,514	66,980	20,256	7,167	3,527	124,797
Governmental subsidies	843	89	2,443				3,375
Administrative subsidies			2,717				2,717
Contributions	20,410	3,160	12,144	20,255			55,969
User fees			49,410				49,410
Commissioned operations			242		7,161	3,521	10,924
Miscellaneous income	2,100	266	24	0	6	6	2,402
Cash inflows from investing activities	5,848						5,848
Cash inflows from financial activities							-
Amount brought forward at the beginning of the mid-term plan period	1,609	247	5,648	4,481	50	150	12,185
Total	30,810	3,761	72,628	24,737	7,217	3,677	142,830

[Note] In principle, all figures have been rounded off; therefore, individual totals shown may not coincide with the actual totals.

Table 10. Planned Financial Statements for FY 2012 and FY 2013

Plan for FY 2012

Budgets — Attachment 1

Budgets for Fiscal Year Plan (FY 2012)

(Unit: million yen)

Classification	Amount of money								
	Adverse drug reactions relief account	Infection relief account	Review account			Specified relief account	Commission and loan account	Commission payment account	Total
			Review segment	Safety segment	Total				
Income									
Administrative subsidies			126	218	344				344
Governmental subsidies	168	142	267	873	1,141				1,450
Contributions	4,146	777		2,691	2,691	5,550			13,165
User fees			9,510		9,510				9,510
Commissioned operations							1,323	662	1,986
Management income	386	64							450
Miscellaneous income	2	0	29	7	36	0	2	1	41
Total	4,702	982	9,932	3,790	13,722	5,550	1,325	663	26,945
Expenditure									
Operating expenses	2,942	246	9,982	4,068	14,050	10,251	1,319	659	29,466
Personnel expenses	209	23	4,342	1,110	5,453	18	37	22	5,761
Administrative expenses	2,733	223	5,640	2,958	8,597	10,234	1,282	637	23,705
General administrative expenses	110	11	1,495	334	1,828	2	6	5	1,963
Personnel expenses	66		530	135	665				731
Non-personnel expenses	44	11	965	199	1,164	2	6	5	1,232
Total	3,052	257	11,477	4,402	15,878	10,253	1,325	663	31,429

[Note] As each count was obtained by rounding off in principle, some fractions are not consistent with the total.

Plan for FY 2013

Budgets — Attachment 1

Budgets for Fiscal Year Plan (FY 2013)

(Unit: million yen)

Classification	Amount of money								
	Adverse drug reactions relief account	Infection relief account	Review account			Specified relief account	Commission and loan account	Commission payment account	Total
			Review segment	Safety segment	Total				
Income									
Administrative subsidies			118	211	329				329
Governmental subsidies	145	140	301	903	1,204				1,489
Contributions	3,533	877		2,864	2,864	6,415			13,690
User fees			10,590		10,590				10,590
Commissioned operations			150		150		1,260	649	2,059
Management income	397	71							468
Miscellaneous income	1	0	24	5	29	0	2	22	55
Total	4,077	1,088	11,183	3,984	15,167	6,415	1,262	671	28,680
Expenditure									
Operating expenses	2,681	233	11,154	4,875	16,029	13,142	1,255	666	34,006
Personnel expenses	199	23	4,205	1,023	5,228	16	34	18	5,518
Administrative expenses	2,482	209	6,949	3,852	10,801	13,126	1,221	648	28,488
General administrative expenses	93	14	2,217	528	2,745	2	7	4	2,865
Personnel expenses	49		512	133	645				694
Non-personnel expenses	45	14	1,704	395	2,100	2	7	4	2,171
Total	2,774	246	13,371	5,403	18,774	13,144	1,262	671	36,871

[Note] As each count was obtained by rounding off in principle, some fractions are not consistent with the total.

Plan for FY 2012

Income and Expenditure Plan — Attachment 2

Income and Expenditure Plan for Fiscal Year Plan (FY 2012)

(Unit: million yen)

Classification	Amount									
			Review account							
	Adverse drug reactions relief account	Infection relief account	Review segment	Safety segment	Adjusted	Total	Specified relief account	Commission and loan account	Commission payment account	Total
Ordinary expenses	4,308	345	9,831	3,628	△ 5	13,455	10,257	1,326	662	30,353
Relief benefits	2,150	31								2,181
Operating expenses for health and welfare	38	124								162
Operating expenses for reviews			2,702			2,702				2,702
Operating expenses for safety measures				1,564		1,564				1,564
Specified relief benefits							10,212			10,212
Benefits (healthcare allowances, etc.)								1,266		1,266
Benefits (special allowances, etc.)									261	261
Operating expenses for research and study									361	361
Provision for liability reserve	1,398	107								1,505
Other administrative expenses	609	70	5,583	1,711		7,294	43	52	35	8,103
Personnel expenses	195	21	3,965	1,037		5,002	16	33	20	5,289
Depreciation expenses	59	7	198	369		568	4	0	1	638
Retirement benefit expenses	7	1	157	39		195	0	1	1	205
Provision for accrued bonuses	6	1	236	41		277	1	2	1	289
Other expenses	342	41	1,027	225		1,252	22	15	12	1,683
General administrative expenses	111	11	1,513	340	△ 5	1,848	2	6	5	1,984
Personnel expenses	62		484	126		610				673
Depreciation expenses	0		44			44				44
Retirement benefit expenses	2		16	3		19				21
Provision for accrued bonuses	2		32	7		39				41
Other expenses	45	11	936	204	△ 5	1,135	2	6	5	1,205
Financial expenses	1		34	13		46				47
Miscellaneous losses	1	1		1		1		2	1	6
Ordinary income	4,697	984	9,991	3,477	△ 5	13,463	10,257	1,325	663	31,389
Governmental subsidies	168	142	267	523		790				1,100
Administrative subsidies			182	220		402				402
Other governmental grants							41			41
Contributions	4,146	777		2,691		2,691				7,614
User fees			9,510			9,510				9,510
Gain on reversal of specified relief fund deposit received							10,212			10,212
Commissioned operations								1,323	662	1,986
Reversal of asset offset subsidies	0		16	35		51	4			55
Reversal of asset offset administrative subsidies			8	8		16				16
Reversal of asset offset gifts received			0			0				0
Financial income (no operating income)	382	65								447
Miscellaneous income	0	0	8	0	△ 5	3		2	1	6
Ordinary net income (△ net loss)	389	639	159	△ 152		8	0	△ 1	1	1,036
Current net income before tax (△ net loss)	389	639	159	△ 152		8	0	△ 1	1	1,036
Current net income (△ net loss)	389	639	159	△ 152		8	0	△ 1	1	1,036
Current gross income (△ gross loss)	389	639	159	△ 152		8	0	△ 1	1	1,036

[Note] As each count was obtained by rounding off in principle, some fractions are not consistent with the total.

Plan for FY 2013

Income and Expenditure Plan — Attachment 2

Income and Expenditure Plan for Fiscal Year Plan (FY 2013)

(Unit: million yen)

Classification	Amount									
			Review account							
	Adverse drug reactions relief account	Infection relief account	Review segment	Safety segment	Adjusted	Total	Specified relief account	Commission and loan account	Commission payment account	Total
Ordinary expenses	4,129	362	11,474	4,547	△ 3	16,018	13,148	1,262	672	35,591
Relief benefits	1,984	31								2,015
Operating expenses for health and welfare	38	124								162
Operating expenses for reviews			4,522			4,522				4,522
Operating expenses for safety measures				2,647		2,647				2,647
Specified relief benefits							13,104			13,104
Benefits (healthcare allowances, etc.)								1,201		1,201
Benefits (special allowances, etc.)									259	259
Operating expenses for research and study									354	354
Provision for liability reserve	1,317	110								1,426
Other administrative expenses	695	82	5,624	1,551		7,176	41	53	33	8,080
Personnel expenses	187	22	3,937	953		4,890	15	31	17	5,161
Depreciation expenses	52	6	266	305		571	4	1	1	634
Retirement benefit expenses	6	1	165	38		204	0	1	1	213
Provision for accrued bonuses	7	1	246	41		287	1	2	1	298
Other expenses	443	53	1,009	215		1,224	22	18	14	1,774
General administrative expenses	94	14	1,300	345	△ 3	1,643	2	7	4	1,764
Personnel expenses	45		469	124		593				638
Depreciation expenses	0		49	8		57				57
Retirement benefit expenses	2		17	3		21				23
Provision for accrued bonuses	2		33	8		41				43
Other expenses	45	14	732	202	△ 3	931	2	7	4	1,003
Financial expenses	0		27	3		29				30
Miscellaneous losses	1	1		1		1		2	22	27
Ordinary income	4,061	1,088	11,217	3,920	△ 3	15,134	13,148	1,261	671	35,363
Governmental subsidies	145	140	301	772		1,073				1,358
Administrative subsidies			155	201		357				357
Other governmental grants							40			40
Contributions	3,533	877		2,864		2,864				7,275
User fees			10,590			10,590				10,590
Gain on reversal of specified relief fund deposit received							13,104			13,104
Commissioned operations			150			150		1,260	649	2,059
Reversal of asset offset subsidies	0		16	80		96	4			99
Reversal of asset offset administrative subsidies			0	3		3				3
Reversal of asset offset gifts received			0			0				0
Financial income (no operating income)	383	70								453
Miscellaneous income	0	0	4	0	△ 3	2		2	22	25
Ordinary net income (△ net loss)	△ 67	726	△ 257	△ 628		△ 884	0	△ 1	△ 1	△ 228
Current net income before tax (△ net loss)	△ 67	726	△ 257	△ 628		△ 884	0	△ 1	△ 1	△ 228
Current net income (△ net loss)	△ 67	726	△ 257	△ 628		△ 884	0	△ 1	△ 1	△ 228
Reversal of appropriated surplus	-	-	555	62		617	-	-	-	617
Current gross income (△ gross loss)	△ 67	726	298	△ 565		△ 267	0	△ 1	△ 1	389

[Note] As each count was obtained by rounding off in principle, some fractions are not consistent with the total.

Plan for FY 2012

Cash Flow Plan — Attachment

Cash Flow Plan for Fiscal Year Plan (FY 2012)

(Unit: million yen)

Classification	Amount									
			Review account							
	Adverse drug reactions relief account	Infection relief account	Review segment	Safety segment	Adjusted	Total	Specified relief account	Commission and loan account	Commission payment account	Total
Cash Outflows										
Cash outflows from operating activities	2,910	242	9,747	3,595	△ 7	13,335	10,253	1,339	667	28,747
Relief benefits	2,146	30								2,176
Operating expenses for health and welfare	38	124								162
Operating expenses for reviews			3,895			3,895				3,895
Operating expenses for safety measures				2,135		2,135				2,135
Administrative expenses	383	44					22	15	12	476
Specified relief benefits							10,212			10,212
Benefits (healthcare allowances, etc.)								1,268		1,268
Benefits (special allowances, etc.)									261	261
Operating expenses for research and study									361	361
General administrative expenses	44	11	965	199		1,164	2	6	5	1,232
Personnel expenses	265	22	4,670	1,197		5,867	17	35	21	6,228
Repayment money	1	1		1		1		2	1	6
Other cash outflow from operating activities	33	9	216	63	△ 7	273	0	13	6	334
Cash outflow from investing activities	3,286	525	1,738	1,005		2,744			2	6,556
Amount carried forward to next fiscal year	2,051	502	8,284	2,107		10,391	3,931	39	134	17,048
Total	8,247	1,269	19,769	6,707	△ 7	26,470	14,184	1,378	802	52,351
Cash Inflows										
Cash inflows from operating activities	4,704	982	9,537	3,797	△ 7	13,328	5,497	1,328	663	26,502
Contributions	4,146	777		2,691		2,691	5,497			13,111
Administrative subsidies			126	218		344				344
Governmental subsidies	168	142	267	873		1,141				1,450
User fees			9,079			9,079				9,079
Commissioned operations								1,326	662	1,988
Amount of interests received	386	64								450
Miscellaneous incomes	0	0	57	14		71		2	1	74
Other incomes	3	0	9		△ 7	2	0	0	0	6
Cash inflows from investing activities	2,000									2,000
Amount brought forward from preceding fiscal year	1,543	287	10,232	2,910		13,142	8,687	50	139	23,849
Total	8,247	1,269	19,769	6,707	△ 7	26,470	14,184	1,378	802	52,351

[Note] As each count was obtained by rounding off in principle, some fractions are not consistent with the total.

Plan for FY 2013

Cash Flow Plan — Attachment

Cash Flow Plan for Fiscal Year Plan (FY 2013)

(Unit: million yen)

Classification	Amount									
			Review account							
	Adverse drug reactions relief account	Infection relief account	Review segment	Safety segment	Adjusted	Total	Specified relief account	Commission and loan account	Commission payment account	Total
Cash Outflows										
Cash outflows from operating activities	2,856	280	12,121	4,034	△ 4	16,150	13,144	1,281	679	34,390
Relief benefits	1,987	30								2,017
Operating expenses for health and welfare	38	124								162
Operating expenses for reviews			5,660			5,660				5,660
Operating expenses for safety measures				2,674		2,674				2,674
Administrative expenses	513	60					22	19	15	629
Specified relief benefits							13,104			13,104
Benefits (healthcare allowances, etc.)								1,204		1,204
Benefits (special allowances, etc.)									259	259
Operating expenses for research and study									354	354
General administrative expenses	46	14	1,751	16		1,767	2	7	5	1,840
Personnel expenses	238	22	4,514	1,110		5,625	15	33	17	5,951
Repayment money	1	1		1		1		3	22	28
Other cash outflow from operating activities	33	28	195	232	△ 4	423	0	16	8	508
Cash outflow from investing activities	3,300	700	1,188	1,136		2,324			0	6,324
Amount carried forward to next fiscal year	2,126	463	8,972	2,763		11,735	299	37	132	14,793
Total	8,282	1,443	22,281	7,933	△ 4	30,209	13,443	1,318	811	55,507
Cash Inflows										
Cash inflows from operating activities	4,081	1,091	10,880	3,993	△ 4	14,868	6,429	1,265	671	28,405
Contributions	3,533	877		2,864		2,864	6,429			13,704
Administrative subsidies			118	211		329				329
Governmental subsidies	145	140	301	903		1,204				1,489
User fees			10,322			10,322				10,322
Commissioned operations			73			73		1,263	649	1,985
Amount of interests received	397	71								468
Miscellaneous incomes	0	0	60	14		74		2	22	98
Other incomes	5	3	6		△ 4	1	0	0	0	10
Cash inflows from investing activities	2,180									2,180
Amount brought forward from preceding fiscal year	2,022	352	11,400	3,940		15,340	7,014	53	139	24,921
Total	8,282	1,443	22,281	7,933	△ 4	30,209	13,443	1,318	810	55,506

[Note] As each count was obtained by rounding off in principle, some fractions are not consistent with the total.

Table 11. Balance Sheet for FY 2013

Balance Sheet (corporate basis)

(As of March 31, 2014)

(Unit: yen)

Account item	Amount		Account item	Amount	
Assets			Liabilities		
I Current assets			I Current liabilities		
Cash and deposits		25,452,409,754	Deposit subsidy, etc.		266,803,037
Securities		3,200,332,780	Accrued benefits		326,502,713
Expenses for work-in-process reviews, etc.		1,334,737,105	Accounts payable		2,636,679,763
Prepaid expenses		196,088	Advances received		7,463,601,575
Accounts due		972,853,421	Deposits received		120,101,432
Accrued income		52,712,708	Lease obligations		106,005,103
Deposits paid		2,670,000	Allowance		
Other current assets		534,244	Accrued bonuses	427,792,117	427,792,117
Total of current assets		31,016,446,100	Total of current liabilities		11,347,485,740
II Fixed assets			II Fixed liabilities		
Tangible fixed assets			Per contra liabilities for property acquisition		
Tools, equipment and fixtures	2,139,833,028		Administrative subsidies for assets as per contra	58,974,605	
Cumulative total of depreciation	△ 1,061,365,923	1,078,467,105	Governmental subsidies, etc. for assets as per contra	586,348,148	
Construction in progress		370,195,822	Amount of received goods for assets as per contra	185,308	645,508,061
Total of tangible fixed assets		1,448,662,927	Deposits of specific relief funds		
Intangible fixed assets			Long-term deposit subsidy, etc.	216,222,049	
Software		1,774,326,278	Deposit contribution	6,072,036,642	6,288,258,691
Software in progress		2,331,199,733	Long-term lease obligations		96,830,724
Telephone subscription right		286,000	Allowances		
Total of intangible fixed assets		4,105,812,011	Allowances for retirement benefits	1,602,913,856	1,602,913,856
Investments and other assets			Liability reserve		17,942,610,043
Investment securities		32,460,630,466	Total of fixed liabilities		26,576,121,375
Rental deposit		4,670,640	Total of liabilities		37,923,607,115
Total of investments and other assets		32,465,301,106	Net assets		
Total of fixed assets		38,019,776,044	I Capital funds		
			Government investment		1,179,844,924
			Total of capital funds		1,179,844,924
			II Capital surplus		
			Capital reserves		4,670,640
			Cumulative total of depreciation that are not recorded as expenses (△)		△ 670,431,080
			Loss on retirement or sale of fixed assets that are not recorded as expenses (△)		△ 73,191,116
			Total of capital surplus		△ 738,951,556
			III Retained earnings		30,671,721,661
			Total of net assets		31,112,615,029
Total of assets		69,036,222,144	Total of liabilities and net assets		69,036,222,144

Table 12. Profit and Loss Statement for FY 2013

Profit and Loss Statement (Corporate basis)

(From April 1, 2013 to March 31, 2014)

(Unit: yen)

Account item	Amount		
Ordinary expenses			
Adverse drug reaction relief benefits		1,959,184,025	
Infection relief benefits		2,967,268	
Health and welfare services		128,965,696	
Reviews and related services		3,083,416,209	
Safety measures, etc.		1,259,736,571	
Specific relief benefits		2,888,000,000	
Benefits for healthcare allowances, etc.		1,160,994,014	
Benefits for special allowances, etc.		205,881,600	
Investigative research		292,348,600	
Other operating expenses			
Personnel expenses	4,747,606,008		
Depreciation expenses	694,343,673		
Retirement benefit expenses	392,412,524		
Provision for accrued bonuses	290,175,775		
Estate rental fees	1,227,830,776		
Other expenses	386,581,508	7,738,950,264	
General administrative expenses			
Personnel expenses	587,722,452		
Depreciation expenses	72,841,666		
Retirement benefit expenses	39,698,168		
Provision for accrued bonuses	37,025,447		
Estate rental fees	241,397,922		
Other expenses	782,889,568	1,761,575,223	
Financial expenses			
Interests paid		28,968,449	
Miscellaneous losses		18,312,990	
Total of ordinary expenses			20,529,300,909
Ordinary revenues			
Administrative subsidies		541,757,760	
Reversal of provision for deposits of specific relief funds			
Revenues from grants for payment of specific relief benefits		2,144,000,000	
Revenues from contributions		744,000,000	
User fees		10,323,990,876	
Contributions		7,280,686,300	
Revenue from governmental subsidies		1,006,684,420	
Commissioned operations for government		77,427,766	
Commissioned operations for others		1,817,549,881	
Return of administrative subsidies for assets as per contra		1,119,105	
Return of subsidies, etc. for assets as per contra		93,878,543	
Return of amount of received goods for assets as per contra		34,399	
Return of liability reserves		186,187,656	
Financial revenue			
Interests received	10,047,946		
Interests on securities	443,440,640	453,488,586	
Miscellaneous gains		22,050,284	
Total of ordinary revenues			24,692,855,576
Ordinary profits			4,163,554,667
Extraordinary losses			
Loss on retirement of fixed assets		13,124,318	13,124,318
Current net profits			4,150,430,349
Reversal of reserve for specific purposes			521,303,022
Current gross profits			4,671,733,371

Table 13. Cash Flow Statement for FY2013

Cash Flow Statement (Corporate basis)

(From April 1, 2013 to March 31, 2014)

(Unit: yen)

Account item	Amount of money
I. Cash flow from operating activities	
Expenditure for adverse drug reaction relief benefits	△ 1,957,206,412
Expenditure for infection relief benefits	△ 2,968,668
Expenditure for health and welfare services	△ 128,976,012
Expenditure for reviews and related services	△ 2,430,741,422
Expenditure for safety measures, etc.	△ 1,336,725,539
Expenditure for specific relief benefits	△ 2,888,000,000
Expenditure for benefits for healthcare allowances, etc.	△ 1,167,225,744
Expenditure for benefits for special allowances, etc.	△ 205,885,400
Expenditure for expenses for investigative research	△ 293,623,300
Expenditure for personnel expenses	△ 5,615,586,631
Expenditure for money refunded for settlement of subsidies, etc.	△ 225,760,427
Other operating expenditures	△ 2,871,283,895
Income from administrative subsidies	328,980,000
Income from governmental subsidies	1,179,256,000
Income from contributions	7,926,788,300
Income from user fees	9,840,515,085
Income from commissioned operations for government	77,427,766
Income from commissioned operations for others	1,736,464,382
Other incomes	110,783,248
Subtotal	2,076,231,331
Amount of interests paid	△ 28,968,449
Amount of interests received	468,018,040
Cash flow from operating activities	2,515,280,922
II. Cash flow from investing activities	
Income from refund of long-term deposits with fiscal loan fund	1,000,000,000
Expenditure for acquisition of investment securities	△ 4,734,233,000
Income from redemption of investment securities at maturity	1,200,000,000
Expenditure for acquisition of tangible fixed assets	△ 831,333,504
Expenditure for acquisition of intangible fixed assets	△ 2,481,785,355
Expenditure for payment of lease deposits	△ 4,670,640
Cash flow from investing activities	△ 5,852,022,499
III. Cash flow from financing activities	
Expenditure for repayment of finance lease obligations	△ 223,981,164
Cash flow from financing activities	△ 223,981,164
IV. Increase in funds	△ 3,560,722,741
V. Beginning-of-term balance of funds	29,013,132,495
VI. End-of-term balance of funds	25,452,409,754

Table 14. Government Service Implementation Cost Statement for FY2013

Government Service Implementation Cost Statement (Corporate basis)

(From April 1, 2013 to March 31, 2014)

(Unit: yen)

Account item	Amount of money		
I. Operating expenses			
(1) Expenses in the profit and loss statement			
Adverse drug reaction relief benefits	1,959,184,025		
Infection relief benefits	2,967,268		
Expenses for health and welfare services	128,965,696		
Expenses for reviews and related services	3,083,416,209		
Expenses for safety measures, etc.	1,259,736,571		
Specific relief benefits	2,888,000,000		
Benefits for healthcare allowances, etc.	1,160,994,014		
Benefits for special allowances, etc.	205,881,600		
Expenses for investigative research	292,348,600		
Other operating expenses	7,738,950,264		
General administrative expenses	1,761,575,223		
Financial expenses	28,968,449		
Miscellaneous losses	18,312,990		
Loss on retirement of fixed assets	13,124,318	20,542,425,227	
(2) (Exemption) Self-generated income, etc.			
Income from contributions	△ 8,024,686,300		
Income from user fees	△ 10,323,990,876		
Income from commissioned operations for government	△ 77,427,766		
Income from commissioned operations for others	△ 1,817,549,881		
Return of liability reserves	△ 186,187,656		
Financial revenue	△ 453,488,586		
Miscellaneous gains	△ 22,050,284	△ 20,905,381,349	
Total of operating expenses			△ 362,956,122
II. Amount equivalent to depreciation that are not recorded as expenses			15,397,250
III. Amount equivalent to loss on retirement or sale of fixed assets that are not recorded as expenses			22,330,182
IV. Estimated amount of non-allowance bonuses			15,864,790
V. Estimated increased amount of non-allowance retirement benefits			80,943,191
VI. Opportunity costs			
Opportunity costs of investments by the government or local governments, etc.			2,912,554
VII. Government service implementation costs			△ 225,508,155

Notes

I. Important Accounting Policies

1. Criteria for allocation of revenue from administrative subsidies
   Percentage-of-expense method has been employed.
   Services implemented by the PMDA do not progress with a certain period of time and it is difficult to reasonably estimate the degree of achievement of results, and therefore it is difficult to clearly show a correspondence relationship between certain services, etc., and the financial resource of administrative subsidies.
   It is most reasonable to grasp the actual status of progress of services based on the amount of expenses required for activities, and therefore the percentage-of-expense method has been employed.

2. Evaluation criteria and evaluation methods for securities
   Held-to-maturity bonds
   They are handed by the amortized cost method (straight-line method).

3. Evaluation criteria and evaluation methods for expenses for work-in-process reviews, etc.
   They are handled by the lower-of-cost-or-market method based on specific identification method.

4. Methods of accounting for depreciation
   (1) Tangible fixed assets
      [1] Tangible fixed assets other than lease assets
         The straight-line method has been employed.
         Durable years of main assets are as follows.
            Tools, equipment and fixtures 2 - 18 years
         The amount equivalent to depreciation of particular depreciable assets (Accounting Standards for Incorporated Administrative Agencies No. 87) is shown to be deducted from the capital surplus as cumulative total of depreciation that are not recoreded as expenses.
      [2] Lease assets
         Lease assets related to non-ownership-transfer finance lease transactions
         The straight-line method, in which the lease period is durable years and the residual value is zero, has been employed.
   (2) Intangible fixed assets
      The straight-line method has been employed.
      Software is used within the corporate body based on an available period (5 years) within the corporate body.

5. Criteria for allocation of allowances and estimated amounts related to bonuses
   Amounts occurring for the current term are allocated from among the expected amounts of payment of bonuses for the next term to executives, regular employees, etc.
   However, allowances are not allocated for amounts which are funded from the administrative subsidies and governmental subsidies from among the said expected amounts of payment.

6. Criteria for allocation of allowances and estimated amounts related to retirement benefits
   To prepare for retirement benefits for executives and regular employees, the allowances and estimated amounts are allocated based on the expected amounts of retirement benefit obligations at the end of the current fiscal year. Actuarial differences are to be collectively amortized in the next fiscal year after the

occurrence. However, allowances related to retirement benefits are not allocated for amounts which are funded from the administrative subsidies.

7. Criteria for allocation of liability reserves
To prepare for the payment of relief benefits in the future, amounts specified in the statement of operation procedures are allocated pursuant to the provisions of Article 30 of the Act on Pharmaceuticals and Medical Devices Agency (Act No.192 of 2002).

8. Method of allocating opportunity costs in government service implementation cost statements
Interest rate used for calculation of opportunity costs of investments by the government or local governments, etc.:
Costs are calculated at a rate of 0.640% with reference to the yield rate at the end of March 2014 for 10-year fixed rate government bond.

9. Methods of accounting for lease transactions
Finance release transactions for which the total of lease fees is 3 million yen or more are handled by accounting method according to the method for usual sales transactions.
Finance release transactions for which the total of lease fees is less than 3 million yen are handled by accounting method according to the method for usual lease transactions.

10. Methods of accounting for consumption tax, etc.
These are handled by the tax-included method.

II. Items to note

1. Notes for balance sheets
(1) Notes regarding matters including current prices of financial products
[1] Items related to the status of financial products
Deposits are to be deposits for settlement.
Also, financial products invested for fund management are limited to long-lived deposits, public and corporate bonds, etc. As investment securities, the PMDA holds only public bonds, FILP agency bonds, and class A or higher corporate bonds and does not hold stocks, etc. based on rules such as the provisions of Article 47 of the Act on General Rules for Incorporated Administrative Agencies.
[2] Items related to matters including current prices of financial products
Balance sheet amounts, current prices, and amounts of difference between them on closing date are as follows.

(Unit: yen)

Classification	Balance sheet amount (*)	Current price on closing date (*)	Amount of difference
A. Cash and deposits	25,452,409,754	25,452,409,754	0
B. Securities and investment securities	35,660,963,246	36,765,540,000	1,104,576,754
C. Accounts payable	(2,636,679,763)	(2,636,679,763)	0

(*) Those allocated in liabilities are shown in ( ).

(Notes) Method of calculating current prices of financial products and items related to securities, etc.
A. Cash and deposits
Current prices approximate book values, and therefore are based on these book values.

B. Securities and investment securities
Current prices are based on prices at the stock exchange or prices offered by correspondent financial institutions.
Items to note for securities are as follows.

1) Held-to-maturity bonds with current price

(Unit: yen)

Classification	Balance sheet amount	Current price on closing date	Amount of difference
Bonds with current prices exceeding balance sheet amount	31,074,706,504	32,219,520,000	1,144,813,496
Bonds with current prices not exceeding balance sheet amount	4,586,256,742	4,546,020,000	-40,236,742
Total	35,660,963,246	36,765,540,000	1,104,576,754

2) Scheduled amounts of redemption after closing date for held-to-maturity bonds

(Unit: yen)

Classification	≤ 1 year	> 1 year ≤ 5 years	> 5 years ≤ 10 years	> 10 years
Government bonds	0	2,100,000,000	8,400,000,000	0
Government-guaranteed bonds	0	3,100,000,000	10,400,000,000	0
Local government bonds	1,000,000,000	2,500,000,000	0	0
Corporate bonds	100,000,000	2,000,000,000	0	0
FILP agency bonds	0	3,800,000,000	0	0
Bonds issued by agency under a special act	2,100,000,000	0	0	0
Total	3,200,000,000	13,500,000,000	18,800,000,000	0

C. Accounts payable
The accounts are settled in short period and current prices approximate book values, and therefore are based on these book values.

(2) Estimated amount of non-allowance bonuses
Estimated amount of bonuses to be covered by the administrative subsidies and governmental subsidies: 52,118,364 yen

(3) Estimated amount of non-allowance retirement benefits
Estimated amount of retirement benefits to be covered by the administrative subsidies: 26,424,559 yen

2. Notes for profit and loss statements

(1) Expenses for health and welfare services are expenses required for investigative research conducted to improve the QOL (Quality of Life) of people such as those covered by the system who suffered a serious and rare adverse drug reaction for which supports are not necessary sufficient when taking general measures intended for disabled people. These expenses consist of rewards for cooperation for investigation, etc.

(2) Expenses for reviews and related services are expenses required for the operation of reviews and related services for drugs, medical devices, etc. These expenses consist of rewards, travel expenses, expenses at government offices in charge of clerical works, etc. Also, expenses for safety measures, etc. are expenses required for the operation of post-marketing safety measures

for drugs, medical devices, etc. These expenses consist of rewards, travel expenses, expenses at government offices in charge of clerical works, etc.

(3) Expenses for investigative research are expenses required for investigative research of persons infected with HIV through blood products which is intended to contribute to the prevention of onset of AIDS. All of these expenses are healthcare expenses for HIV-infected persons.

(4) Income from user fees is an income paid by applicants for approval as a financial source for conducting review services for drugs, etc.

(5) Income from contributions is an income paid by marketing authorization holders of drugs, etc. as a financial resource for conducting relief services for adverse health effects and post-marketing safety measure services.

3. Notes for cash flow statements

Relationship between the end-of-term balance of funds and money amounts of accounting items shown in the balance sheet

Cash and deposits: 25,452,409,754 yen

End-of-term balance of funds: 25,452,409,754 yen

4. Notes for government service implementation cost statements

The estimated increased amount of non-allowance retirement benefits includes 73,857,000 yen for executives and regular employees temporally transfered from the government.

5. Notes for asset retirement obligations

The PMDA has obligations for restoration to original state at the time of leaving business office based on the real estate leasehold contract, but the actual period of use of lease assets related to these obligations are not clear.

Therefore, it is difficult to predict the timing of implementing these obligations and it is not possible to reasonably estimate asset retirement obligations. For this reason, asset retirement obligations that match these obligations have not been allocated.

6. Notes for allowances for retirement benefits

(1) Outline of the retirement benefits system employed

The PMDA has established a retirement lump sum grants system as a defined-benefit system.

(2) Items related to retirement benefit obligations

(Unit: yen)

Classification	As of March 31, 2014
[1] Retirement benefit obligations	1,593,479,850
[2] Unrecognized actuarial difference	9,434,006
[3] Allowance for retirement benefits ([1] + [2])	1,602,913,856

(3) Items related to retirement benefits expenses

(Unit: yen)

Classification	April 1, 2013 - March 31, 2014
[1] Service expenses	267,220,706
[2] Interest expenses	14,897,857
[3] Amortization expenses for actuarial difference	149,992,129
[4] Retirement benefits expenses ([1] + [2] + [3])	432,110,692

(Note) As burdens of retirement benefits expenses for workers temporally transferred from other institution, [1] 3,429,016 yen for service expenses and [2] 251,962 yen for interest expenses were allocated.

(4) Items related to the basis for calculation of retirement benefit obligations, etc.

Classification	As of March 31, 2014
Discount rate	1.1%
Method of periodic allocation of estimated amounts of retirement benefits	Straight-line attribution
Amortized period of actuarial difference	1 year Actuarial differences are to be collectively amortized in the next fiscal year after the occurrence.

III. Important Acts of Bearing Obligation

Important acts of bearing obligation for which payment is scheduled for the next fiscal year or after are as follows.

System design/development works for implementation of work system optimization (next-gen application/review system)	819,000,000 yen

IV. Important Subsequent Events

There are no corresponding events.

Mid-Term Target of the Pharmaceuticals and Medical Devices Agency

Mid-term Targets of the Pharmaceuticals and Medical Devices Agency (PMDA)
(Provisional Translation)

** This translation of the original Japanese text is for information purposes only*
(in the event of inconsistency, the Japanese text shall prevail).

Instruction No. 0307-73 (dated March 7, 2014) of
Pharmaceutical and Food Safety Bureau,
Ministry of Health, Labour and Welfare (MHLW)

Targets to be achieved by the Pharmaceuticals and Medical Devices Agency in its operation management shall be established as below, based on the provision of Article 29, Paragraph 1 of the Act on General Rules for Incorporated Administrative Agency for Incorporated Administrative Agency (Act No. 103, 1999),.

March 7, 2014

Minister of Health, Labour and Welfare
Norihisa Tamura

Part 1
Effective Period for Mid-term Targets
The effective period for Mid-term Targets according to Article 29, Paragraph 2, Item 1 of the Act on General Rules for Incorporated Administrative Agency (Act No. 103, 1999) shall be 5 years, from April 2014 through March 2019.

Part 2
Matters Regarding Improvement in Operation Management of the Overall Corporation and Matters Regarding Improvement in the Quality of Services and Other Operations Rendered to the Public
The targets related to the overall corporation regarding improvement in efficiency of operations, as stipulated in Article 29, Paragraph 2, Item 2 of the Act on General Rules for Incorporated Administrative Agency, and the targets regarding improvement in the quality of services and other operations rendered to the public, as stipulated in Article 29, Paragraph 2, Item 3 of the Act on General Rules for Incorporated Administrative Agency, shall be as follows.

1) Efficient and Flexible Management of Operations
   a) The Pharmaceuticals and Medical Devices Agency (hereinafter referred to as the “PMDA”) shall establish an efficient and flexible system for managing operations, confirm the way of operational control and methods for implementing operations through external evaluation, and improve the management of operations based on the following points.
      - Improve internal controls including the way of implementing duties in accordance with instructions from accounting auditors, and proactively disclose measures taken.
      - Examine the way of internal control by utilizing professional knowledge from experts of third-parties.

- PMDA shall refer to the matters that were notified to each evaluation committee of the incorporated administrative agencies of the government ministries, which are opinions on the report (*Internal Control and Evaluation in Incorporated Administrative Agencies*) released by the Study Group on Internal Control and Evaluation in Incorporated Administrative Agencies held by the Ministry of Internal Affairs and Communications, and opinions on evaluation results of the operating performance in incorporated administrative agencies from the Ministry of Internal Affairs and Communications and the Evaluation Committee of Incorporated Administrative Agencies.

b) Promote computerization of the operations to increase efficiency of the operation management system.

c) Based on a re-examination of systems control operation of the common information and the review operation, PMDA shall control costs by re-examining the system configuration of the overall PMDA and its procurement method, in order to reduce system costs, to ensure transparency of system procurement, and to streamline operation management.

For this reason, PMDA shall promote approaches to optimize operations and systems by integrating the individual review systems and by establishing a system to promote information sharing among review services, post-marketing safety measures, and relief services for adverse health effects, based on the Optimization Plan for Operations and Systems established at the end of FY 2007.

2) Improvement of Operation Management

a) By continuously improving the operation and increasing efficiency in management, the following reduction in the budget for the Mid-term Plan is expected to have been achieved by the end of the effective period for Mid-term Targets, regarding general administrative expenses (excluding personnel expenses) in which the administrative subsides are to be applied.
- No less than 15% as compared to FY 2014.
- Appropriately utilize outsourcing (outsource when possible to prevent increase in personnel, etc.).

b) By increasing efficiency in operations, the following reduction, regarding operating expenses (excluding personnel expenses, and single fiscal-year expenses, etc., that were paid for the establishment of operations) in which the administrative subsidies are to be applied, is expected to be made by the end of the effective period for Mid-term Targets.
- No less than 5% as compared to FY 2014.
- Appropriately utilize outsourcing (outsource when possible to prevent increase of personnel, etc.).

c) Yearly administrative subsidies are to be rigorously calculated with consideration of its debt balance.

d) Promote efficiency and improvements of operations by consolidating the management of the marketing authorization holder's product data, etc. of contributions for adverse drug reaction (ADR), contributions for relief for infections, and contributions for post-marketing safety measures.

e) As a general rule, contracts shall be concluded through open competitive bidding, etc., and the following approaches shall be made.
- Fully secure competitiveness and transparency even when contracts are not concluded by open competitive bidding such as planning competition and invitation to bids.
- Conduct bids and conclude contracts appropriately, by having them thoroughly checked by auditors and accounting auditors as well as by utilizing opinions of experts.

f) Provide and disseminate genuinely useful information from the public perspective

Let the public be aware of the services and role of PMDA by disseminating and providing information from the public's perspective, which enables the public and patients to readily access

to the information they need. Enhance the consultation system and ensure transparency of operations and its details in order to improve the services rendered to the public.

g) Analyze issues of the operation system
Analyze the issues of the operation system appropriately and revise them if necessary.

h) Considerations related to financial base
Consider a financial base that is appropriate for the role of PMDA and take necessary measures.

Part 3

Matters Regarding Improvement in Operation Management of Each Division and Matters Regarding Improvement in the Quality of Services and Other Operations Rendered to the Public

1. Relief Fund Services for Adverse Health Effects

With regard to the relief fund services for Adverse Health Effects (hereinafter referred to as "relief services"), it is important not only to fully disseminate more people the Adverse Drug Reaction Relief System and the Relief System for Infections Acquired through Biological Products (hereinafter referred to as "relief systems") and appropriately operate them, but also adequately and promptly provide relief for those suffering from ADR and infections acquired through biological products or regenerative medical products (hereinafter, including cellular and tissue-based products and gene therapy products).
Based on this concept, the following targets shall be achieved.

1) Enhance Public Relations and Dissemination of Information Regarding the Relief Systems

a) Conduct proactive public relations so that the relief systems are definitely utilized when necessary.

b) Make more efficient operations by reducing the number of cases where inadequate operations of claim documents, etc., result in need of extra processing time.

2) Promptly Process Relief Benefit Claims by Investigating and Organizing the Facts of the Claims

a) Promptly process relief benefit claims

b) Set up standard administrative processing times* and steadily achieve those standards.

* Standard administrative processing time includes a certain period for medical and pharmaceutical judgments of the Ministry of Health, Labour and Welfare. However, administrative processing time shall exclude the period when processing could not be continued because additional or supplementary documents and investigations of the claimant or medical institutions were required to make medical and pharmaceutical judgments.

3) Promote Appropriate Information Transmission in cooperation with Divisions

Cooperation shall be promoted among the divisions of PMDA, and information especially regarding cases of relief payment shall be appropriately disseminated to the Review Divisions and the Safety Measures Divisions, with attention to ensuring protection of personal information.

4) Implement Appropriate Health and Welfare Services

Steadily implement health and welfare services.

5) Appropriately Provide Healthcare Allowances to SMON Patients and Patients infected with HIV through Blood Products

Appropriately conduct services regarding healthcare allowances to SMON patients and HIV-positive patients infected with blood products.

6) Appropriately Pay Benefits to Assist Individuals Affected by Hepatitis C through Specified Fibrinogen Products and Specified Blood Coagulation Factor IX Products Contaminated by Hepatitis C Virus

Appropriately conduct services regarding payment of benefits to assist individuals affected by hepatitis C through specified fibrinogen products and specified blood coagulation factor IX products contaminated by hepatitis C virus.

2. Reviews and Related Services

In the review services and post-marketing safety measures, PMDA shall enable better pharmaceuticals and medical devices, etc., to be provided to medical settings more promptly and safely, so that the public can use global standard pharmaceuticals and medical devices, etc., at ease. It is important to ensure that pharmaceuticals and medical devices, etc., are appropriately used, prevent health hazards from occurring while accurately and promptly taking measures in cases where health hazards occur, and make pharmaceuticals and medical devices, etc., fulfill their mission in the long term.

Along with this conception, and based on the Japan Revitalization Strategy (adopted by the Cabinet on June 14,2013) and the Healthcare and Medical Strategy (an agreement among the Chief Cabinet Secretary, Minister of Health, Labour and Welfare, and Minister of Internal Affairs and Communications on June 14, 2013) , Act to Ensure Quality, Efficacy, and Safety of Pharmaceuticals and Medical Devices (Act No. 145, 1960) that were revised as a result of the Act for Partial Revision of the Pharmaceutical Affairs Act, (Act No. 84, 2013) , as well as the Act to Ensure Safety of Regenerative Medicine (Act No. 85, 2013), etc. , PMDA shall accelerate reviews speed for s and medical devices, aim to achieve elimination of review lag*, and aim to improve the quality of the reviews, etc. Pharmaceutical Affairs Consultation on R&D Strategy, etc., shall also be enhanced as a support to eliminate the developmental lag*.
In order to achieve these targets, PMDA's financial resources shall be utilized in enhancing the system.
*Drug lag and device lag are defined as delay of approvals of pharmaceuticals and medical devices, respectively, from United States in Japan. Drug lag or device lag can be divided into review lag, which are differences in review time (time from application to approval) between the United States and Japan, and development lag, which are differences in time at which the companies submit applications to the regulatory agencies of the United States and Japan (from the Japan Revitalization Strategy [approved by the Cabinet on June 14, 2013]).
The overall lag shall be eliminated by eliminating the review lag and development lag.

Following measures shall be promoted in order for the above mentioned measures to be implemented appropriately and smoothly, while maintaining cooperation with MHLW.

1) Make pharmaceuticals, medical devices, etc. accessible by the public more quickly

Efforts shall be made to enable the public and healthcare professionals to promptly gain advantage of advanced and safe pharmaceuticals and medical devices, etc., based on their needs so that they can receive the maximum benefit from them.

PMDA shall proactively support and cooperate with MHLW and its approaches, including acceleration of clinical trials, to promote development of pharmaceuticals and medical devices that are still unapproved in Japan but are of high medical need, in order to reduce development lag.

a) Conduct various measures, while evaluating and verifying their state of progress, and take additional measures when necessary.
b) In order to achieve reduce review lag while improving the quality of reviews, PMDA shall improve the services by setting time reduction targets (targets at ordinary times without any exceptional cases such as substantial changes in the systems or social conditions) for the processing time of applications (regulatory review time for products approved in the respective years) that were submitted after April 1, 2004. PMDA shall develop a review system to achieve these targets.
c) Promote multiregional clinical trials by cooperating with the United States, Europe, and Asian countries.
d) Prioritize clinical trial consultations for pharmaceuticals and medical devices that are expected to be highly useful by enhancing pre-application consultations, so as to reduce

review period. Correctly understand the accurate needs of companies at the stage of development and reevaluate system of the consultation service whenever necessary.

e) Improve PMDA's own scientific levels for skills of consultations and reviews, with consideration of the rapid development of the latest technologies such as biotechnology, genomics, and regenerative medicine, and shall take necessary measures for the consultations and reviews along with the development of new pharmaceuticals, new medical devices, and regenerative medical products that utilize the latest technologies.

f) Take necessary measures to accelerate reviews for generic drugs, etc., as in the case of new pharmaceuticals.

g) Take measures to accelerate reviews for behind-the-counter (BTC) drugs*, over-the-counter (OTC) drugs, and quasi-drugs as with new pharmaceuticals.

* Behind-the counter (BTC) drugs are defined as switch OTC drugs and powerful OTC drugs which require pharmacist's intervention.

h) Set targets to aim for eliminating review lag for medical devices, as with new pharmaceuticals, and take measures to accelerate reviews. Develop a review system to achieve these targets.

Regarding reviews of improved medical devices and generic medical devices, PMDA shall take measures to systematically and intensively review items which had taken long time for the reviews after submission, and shall make efforts to reduce the applicant's time (the time within the review time that is necessary for the applicants to reply to inquiries from the regulatory side).

i) Take measures to accelerate reviews for regenerative medical products by enhancing the relevant review divisions necessary to conduct accurate and prompt reviews, while introducing conditional and time-limited approval system as well as setting target review times.

j) Appropriately and efficiently conduct conformity inspections.

k) Conduct appropriate and efficient GMP/QMS/GCTP (Good gene, Cellular and Tissue Practice) etc. inspections.

2) Provide Support to be the First in the World to Facilitate Practical Use of Innovative Pharmaceuticals, Medical Devices, and Regenerative Medical Products

Make the following approaches in order to be first in the world to facilitate practical use of innovative pharmaceuticals, medical devices, and regenerative medical products.

a) Establish and update review standards for innovative products.

b) Proactively conduct Pharmaceutical Affairs Consultation on R&D Strategy, etc.

c) Operate the approval system based on the characteristics of regenerative medical products.

3. Safety Measures

In the review services and post-marketing safety measures, PMDA shall promptly and safely provide superior pharmaceuticals and medical devices, etc., to medical settings in order to enable the public to use global standard pharmaceuticals and medical devices, etc., at ease. It is important to ensure that pharmaceuticals and medical devices, etc., are appropriately used, prevent health hazards from occurring while accurately and promptly taking measures in cases where health hazards occur, and make pharmaceuticals and medical devices, etc., fulfill their mission in the long term.

In accordance with this concept, utilize finances including PMDA's own financial resource and enhance the system when necessary to improve post-marketing safety measures of pharmaceuticals and medical devices, etc., based on the Act for Partial Revision of the Pharmaceutical Affairs Act that reflects the details of Japan Revitalization Strategy, the Healthcare and Medical Strategy, the final recommendation of the Committee for Investigation of Pharmaceutical-induced Hepatitis Cases and Appropriate Regulatory Administration to Prevent Similar Sufferings, etc.

a) Systematically and continuously conduct comprehensive evaluations of information on ADR, Malfunction, and Adverse Reaction (here in after ADR, etc.), by substantially enhancing assemble of information on ADR, etc., and its evaluation analysis system in order to accurately respond to the advanced and specialized evaluation of information on ADR, etc. Furthermore, find out new relationships among multiple ADR information, and establish an efficient and effective evaluation system for safety information such as researching and utilizing methods to identify and analyze new safety information, and improved it when necessary, by using IT technology.

b) Have healthcare professionals and companies increase utilization of feedback information on the analysis results of collected safety information, etc., and enhance methods of disseminating information on appropriate use to the patients, in order to enhance the rigorous system for disseminating safety information to improve safety measures at medical institutions. At the same time, PMDA shall also establish standards that enable the accomplishments of safety measures to be more accurately understood in a manner in which the public are able to understand easily.

c) Conduct appropriate post-marketing safety measures based on the Risk Management Plan of pharmaceuticals.

d) Cooperation shall be promoted among the relief services and the review services to enable appropriate assessment of safety.

e) Establish a system that enables confirmation of the current status and effectiveness of post-marketing safety measures taken by PMDA in companies and medical institutions, etc.

f) Appropriately collect information on Adverse Reaction reports regulated in the Preventive Vaccination Act and appropriately conduct investigations and analyses.

4. Promotion of Regulatory Science, Globalization, etc.

Note: Regulatory science = Science for coordinating results of science and technology into the most desirable form for harmonizing people and society, by conducting accurate and evidence-based estimations, evaluations, and decisions in order for the results of science and technology to be used for people and society. (from the Science and Technology Basic Plan, adopted by the Cabinet on August 19, 2011)

a) Enhance regulatory science research

Develop an environment and system for conducting regulatory science research (hereinafter referred to as the “RS research”) aimed at improving the quality of the services provided by PMDA. Make efforts to train human resources to be experts in RS research through conducting it, and make efforts to contribute to increase the efficiency of development of pharmaceuticals, etc., through establishment of guidelines, etc.

b) Response to globalization

Reinforce partnerships with foreign regulatory agencies, promote global harmonization activity to proactively collect foreign information, and make efforts to promote dissemination of information in English.

Furthermore, enhance the English website of PMDA, and enhance measures in order for Asian countries to increase their understanding of Japanese regulations and standards regarding pharmaceutical applications, etc.

c) Enhance staff training

By enhancing staff training, PMDA shall establish a group of engineering supervisors that have a global level in review services and post-marketing safety measures so as to increase the quality of the services, and shall make efforts to train human resources to be experts in RS research.

d) Promote interaction with external researchers and investigative research

Promote investigative research by proactively interacting with external researchers in order to contribute to activate development and to establish guidelines regarding innovative seed-stage resources.

e) Promptly facilitate practical use of pharmaceuticals for intractable diseases and orphan diseases.

f) Promote further transparency of review services and post-marketing safety measures such as revealing in public review reports.

g) Develop an information system basis that ensures reliability and increases efficiency of review services and post-marketing safety measures.

Part 4

Matters Regarding Improvement in Financial Affairs

The following is the target for improving financial affairs specified in Article 29, Paragraph 2, Item 4 of the Act on General Rules for Incorporated Administrative Agency.

For matters specified in Part 2, items 1) and 2) of this Mid-term Targets, a Mid-term budget shall be developed with an estimation of cost reductions, and PMDA shall operate based on this budget.

Part 5

Important Matters Regarding Other Operation Management

The following are important targets regarding other operation management specified in the Article 29, Paragraph 2, Item 5 of the Act on General Rules for Incorporated Administrative Agency.

1) Matters Regarding Personnel Affairs

a) Secure enough personnel necessary to reviews and post-marketing safety measures, based on the Act for Partial Revision of the Pharmaceutical Affairs Act, etc., that reflects the details of Japan Revitalization Strategy, the Healthcare and Medical Strategy, and the final recommendation of the Committee for Investigation of Pharmaceutical-induced Hepatitis Cases and Appropriate Regulatory Administration to Prevent Similar Sufferings, etc.

In order to avoid any suspicion of inappropriate relationships with pharmaceutical companies, etc., PMDA shall take appropriate measures in employment, allocation, post-retirement reemployment, etc., of executives and employees, while thoroughly ensuring its neutrality, etc.

PMDA shall make efforts to adjust the salary levels of the employees to achieve an appropriate and efficient level, taking into consideration competitiveness for stable securement of excellent human resources.

b) Appropriately develop personnel capacities by having them interact with external institutions to increase their expertise, and appropriately conduct personnel evaluations based on their work performance. PMDA shall also increase motivation of the personnel through these measures, etc.

2) Ensure Security

Ensure security of the offices, etc. and take all measures to thoroughly manage information, in order to thoroughly protect information of personal, corporate, etc.

3) Matters Regarding Disposition of the Reserve Funds Specified in Article 31, Paragraph 1 of the Act on the Pharmaceuticals and Medical Devices Agency

Appropriately dispose the reserve funds that are still left even after adjusting profit and loss according to Article 44 of the Act on General Rules for Incorporated Administrative Agency at the end of the last fiscal-year of the effective period for the Second Mid-term Targets.

4) Other Matters

Steadily conduct approaches based on the government policy indicated in past Cabinet decisions, etc.

Mid-Term Plan of the Pharmaceuticals and Medical Devices Agency

Mid-term Plan of the Pharmaceuticals and Medical Devices Agency (PMDA)
*(Provisional Translation)

** This translation of the original Japanese text is for information purposes only (in the event of inconsistency, the Japanese text shall prevail).*

Notification No. 0331-44 (dated March 31, 2014) of
Pharmaceutical and Food Safety Bureau,
Ministry of Health, Labour and Welfare

To achieve the Mid-term Targets of the Pharmaceuticals and Medical Devices Agency assigned on March 7, 2014 by the Minister of Health, Labour and Welfare based on the provisions of Article 29, Paragraph 1 of the Act on General Rules for Incorporated Administrative Agency (Act No. 103, 1999), the Pharmaceuticals and Medical Devices Agency (PMDA) has developed the following Mid-term Plan based on the provisions of Article 30, Paragraph 1 of the same act.

March 7, 2014

Tatsuya Kondo, Chief Executive,
Pharmaceuticals and Medical Devices Agency

Development toward global PMDA based on the PMDA Philosophy

PMDA was established in April 2004, after several times of reorganization by integrating the services of review and post-marketing safety measures, and has its roots in the “Fund for Relief Services for Adverse Drug Reactions”, which was established following tragic pharmaceutical-induced sufferings caused by pharmaceuticals such as thalidomide and diseases such as subacute myelo-optical neuropathy (SMON). Based on this history, and in order to carry out its mission to promptly provide the public with more effective and safer pharmaceuticals and medical devices, PMDA has been dedicating itself to improve its services for review, post-marketing safety measures, and relief services for adverse health effects. Essential targets have been accomplished by accelerating reviews and enhancing post-marketing safety measures in its efforts during the first and second terms. PMDA will need to further strengthen and enhance its system to aim to be a world-class institution responsible for reviews and post-marketing safety measures, in order to equal the United States and Europe in the future.

PMDA will promote comprehensive risk management through “Safety Triangle”, a system based on three major services, which are the review, post-marketing safety measures for pharmaceuticals and medical devices, and relief services for adverse health effects, to secure safety and efficacy, based on the following organizational philosophy of action (PMDA Philosophy).

1) We pursue the development of medical science while performing our duty with greater transparency based on our mission to protect public health and the lives of our citizens.
2) We will be the bridge between the patients and their wishes for faster access to safer and more effective pharmaceuticals and medical devices.
3) We make science-based judgments on quality, safety, and efficacy of medical products by training personnel to have the latest technical knowledge and wisdom in their field of expertise.
4) We play an active role within the global community by promoting global harmonization.
5) We conduct services in a way that is trusted by the public based on our experiences from the past.

In promoting its risk management, PMDA will especially make efforts to develop an environment that enables judgments from an ethical perspective based on regulatory science, and to proactively contribute in improving public health and safety. PMDA will also promote cooperation with the United States, Europe, and Asian countries, etc., and approach issues from a global perspective in order to further improve health of people not only in Japan but also in the world.

Based on the Japan Revitalization Strategy (adopted by the Cabinet on June 14, 2013), the Healthcare and Medical Strategy (an agreement among the Chief Cabinet Secretary, Minister of Health, Labour and Welfare, and Minister of Internal Affairs and Communications, etc., on June 14, 2013), the Act to Ensure Quality, Efficacy, and Safety of Pharmaceuticals and Medical Devices (Act No. 145, 1960; hereinafter referred to as the "Pharmaceutical and Medical Devices Act"), and the Act to Ensure Safety of Regenerative Medicine (Act No. 85, 2013; hereinafter referred to as the "The Act of the Safety of Regenerative Medicine"), etc., PMDA will further accelerate and improve the review services in order to promote to be the first in the world in practical use of innovative pharmaceuticals, medical devices, and regenerative medical products, while taking post-marketing safety measures, such as ensuring quality of post-marketing products and preventing occurrence and spread of health hazards.

In order to achieve these goals, the review and post-marketing safety measures in this term shall be improved by further enhancing the system and by introducing new review methods, etc., while pursuing elimination of review lag. Efforts will be made to have the public be aware of the relief services to ensure utilization of them. With these targets, the Third Mid-term Plan is to be established and implemented as follows:

Part 1

Measures to be taken in Order to Achieve Targets Related to Matters Regarding Improvement in Operation Management of the Overall Corporation and Matters Regarding Improvement in the Quality of Services and Other Operations Rendered to the Public

The following are the measures to be taken in order to achieve targets regarding improvement in efficiency of operations, as stipulated in Article 30, Paragraph 2, Item 1 of the Act on General Rules for Incorporated Administrative Agency (Act No. 103, 1999; hereinafter referred to as the "Act on General Rules"), and to achieve targets regarding improvement in the quality of services and other operations rendered to the public, as stipulated in Article 30, Paragraph 2, Item 2 of the Act on General Rules.

1) Efficient and Flexible Management of Operations

a) Manage transparent and appropriate operations through thorough compliance risk management

- Clarify the operational targets and responsibilities of each division, and identify and resolve problems by managing the operational progress on a daily basis.
- Develop and appropriately utilize internal control processes to achieve efficacy and efficiency of operations, reliability of financial reports, compliance with acts related to operational activities, and maintenance of assets, and proactively disclose the details of those measures that were taken.
- Gather opinions on operational performance for each fiscal year and utilize them in managing the operations.
- Hold advisory councils as an opportunity to exchange opinions with experts from various fields, and seek proposals and improvement measures for operations and the management system, in order to increase efficiency as well as to ensure fairness and transparency of the operations.
- Efficiently manage the operations by flexibly allocating personnel according to situations and by effectively utilizing external experts.
- Utilize manuals for emergency management appropriately by reviewing them from time to time in response to particular situations, in order to thoroughly manage risks in the management of operations.

- Develop a system necessary to support the operations of the review, post-marketing safety measures, and relief service in order to respond to the expansion of the organization due to system reinforcement, and to enable reviewers to concentrate on technical and specialized operations.

b) Standardize operation procedures
- Standardize the procedures of each operation so that they can be conducted appropriately, which will enable utilization of non-regular staff, and as a result limit the number of regular staff members.

c) Develop materials and information databases
- Utilize an electronic format for documentary information whenever possible, and promote the development of databases that enable the information to be systematically organized and stored, as well as to enable material and information to be collected and analyzed.

d) Optimize the system to improve efficiency of operations
- Continue operations based on the basic policies of the Pharmaceuticals and Medical Devices Agency (hereinafter referred to as the "Agency") for developing the system environment.
- Based on the Optimization Plan for Operations and Systems that was established at the end of FY 2007, a system shall be developed to promote information sharing in the operations of review, post-marketing safety measures, and relief services for adverse health effects, and further approaches shall be promoted for the optimization of operations and systems, which was revised in FY 2012 for the purpose of enhancing the accounting and personnel management functions to respond to changes such as increase in personnel. Expenses for system development and improvement shall be invested systematically and efficiently by comprehensively judging at the Committee on Investment in Information Systems from such perspectives as appropriateness, cost-effectiveness, and technical difficulty.
- Along with the Optimization Plan for Operations and Systems, increase efficiency of operations by revising the information system according to the actual status of the operations in each division.

2) Rationalize Operation Management

a) Retrench general administrative expenses (management divisions)
- By continuously improving the operation and increasing efficiency in management, the following reduction in the budget for the Mid-term Plan is expected to have been achieved by the end of the effective period for Mid-term Targets, regarding general administrative expenses (excluding personnel expenses) in which the administrative subsidies are to be applied.
- No less than 15% as compared to FY 2014
- Appropriately utilize consolidation and outsourcing for management operations such as payroll accounting, fund balancing, and calculation of travel expenses.

b) Retrench operating expenses for efficient operation management
- By increasing efficiency in operations such as promoting computerization, the following reduction in the budget for the Mid-term Plan is expected to have been made by the end of the effective period for Mid-term Targets, regarding operating expenses (excluding personnel expenses, and single fiscal-year expenses that were paid for the establishment of operations) in which the administrative subsidies are to be applied.
- No less than 5% as compared to FY 2014
- Appropriately utilize consolidation and outsourcing for management operations such as payroll accounting, fund balancing, and calculation of travel expenses.

c) Calculate administrative subsidies
- Yearly administrative subsidies are to be rigorously calculated with consideration of its debt balance.

d) Stable collection of contributions

- Have the marketing authorization holders (MAHs) of pharmaceuticals and medical devices understand the significance of the contribution system for adverse drug reaction (ADR) fund, relief for infections, and contributions to post-marketing safety measures, in order for contributions to be appropriately declared and paid, and to ensure stable collection of each contribution.
- The collection rate for the contributions of ADR fund, relief for infections, and contributions to post-marketing safety measures shall be no less than 99%.

e) Secure contract competitiveness and transparency
- Contracts shall be concluded through open competitive bidding as a principle, and the following approaches shall be made.
- Fully secure competitiveness and transparency even when contracts are not concluded by general competitive bidding such as planning competition and invitation to bids.
- To conduct biddings and conclusion of contracts appropriately, contracts should be pre-inspected, etc., by the Contract Review Committee and thoroughly checked by auditor and accounting auditor.

f) Provide and disseminate genuinely useful information from the public perspective
- Take the following measures to steadily implement the PMDA Public Relations Strategic Plan.
  1. Enhance dissemination of information by improving the website so that it can be easily understood in order for the public and patients to be able to readily access information regarding safety and efficacy of pharmaceuticals and medical devices.
  2. Conduct public relations using newsletters related to PMDA.
  3. Provide and publish information regarding PMDA in television and magazines.
  4. Create newsletters in English and disseminate information to Foreign Correspondents' Club of Japan and to foreign media.
  5. Enhance and improve the system for responding to consultations and complaints from the public.
- Enhance dissemination of information to the general public by disclosing the details of PMDA's services and achievements when appropriate, through various media including its website in order for the public to better understand the safety of pharmaceuticals and medical devices, as well as the overall services of PMDA.
- Conduct external audit in accordance with the incorporated administrative agencies system, together with systematic internal audit and accounting audit, and disclose those results.
- Disclose PMDA's overall financial standing as well as its financial standing for each account and segment in order to ensure transparency of the expenditures.

g) Analyze issues of the operation system
- Quantitatively analyze and examine issues of each division regarding the current operation processes as well as their systems as much as possible by the midpoint of the effective period for the Third Mid-term Targets, based on the understanding of the past operating performances of the relief service, review, and safety divisions, and those processes and systems shall be revised if necessary in order to confirm whether the personnel are allocated appropriately for the system enhancement and whether the operations are conducted efficiently.

h) Considerations related to financial base
- Consider a financial base that is appropriate for the role of PMDA, and take necessary measures based on the current situation where PMDA's revenue such as user fees from companies accounts for the majority of the financial base of PMDA, because the review and safety services of pharmaceuticals and medical devices greatly influence the life and safety of the public.

Part 2

Measures to be taken in Order to Achieve Targets Related to Matters Regarding Improvement in Operation Management of Each Division and Matters Regarding Improvement in the Quality of Services and Other Operations Rendered to the Public

- Make all efforts to promote the safety triangle of review, safety, and relief as a mission of PMDA -

1. Relief Fund Services for Adverse Health Effects

The Relief System for ADR and the Relief System for Infections Acquired through Biological Products (hereinafter referred to as the "relief systems") are systems unique to Japan, which, along with reviews and post-marketing safety measures, are responsible for being part of the safety triangle. The following measures shall be taken for the necessity of having the relief systems to be definitely utilized through consultations with physicians and pharmacists in case of emergencies of health damage due to ADR of pharmaceuticals or regenerative medical products, or due to infections through biological products or regenerative medical products, as well as for the necessity of continuing appropriate operations, such as prompt processing of relief benefit claims.

1) Enhance Public Relations and Dissemination of Information Regarding the Relief Systems

a) Proactively develop public relations in order for the relief systems to be definitely utilized.

- Consider and proactively conduct effective public relations regarding the relief systems.
- Continue informing more of the public regarding the relief systems by utilizing such media as websites and newspapers.
- Current measures, including dissemination of thorough information with the cooperation of relevant organizations, etc., shall be promoted, and the following measures shall be focused in order to increase the awareness by the end of the effective period for the Mid-term Targets, in order to further gain awareness and understanding from the public, health care professionals and MAHs, etc., regarding the relief systems. Surveys shall be conducted every fiscal year to find out the degree of their awareness, and those results shall be examined.

1. Public relations activities shall be proactively conducted by utilizing the opportunities of training at medical institutions for health care professionals and opportunities of informing pharmacists regarding the systems, in order to properly make patients know the existence of relief systems by healthcare professionals including physicians and pharmacists, in case health damage occurs due to ADR or infections through biological products.
2. Develop public relations nationwide through professional medical organizations.
3. Conduct public relations for the general public using such media as websites, television, and newspapers.
4. Develop effective public relations through other media aside from the above that is appropriate for promoting the relief systems.

b) Announce cases of benefit payment

- Further understanding of the current situation of benefit payment and dissemination of the relief systems to the public, healthcare professionals shall be promoted, by announcing cases of benefit payment and operational statistics on the website.

c) Disseminate information regarding the relief systems

- Review the methods of disseminating information from the perspective of making it user-friendly and easy to be understood, by revising the pamphlets and claim guidelines, by improving the content of information disseminated through the Internet, etc.

d) Ensure an efficient system for the consultation services
   - Allocate regular staff for the consultation services, and ensure a system where specialized consultations can be received regarding use of the relief systems as well as the procedures to process benefit payments for ADR and infections.

2) Accelerate the Processing of Relief Benefit Claims
   a) Investigate and organize the facts of the claim
      - In order for relief benefit claims to be promptly processed, the facts of the claims shall be investigated and organized when received, before requesting the Minister of Health, Labour and Welfare for medical and pharmaceutical judgment.
   b) Promptly process within the standard administrative processing time
      - The target administrative processing time from receipt of the claim until the decision of payment (within 6 months, more than 60%) shall be maintained even in situations where the number of claims is expected to increase, by taking appropriate measures such as by enhancing the system for receiving and investigating claims, further enhancing and improving instructions for filling medical certificates, and accurately managing the time to use a system.
      - Administrative processing time shall exclude the period when processing could not be continued because additional or supplementary documents and investigations of the claimant or medical institutions were necessary in order to make medical and pharmaceutical judgments.
   c) Promote efficient operation with the use of databases
      - Data of information related to the operation of relief services of ADR, especially information on the causative pharmaceutical, etc., and health damages shall be accumulated on the database, and those accumulated data shall be statistically processed so that they can be analyzed from various perspectives, in order to operate a system that enables prompt and efficient payment of relief benefits using those results.
      - Upgrade the systems, develop operation support tools, and enhance systems if necessary, in order to respond to increases in relief benefit claims and to operational situations accordingly.

3) Promote Cooperation with the Review Divisions and the Safety Divisions
   - Cooperate with each division of PMDA and appropriately disseminate information, especially regarding cases of relief payment to the divisions of review and the post-marketing safety measures, with attention to ensuring protection of personal information.

4) Implement Appropriate Health and Welfare Services
   - Based on the results of a survey that investigated the current situation of health damages due to ADR, investigative research shall be continued in order to obtain information for considering measures to improve QOL of patients suffering from serious and rare health damages.
   - Steadily conduct consultations regarding mental issues.

5) Provide Healthcare Allowances for SMON Patients and HIV-positive Patients Infected with Blood Products Appropriately
   - In providing healthcare allowances to SMON patients and HIV-positive patients infected with blood products, appropriate services shall be implemented based on the details of the consignment contract, with special attention to ensuring protection of personal information.

6) Pay Benefits to Assist Individuals Affected by Hepatitis C through Specified Fibrinogen Products and Specified Blood Coagulation Factor IX Products Contaminated by Hepatitis C virus Appropriately
   - In providing benefits to assist individuals affected by hepatitis C through specified fibrinogen products and specified blood coagulation factor IX products contaminated by hepatitis C virus, appropriate operations shall be implemented, with special attention to ensure protection of personal information.

2. Reviews and Related Services

Based on the Japan Revitalization Strategy and the Healthcare and Medical Strategy, as well as the Pharmaceutical and Medical Devices Act and the Regenerative Medicine Act that were revised as a result of the Act for Partial Revision of the Pharmaceutical Affairs Act, (Act No. 84, 2013), reviewing speed shall be accelerated, aiming to reduce review lag*, and the quality of the reviews shall be improved through approaches according to the characteristic of each pharmaceutical, medical device, and regenerative medical product (hereinafter, including cellular and tissue-based product and gene therapy product). Pharmaceutical Affairs Consultation on R&D Strategy shall also be enhanced as a support to eliminate the development lag*.

In order to achieve these targets, PMDA's financial resources shall be utilized in enhancing the system.

* Drug lag and device lag are defined as delay of approvals of pharmaceuticals and medical devices, respectively, from United States in Japan. Drug lag or device lag can be divided into review lag, which are differences in review time (time from application to approval) between the United States and Japan, and development lag, which are the differences in time at which the companies submit application to the regulatory agencies of the United States and Japan (from the Japan Revitalization Strategy [approved by the Cabinet on June 14, 2013]). The overall lag shall be eliminated by eliminating the review lag and development lag.

Following measures shall be promoted in order for the above mentioned measures to be implemented appropriately and smoothly, while maintaining cooperation with MHLW.

Note: The organization responsible for implementing the following measures is PMDA unless otherwise stated as MHLW, or other corporations.

1) Make pharmaceuticals, medical devices, etc. accessible by the public more quickly

New pharmaceuticals

a) Conduct accurate and prompt reviews

- Enhance system in order to improve quality of the reviews by utilizing the Science Board and by enhancing training, with aiming to achieve elimination of review lag.
- Steadily implement the project management system in order to improve the progress management function of the review services and to increase transparency of the progress and outlook of reviews for applicants as well.
- Continue considering the efficiency and transparency of the review services and processes through exchange of opinions with the industry.
- Strengthen cooperation with academia and healthcare professionals in order to conduct consultations and reviews based on the latest medical care trends and needs, and to promote cooperation toward appropriate use of pharmaceuticals.
- Proactively support and cooperate in discussions and in requesting development for unapproved pharmaceuticals etc., at the Study Group on Unapproved and Off-label Pharmaceuticals of High Medical Need organized by MHLW.
- Continue making approaches to reduce unapproved pharmaceuticals and off-label pharmaceuticals by enhancing database for the current status of pharmaceutical approval in major overseas nations.
- Secure consistency between clinical trial consultations and reviews by maintaining cooperation between these two services, and flexibly organize groups to conduct accurate and prompt reviews and consultations.
- Conduct accurate and prompt re-examinations for new pharmaceuticals. Take appropriate measures for re-evaluations as well.

- Promote establishment of standards regarding quality of pharmaceuticals, such as the Japanese Pharmacopoeia established by MHLW, in order to conduct accurate and prompt reviews.

b) Introduce new methods for reviews and others

- Systematically enhance the system for prior assessment consultations and respond to all consultations that were requested regarding superior pharmaceuticals of high medical need by the FY 2018.
- Develop a system in PMDA that enables to accept electronic submission of clinical study data regarding new pharmaceutical applications after FY 2016.
- Improve the quality of reviews and consultations by conducting PMDA-initiated analyses using the clinical trial data and by giving indications and suggestions based on those analyses results. Consider a system that enables cross-sectional analyses of products using advanced methods of analysis and prediction evaluation, and further improve reviews and consultation by establishing guidelines, etc., and increase efficiency of pharmaceutical development.

c) Targets to aim for eliminating review lag in pharmaceuticals

- Regarding pharmaceuticals which new pharmaceutical applications were submitted after April 1, 2004, the percentile of the standard total review time from application to approval for the items approved in respective fiscal years, shall rise in stages as shown in the following table. The review time of 9 months for priority review products and 12 months for standard review products shall be achieved at 80th percentile by FY 2018.
  The review services shall be enhanced to achieve these targets.

1. Review time for new pharmaceuticals (priority review products)

Fiscal year	Percentile	Review time
FY 2014	60%	9 months
FY 2015	60%	9 months
FY 2016	70%	9 months
FY 2017	70%	9 months
FY 2018	80%	9 months

2. Review time for new pharmaceuticals (standard review products)

Fiscal year	Percentile	Review time
FY 2014	60%	12 months
FY 2015	70%	12 months
FY 2016	70%	12 months
FY 2017	80%	12 months
FY 2018	80%	12 months

- Regarding re-examination of new pharmaceuticals, the review time shall be reduced in stages regarding pharmaceuticals that are to be submitted for re-examination after FY 2014, with review results issued in respective fiscal years, and the total review time of 18 months shall be achieved at 50th percentile (median) by FY 2018. Products re-examined before FY 2014 shall also be sequentially processed.
- Regarding re-evaluations, evaluation and confirmation shall be conducted without delay by setting the appropriate standard review time to each pharmaceutical, based on the points of the application.

d) Promote multi-regional clinical trials
- In order to promote multi-regional clinical trials, appropriately respond to requests for consultations related to multi-regional clinical trials, based on the guidance regarding study design, etc.
- In order to promote multi-regional clinical trials especially in Asian countries, PMDA shall support the approaches of the Multi Regional Clinical Trial Roadmap led by MHLW at APEC RHSC, and develop an environment for conducting multi-regional clinical trials in Asian countries.
- PMDA shall promote multi-regional clinical trials in clinical trial consultations, etc., including information sharing with foreign regulatory agencies so as to increase the rate of conducting multi-regional clinical trials that Japan will participate amongst foreign clinical trials by FY 2018, to eliminate pharmaceutical development lag.

e) Conduct smooth clinical trial consultations, etc.
- Priority consultations and advance confirmation of application documents shall be continued, in order to increase opportunities to provide guidance and consultations before applications.
- Firmly maintain the time it currently takes from request for clinical trial consultation of new pharmaceuticals to direct consultation (about 2 months), while at any time accepting requests for priority clinical trial consultations so as to accelerate procedures for clinical trial consultations on new pharmaceuticals.
- Regarding categories such as prior assessment consultations, Pharmaceutical Affairs Consultation on R&D Strategy, and simple consultations, categories shall be added or altered according to the needs of the applicants by exchanging opinions with relevant industries and by analyzing the content of consultations, so as to enhance clinical trial consultations.

f) Promote evaluation of new technologies, etc.
- For pharmaceuticals developed using new technologies, concepts regarding development and evaluation shall be established in cross-sectional projects, along with guidelines if necessary, by using the knowledge of the Science Board and opinions of external experts.
- PMDA shall increase its scientific knowledge in order to lead the development of pharmaceuticals using latest technologies such as iPS cells.
- Cooperate with MHLW in establishing guidelines for evaluating products using the latest technologies, and proactively disclose the points to consider for evaluations.
- For preliminary reviews regarding the Act Concerning the Conservation and Sustainable Use of Biological Diversity through Regulations on the Use of Living Modified Organisms (hereinafter referred to as the “Cartagena Act”), the regulatory review time shall be 6 months for approval of first-class use and 2 months for confirmation of second-class use, with a target of achieving 50th percentile (median) for each class.
- Enhance the Pharmaceutical Affairs Consultation on R&D Strategy by conducting consultations where suggestions can be made on development processes (roadmap) as well as confirmatory trial protocols, and by conducting consultations for pharmaceutical companies on developmental strategies.

Generic drugs, etc.

The following measures shall be taken to promote wide use of generic drugs, etc.

a) Conduct accurate and prompt reviews

1. Establish a new office for generic drugs, etc.
   - Enhance and accelerate reviews by appropriately increasing and allocating members for the generic drug, etc. group and by establishing a new office.
2. Ensure efficient and transparent reviews
   - Strengthen cooperation with academia and healthcare professionals, etc. to conduct consultations and reviews based on the latest medical care trends and needs, and to promote cooperation toward appropriate use of pharmaceuticals.
   - Promote establishment of standards regarding quality of pharmaceuticals, etc., such as the Japanese Pharmacopoeia, etc., established by MHLW, in order to conduct accurate and prompt reviews.
   - Recommend application by CTD/eCTD format in order to increase efficiency in reviews.
   - Ensure transparency of the reviews by preparing and disclosing review reports on new generic drugs.
   - Establish guidelines for bioequivalence testing in order to respond to the increased complexity of bioequivalence assessments and the diverse pharmaceutical products that are being developed.
   - Cooperate with relevant offices to take appropriate measures to steadily implement the risk management plan.

b) Targets for reducing review time

- Regarding pharmaceuticals which applications were submitted after April 1, 2004, the target review times for the items approved in respective fiscal years, shall be as shown in the following table. The regulatory authority shall make efforts to achieve these targets with the cooperation of the applicants. The review system shall be enhanced to achieve these targets.

1. Review time for new application of generic drugs

   The following targets shall be achieved at 50th percentile (median) by FY 2018.

Product	Regulatory review time
New generic drugs	10 months

2. Review time of application for partial change approval in generic drugs, etc. (standard review products)

   Targets shall be achieved at 50th percentile (median) by FY 2018, based on the following plan.

Fiscal year	Total review time
FY 2014	15 months
FY 2015	14 months
FY 2016	13 months
FY 2017	12 months
FY 2018	10 months

3. Review time of application for partial change approval in generic drugs, etc. (products other than standard review products)

The following targets shall be achieved at 50th percentile (median) by FY 2018.

Products	Total review time
Products applied for partial change approval (change in procedure of study, etc.)	6 months
Products applied for partial change approval (prompt review)	3 months

c) Conduct smooth clinical study consultations, etc.

- All consultations shall be conducted for those requested for quality consultation or bioequivalence consultation (face to face consultation).
- Enhance consultation services by considering whether setting up new consultation categories are necessary to meet the needs of the applicants.

Behind-the-counter (BTC) drugs*, over-the-counter (OTC) drugs, and quasi-drugs

The following measures shall be taken to promote public self-medication.

a) Conduct accurate and prompt reviews

- In order to conduct accurate and prompt reviews for BTC drugs, OTC drugs, and quasi-drugs, etc., the following measures shall be taken to enhance the review system, etc., including safety assessments.

1. Enhance system for BTC drugs and OTC drugs, etc.
   - In order to respond to the establishment of BTC drugs system, etc., that was newly developed by the Act for Partial Revision of the Pharmaceutical Affairs Act and the Pharmacists Act (Act No. 103 of 2013), the review system shall be enhanced by allocating reviewers for toxicity and clinical matters (including biostatistics), and by securing human resources who have experience in post-marketing safety measures and conformity assessment.
   - Strengthen cooperation with academia and healthcare professionals, etc., in order to conduct consultations and reviews based on the latest medical care trends and needs, and to promote cooperation toward appropriate use of BTC drugs and OTC drugs.
   - Conduct accurate and prompt reviews by establishing standards regarding quality of pharmaceuticals, such as the Japanese Pharmacopoeia as well as official specification for excipients.
   - Increase efficiency and enhance the review service for Chinese herbal medicines and crude drugs.
2. Enhance system for quasi-drugs, etc.
   - Increase the number of reviewers in order to accelerate reviews for innovative products.
   - Increase efficiency of the reviews by establishing standards for quasi-drugs, such as the Japanese Standards of Quasi-drug Ingredients established by MHLW, as well as establishing quality standards for excipients, etc.
   - Improve quality of the reviewers through training, etc.
   - Strengthen cooperation with academia and healthcare professionals, etc., in order to conduct consultations and reviews based on the latest medical care trends and needs, and to promote cooperation toward appropriate use of quasi-drugs.

* Behind-the-counter (BTC) drugs are defined as switch OTC drugs and powerful OTC drugs which require pharmacist's intervention.

b) Targets for reducing review time

- Regarding BTC drugs, OTC drugs and quasi-drugs which applications were submitted after April 1, 2004, and were approved in respective fiscal years, the target review times shall be as shown in the following table. Approaches shall be made to achieve these targets.

1. Review time for BTC drugs and OTC drugs

The following target shall be achieved at 50th percentile (median) by FY 2018.

Product	Regulatory review time
BTC drugs and OTC drugs	7 months

2. Review time for quasi-drugs

The following target shall be continuously achieved at 50th percentile (median) by FY 2018.

Product	Regulatory review time
Quasi-drugs	5.5 months

c) Conduct smooth consultation services

- For BTC drugs and OTC drugs, conduct consultations on the appropriateness of developing new OTC drugs, etc., pre-application consultations for switch OTC drugs, and consultations on confirming the key points of the protocols.
- For quasi-drugs, develop and conduct pre-application consultations.

Medical devices

a) Conduct accurate and prompt reviews

- Systematically enhance the review system for new medical devices in order to accelerate the reviews for innovative medical devices.
- Accelerate reviews by making efforts to conduct rational reviews based on the characteristic of medical devices which constantly being improved, etc.
- Strengthen cooperation with academia and healthcare professionals in order to conduct consultations and reviews based on the latest medical care trends and needs, and to promote cooperation toward appropriate use of medical devices.
- Proactively support and cooperate in requesting development for medical devices, including unapproved medical devices, at the Study Group on the Early Introduction of Medical Devices, etc. with High Medical Need held by MHLW.
- Make efforts to smoothly operate and implement the new use-results evaluation system for medical devices.
- For new medical devices, improved medical devices, and generic medical devices, thoroughly manage the timeline for the standard review process so as to be conducted adequately.

b) Clarify review standards, etc.

- Compile and disclose the concept regarding clinical evaluation.
- In order to accelerate the reviews, cooperate with MHLW in establishing approval standards, certification standards, and review guidelines for medical devices, and disclose those standards and guidelines on the website, etc.
- Clarify, share, and establish the concept of substantial equivalence for generic medical devices.

c) Smoothly transfer specially controlled medical devices to the third party certification system

- Transfer to the third party certification system sequentially from the products whose standards have been established among specially controlled medical devices (class III).

d) Targets to aim for eliminating review lag in medical devices

- Regarding medical devices which applications were submitted after April 1, 2004, the percentile of the standard total review time from application to approval for the items approved in respective fiscal years, shall be raised in stages as shown in the following table, in order for the targets to be achieved by FY 2018. Approaches shall be made to achieve these targets by systematically and intensively completing processing of the devices that were submitted for application in the past as soon as possible, and the regulatory authority shall make efforts to improve the lag with the cooperation of the applicants.

1. Review time for new medical devices (priority review products)
   Achieve 10 months at 80th percentile by FY 2018 based on the following plan.

Fiscal year	Percentile	Review time
FY 2014	60%	10 months
FY 2015	60%	10 months
FY 2016	70%	10 months
FY 2017	70%	10 months
FY 2018	80%	10 months

2. Review time for new medical devices (standard review products)
   Achieve 14 months at 80th percentile by FY 2018 based on the following plan.

Fiscal year	Percentile	Review time
FY 2014	60%	14 months
FY 2015	60%	14 months
FY 2016	70%	14 months
FY 2017	70%	14 months
FY 2018	80%	14 months

3. Review time for improved medical devices (with clinical data)
   Achieve 10 months at 60th percentile by FY 2018 based on the following plan.

Fiscal year	Percentile	Review time
FY 2014	52%	10 months
FY 2015	54%	10 months
FY 2016	56 %	10 months
FY 2017	58 %	10 months
FY 2018	60 %	10 months

4. Review time for improved medical devices (without clinical data)
   Achieve 6 months at 60th percentile by FY 2018 based on the following plan.

Fiscal year	Percentile	Review time
FY 2014	52%	6 months
FY 2015	54%	6 months
FY 2016	56 %	6 months
FY 2017	58 %	6 months
FY 2018	60 %	6 months

5. Review time for generic medical devices

Achieve 4 months at 60th percentile by FY 2018 based on the following plan.

Fiscal year	Percentile	Review time
FY 2014	52%	4 months
FY 2015	54%	4 months
FY 2016	56 %	4 months
FY 2017	58 %	4 months
FY 2018	60 %	4 months

e) Conduct smooth clinical trial consultations, etc.
- Reconsider the consultation category and improve consultation methods in order for the consultation service to be easier to utilize, and to be efficient and effective.
- Address the relevant industries to proactively utilize the consultation service, in order to eliminate review lag and development lag.

f) Promote evaluation of new technologies, etc.
- For medical devices using new technologies, guidelines, etc., shall be established if necessary, utilizing knowledge of the Science Board and opinions of external experts.
- Make efforts to accumulate relevant knowledge, etc., in order to appropriately respond to the development of medical devices using the latest technologies.
- Cooperate with MHLW in establishing guidelines for evaluating products that were developed using the latest technologies, and proactively disclose the points to consider for evaluations.
- For preliminary reviews regarding the Cartagena Act, the regulatory review time shall be 6 months for approval of first-class use and 2 months for confirmation of second-class use, with a target of achieving 50th percentile (median) for each class.
- Enhance the Pharmaceutical Affairs Consultation on R&D Strategy by conducting consultations where suggestions can be made on development processes (roadmap) and confirmatory trial protocol, and by conducting consultations for medical devices related companies on developmental strategies.

***In vitro* diagnostics**

a) Conduct accurate and prompt reviews
- Appropriately increase and allocate members for the *in vitro* diagnostics group, in order to accelerate and increase transparency of the reviews.
- Strengthen cooperation with the academia and healthcare professionals, etc., to conduct consultations and reviews based on the latest medical care trends and needs, and to promote cooperation toward appropriate use of *in vitro* diagnostics.
- Proactively support and cooperate in requesting development of *in vitro* diagnostics, including those that are still unapproved, that were discussed at the Study Group on the Early Introduction of Medical Devices, etc., with High Medical Need held by MHLW.

b) Enhance consultation service
- Reconsider the consultation category and improve consultation methods in order for the consultation service to be easier to utilize, and to be efficient and effective.

Regenerative medical products

a) Conduct accurate and prompt reviews
- Enhance the services of the division of Pharmaceutical Affairs Consultation and its relevant divisions, as well as the division of biologics reviews. Strengthen cooperation with academia such as the Japanese Society for Regenerative Medicine, the National Institute of Health Sciences, and the

Center for iPS Cell Research and Application (CiRA), etc., in order to conduct consultations and reviews based on the latest medical care trends and needs.
- Conduct consultations.

b) Introduce new review methods
- With the implementation of the Act for Partial Revision of the Pharmaceutical Affairs Act, respond appropriately to conditions related to regenerative medical products and to the introduction of time-limited approvals. Develop a system for this, along with its review process, and conduct them accurately.

c) Target review time
- For regenerative medical products which applications were submitted based on the Pharmaceutical Medical Devices Act, standard review time (regulatory time) for the items approved in respective fiscal years shall be set to 9 months.
  The review system shall be enhanced to achieve this target.

d) Conduct smooth clinical study consultations, etc.
- Make efforts to conduct thorough consultations so as to be understood easily, since regenerative medical products are a new field.
- Conduct high-quality consultations by utilizing the Science Board for considering evaluation methods, etc., and highly-qualified external experts, etc., to obtain the latest knowledge.
- PMDA shall make efforts to have applications of regenerative medical products after going through consultations such as the Pharmaceutical Affairs Consultation on R&D Strategy (as the substitute of pre-confirmation application) and pre-application consultations, and develop a system necessary to conduct prompt and smooth reviews considering the current situation of consultations and reviews.
- In order to enable the academia and ventures to consult easily, the target details, etc., of the Pharmaceutical Affairs Consultation on R&D Strategy shall be considered for regenerative medical products, based on the current situation.

e) Promote evaluation of new technologies, etc.
- Conduct appropriate evaluations for regenerative medical products, by utilizing the Science Board for considering evaluation methods, etc., and highly-qualified external experts.
- Make efforts to accumulate relevant knowledge, etc., in order to be able to appropriately respond to the development of regenerative medical products using the latest technologies, such as iPS cells, etc.
- Clarify and rationalize the review standards by promoting the initiative to facilitate development and designated research.
- Enhance the post-marketing surveillance, considering especially the surveillance methods for those conducted after conditional and time-limited approvals, cooperating with the safety division.
- Cooperate with the MHLW in establishing evaluation guidelines regarding products using the latest technologies, and proactively disclose the points to consider for evaluations.
- Enhance consultations to enable proactive utilization of Pharmaceutical Affairs Consultation on R&D Strategy as the substitute of preliminary reviews conducted before clinical trials regarding regenerative medical products and gene therapy products.
- For preliminary reviews regarding the Cartagena Act, the regulatory review time shall be 6 months for approval of first-class use and 2 months for confirmation of second-class use, with a target of achieving 50th percentile (median) for each class.

Promotion of conformity assessments and clinical trials, etc.

The following measures shall be taken to enhance, with strengthening the organization, studies related to the application such as clinical trials, and to ensure reliability of submitted application documents, with focus on an importance of ensuring the reliability of clinical trial data, etc., at the application of pharmaceuticals and medical devices.

a) Implement smooth and efficient conformity assessments for new pharmaceuticals, etc.
   - Strengthen the organization to conduct timely assessments which will not affect the time of approval. New assessment methods with efficiency and effectiveness shall also be introduced.
   - As for the items concurrently submitted with the applications in the world, etc., strengthen the coordination on partnership with foreign regulatory agencies and strengthen the organization, for example, considering the assessment in collaboration with them.
   - Make clear policy on the procedure for clinical trials in which CDISC was introduced from data gathering step.

b) Implement smooth and efficient conformity assessments for medical devices
   - Strengthen the organization to conduct timely assessments which will not affect the time of approval.
   - Strengthen the organization conduct GCP on-site assessment, in particular, focus on innovative medical devices and multi-regional clinical trials, etc.
   - Establish and disseminate detailed requirements that are necessary for applications, in order to implement conformity assessments smoothly and promptly.

c) Implement smooth and efficient conformity assessments for regenerative medical products
   - Cope with the introduction of a conditional and time-limited approval system.
   - In order to implement appropriate conformity assessments, coordinate with the division of biologics review sufficiently considering assessment methods and processes that are based on the characteristics of regenerative medical products.

d) Implement smooth and efficient GLP compliance assessment
   - Train GLP inspectors that has global competency.
   - Examine how to establish a smooth operation of the GLP regulation considering global consistency, and implement the GLP compliance assessment more appropriately and efficiently.

e) Implement smooth and efficient conformity assessment for re-examinations (including conformity assessment on use-results evaluation)
   - Implement efficient and effective GPSP on-site assessments and document-based conformity assessments.
   - To enable high quality post-marketing surveillances, examine to establish such as consultation to provide guidance and advices regarding the compliance for GPSP, etc., during the re-examination period.
   - Examine and disseminate effective assessment methods, to enable smooth and prompt conformity assessments for re-examination, etc.

f) Promote appropriate clinical trials, etc.
   - Enlighten the further promotion for implementation of appropriate clinical trials, etc., through the conformity assessment at medical institutions and sponsors, and training course, etc., in the period of the Mid-term targets, to ensure the quality of clinical trials, etc. in Japan.
   - Examine the establishment of advice system that enables individual cases on GCP, etc.

Promotion of GMP/QMS/GCTP inspection

In order for manufacturers to appropriately maintain and control manufacturing processes and the quality management system for pharmaceuticals, medical devices, and regenerative medical products, the following improvements shall be made to improve inspectional quality.

a) Conduct efficient GMP inspections
   - In response to accelerated reviews and increased numbers of bio-products, methods to improve GMP inspection efficiency shall be considered and conducted. This includes system enhancements to conduct timely inspections and clarify application time, while not affecting the time of approval.
   - Increase the efficiency of inspections by using the assessment results of other regulatory agencies under PIC/S etc., in risk evaluation to decide if inspections shall be conducted on-site or off-site.
   - In response to globalization of active pharmaceutical ingredients supply, partnerships with foreign regulatory agencies shall be reinforced and inspectional information shall be exchanged. A system to enhance on-site inspections at manufacturers overseas, especially in Asian countries, shall be developed.
   - Quality of inspections shall be improved by having reviewers accompany the GMP inspection team and by promoting cooperation between GMP inspectors and reviewers.
   - Enhance staff training for GMP inspectors by letting them proactively participate in training and meetings conducted overseas. Overseas training will increase staff with knowledge of global GMP harmonization and practices.

b) Conduct smooth and efficient QMS inspections
   - QMS inspection and related operations streamlined by the Act for Partial Revision shall be established.
   - Promote cooperation between the review groups and the QMS inspection group.
   - Standardize inspection methods with other domestic and overseas inspection agencies, such as registered certification bodies.
   - Build expertise in global QMS harmonization and practices, through enhancing training for QMS inspectors and let them proactively participate in training and meetings conducted overseas, etc.
   - Share inspection information with relevant domestic authorities to efficiently use resources.

c) Conduct smooth GCTP inspections
   - For accurate and prompt GCTP (Good gene, Cellular and Tissue Practice) inspections by PMDA that will start after enactment of the Act for Partial Revision, appropriate inspection methodology and necessary resources shall be established and secured.
   - For buildings/facilities conformity assessments and relevant on-site inspections by PMDA into establishments that are processing cell/tissue products, that will start after enactment of the Regenerative Medicines Safety Act. Necessary resources shall be immediately secured and managed and current domestic and overseas situation regarding production of such products shall be figured out.

d) Increase efficiency of inspectional efficiency by utilizing the Kansai Branch and by conducting GMP inspections.

Establishment of control function for the registered certification bodies

1) Improve the quality of certification bodies by ensuring the quality of the inspectors and by conducting appropriate training, etc., for those bodies.

2) Provide Support to be the First in the World to Facilitate Practical Use of Innovative Pharmaceuticals, Medical Devices, and Regenerative Medical Products
   a) Establish and update review standards regarding innovative products
      - Utilize the Science Board, the initiative to facilitate practical use of innovative pharmaceuticals, medical devices, and regenerative medical products, and regulatory science research

(hereinafter referred to as the “RS research”), etc., in order to establish guidelines and guidance and to consider RS research, etc., that PMDA shall make approaches on.
- Establish guidelines and guidance, etc., in cross-sectional projects regarding development and evaluation of pharmaceuticals, etc., that uses new technologies, and make necessary approaches in order to smoothly implement them.

b) Proactively conduct Pharmaceutical Affairs Consultation on R&D Strategy, etc.
- Conduct consultations where suggestions can be made on development processes (roadmap) and confirmatory trial protocol. Conduct consultations for pharmaceutical companies on developmental strategies as well.
- Promote medical innovations by utilizing the Kansai Branch to fully educe technological capacity of Japan regarding biopharmaceuticals, medical devices, and regenerative medical products, etc.
- Regarding PMDA’s function to mediate between clinical study and practical use, support, etc., shall be proactively provided through Pharmaceutical Affairs Consultation on R&D Strategy, etc., in establishing exit strategies, with the cooperation of the Japan National Institutes of Health, etc.

c) Operation of approval system based on the characteristics of regenerative medical products
- In order to appropriately cope with conditions related to regenerative medical products as well as the system for time-limited approval that were both introduced by the enforcement of the Act for Partial Revision of the Pharmaceutical Affairs Act, information dissemination and utilization of the consultations shall be promoted, by enhancing Pharmaceutical Affairs Consultation on R&D Strategy and by cooperating with relevant academia and industry.

3. Safety Measures

Utilize finances including PMDA’s own financial resource and enhance system necessary to improve post-marketing safety measures of pharmaceuticals, medical devices, etc., based on the Act for Partial Revision of the Pharmaceutical Affairs Act that reflects the details of Japan Revitalization Strategy, the Healthcare and Medical Strategy, the final recommendation by the Committee for Investigation of Pharmaceutical-induced Hepatitis Cases and Appropriate Regulatory Administration to Prevent Similar Sufferings, the discussions held by the Investigational Sub-committee on Revision of Pharmaceutical Regulatory Systems of the Health Science Council, etc.

The following measures shall be taken in order to promote appropriate and efficient approaches mentioned above, with close cooperation with MHLW.

Note: The organization responsible for implementing the following measures is PMDA unless otherwise stated to be MHLW, etc., or other corporations, etc.

1) Enhance Collection of ADR and Malfunction Information
- Establish a system in which patients can easily report ADR, based on opinions, etc., from the patients and patients’ families, etc., who have reported them, and officially commence accepting and evaluating ADR reports, including reports on OTC drugs and Switch OTC and powerful drugs.
- Accept reports from MAHs as well as healthcare professionals, and take measures to increase reports from healthcare professionals with the cooperation of MHLW.
- Enhance and improve the systems to report information on ADR and malfunctions, etc., based on the current situation of global development such as ICH E2B and on the advancement of information technology, etc., and promote efficient and effective collection of safety information, etc.
- Enhance measures to collect information on ADR of quasi-drugs and cosmetics.

2) Systematize Information of ADR, etc., and Its Evaluation Analysis
   - In order to appropriately respond to the evaluation approach for ADR which is increasingly sophisticated and specialized, substantially enhance current framework to assemble and analyze information on ADR. For this purpose, it is necessary to increase the number of staff members in each group organized according to pharmaceutical effect classification and area of medical practice that correspond to the review divisions. Measures, such as utilizing IT technology, shall also be taken to carefully investigate the overall domestic reports on ADR and infections.
   - Modify a PMDA-initiated system step-by-step to follow-up on ADR reported from medical institutions, and ensure its application for all reports that needs investigation by FY 2018.
   - Standardize and increase transparency of the process from obtaining information of ADR to take post-marketing safety measures including revision of package inserts, and increase accuracy and expediting of the process.
   - Steadily accelerate the process taken to prepare post-marketing safety measures by setting a target time, and by increasing efficiency of the process with standardization. For the target time, consider, reducing the current median time from the first meeting with the MAHs until notification of investigation results.
   - Modify submission process for package inserts to enable MAHs to smoothly submit package inserts.
     Establish a system to check contents of submitted package inserts and ensure that the submitted information is based on the latest knowledge.
   - Respond promptly to consultations from MAHs when it voluntarily develop or revise either package inserts or communication tools for healthcare professionals and patients.
   - Respond promptly to medical safety consultations from MAHs regarding safer use of pharmaceuticals and medical devices at clinical practice.
3) Establish Database, etc., for Medical Information
   - Conduct pharmacoepidemiological analyses using electronic medical information, such as the Medical Information Database Network, and improve those analysis methods to promote its utilization for risk/benefit assessments of pharmaceuticals and for post-marketing safety measures.
   - Promote MAHs to utilize the Medical Information Database Network for post-marketing safety measures, with its conditions of utilization determined by MHLW for post-marketing surveillance, etc., based on results of utilization obtained through pilot studies.
   - Data accumulation shall be promoted in order to improve the quantity and quality of the Medical Information Database Network as well as to improve post-marketing safety measures.
   - In order to promptly and safely provide useful medical devices and regenerative medical products, discussions up to the previous effective period for the Mid-term Targets shall be put into consideration to enhance the system of collecting post-marketing information, for example, by establishing a patient registry system for confirming long-term safety, with the cooperation of relevant academia and companies, etc.
   - Promote investigational research regarding utilization of pharmacogenomics in post-marketing safety measures.
4) Establish a System for Post-marketing Safety Measures by Providing Information Feedback, etc.
   - Regarding line listing of ADR, the time from ADR reporting to disclosure shall remain as within 4 months.
   - ADR reports from medical institutions shall be promptly disclosed in the line listing for those that have been investigated by PMDA.
   - The instructions for revising the package inserts shall be published on the website within 2 days after issuance of those instructions.

- Disseminate information related to cases of ADR and malfunction, etc., for those that served as the basis for revising package inserts for prescription pharmaceuticals and medical devices, etc.
- Consider with MHLW about measures to enable medical institutions to discern the urgency and importance of the disseminated information more easily.
- Enhance dissemination of information to promote appropriate use of generic drugs.
- Regularly disseminate medical safer information so that pharmaceuticals and medical devices, etc., will be used safely at clinical settings.
- Collect medical safety information from vocational groups, etc., and enhance dissemination of the information.
- Aim for a wider use of the Pharmaceuticals and Medical Devices Information E-Mail Alert Service by enhancing the content of the service and by increasing the number of registries at an early period before the end of FY 2018 by more than 1.5 times that at the end of FY 2013, by means of strongly promoting registry of healthcare professionals working at medical institutions and pharmacies with the cooperation of relevant organizations, and so on.
- Let healthcare professionals, including physicians and pharmacists, etc., increase understanding of the information that PMDA provides.

5) Enhance Dissemination of Information to the Public Regarding Safety of Pharmaceuticals and Medical Devices, etc.
- Improve the method of disseminating information on the website regarding safety of pharmaceuticals and medical devices, etc., in order to respond to changes in the environment in which pharmaceuticals, medical devices, and regenerative medical products are provided, such as internet marketing of OTC drugs.
- Promptly release important safety information in a manner that is easy to understand from the patients' perspective.
- Enhance dissemination of information to patients by further increasing patient's awareness of the Pharmaceutical Guide for Patients and by increasing its convenience.
- Enhance dissemination of information that can be used for medication instructions for patients.
- Conduct consultations services for general consumers and patients for a safe and secure use of pharmaceuticals and medical devices, etc.
- Further improve the contents of information to the public, etc.

6) Conduct Appropriate Post-marketing Safety Measures Based on the Risk Management Plan of Pharmaceuticals
- Consultation and instruction systems shall be strengthened and enhanced to appropriately conduct pharmacovigilance activities and risk minimization activities, based on the new Risk Management Plan (RMP) of pharmaceuticals.
- The new pharmaceuticals review divisions and the safety divisions shall cooperate together through discussions with the applicant in confirming RMP before reviews of new pharmaceuticals concludes.
- Regarding generic drugs, the generic drugs review division and the safety divisions shall cooperate together in order to confirm in the reviews the pharmacovigilance activity and the risk minimization activity that the MAHs are required to conduct.

7) Enhance Safety Measures in Response to the Introduction of New Review Service, and a Safety Management System Consistent from the Review Stage
- Safety management system shall strengthen cooperation with the relief services and maintain consistency from the review stage. Information from the relief services shall be utilized in the post-marketing safety measure operation, with special attention to ensuring protection of personal information.

- The safety divisions and the review divisions shall share information on adverse reactions caused by regenerative medical products (including time during conditional and time-limited approvals), and shall cooperate in taking post-marketing safety measures.
- Information on malfunctions of new medical devices and certified medical devices shall be shared among the safety divisions, the review divisions, and the registered certification body assessment division, for taking post-marketing safety measures.
- The system of safety management shall be enhanced in order to maintain consistency from the review stage, by allocating multiple risk managers for each field according to the number of new pharmaceutical products.
- The management function of the overall post-marketing safety measures shall be enhanced and the groups shall coordinately cooperate, to conduct appropriate operation.
- For products which need investigation on all cases as an approval condition, safety and efficacy information obtained from post-marketing surveillance shall be promptly provided to the public and health care professionals.

8) Enhance Follow-ups of the Safety Measures Conducted
- Conduct investigations to confirm the current status of post-marketing safety measures in MAHs, for example, whether information is definitely conveyed from the MAHs to medical institutions, and to confirm whether information from MAHs is conveyed and utilized within medical institutions and pharmacies. Based on the investigation results, information regarding methods of utilizing safety information in medical institutions and pharmacies shall be disseminated as best practices to use pharmaceuticals and medical devices safely.
- Investigate the status of whether the information provided from PMDA is utilized by general consumers and healthcare professionals, and analyze their needs and satisfaction level, to reflect them in the information service improvement.

9) Data Collection, Investigation, and Analysis on Adverse Reactions Reports in Accordance with the Preventive Vaccination Act
- Adverse reactions shall be promptly disclosed on the website for those that were reported from medical institutions and were investigated by PMDA.
- Details of adverse reactions reports shall be investigated in accordance with the Preventive Vaccination Act, with special attention to ensuring protection of personal information, and investigations and analyses shall be conducted in order to ensure safety of vaccination.

4. Promotion of Regulatory Science and Globalization, etc.

In order to promptly provide clinical settings with necessary pharmaceuticals and medical devices, etc., it is essential for the quality, efficacy, and safety of pharmaceuticals and devices to be accurately estimated, evaluated, and determined based on scientific rationale and to be ascertained from an ethical perspective on whether to allow the public to use them. Regulatory science (RS) pursue this, and it has become increasingly important to be promoted, and research needs to be conducted on establishing prompt and accurate evaluation methods, etc., based on the latest results of technology, by utilizing external experts and by improving PMDA's capability.

In the midst of global development, manufacturing, distribution, and marketing of pharmaceuticals and medical devices, the services of PMDA have increasingly become globalized. Under these circumstances, improvement in medical services as well as establishment of PMDA's global standing shall be made by cooperating with MHLW, the United States, Europe, and Asian countries, etc., and by proactively promoting global activities based on the PMDA International Strategic Plan, PMDA International Vision, and Road map for the PMDA International Vision.

Note: Regulatory science = Science for coordinating results of science and technology into the most desirable form for harmonizing people and the society, by conducting accurate and evidence-based estimations, evaluations, and decisions in order for the results of science and technology to be used for

the people and the society (from the Science and Technology Basic Plan, adopted by the Cabinet on August 19, 2011).

1) Promotion of Regulatory Science

1. Utilize the Science Board
   - Proactively utilize the Science Board comprising external experts from the fields of medical science, dentistry, pharmaceutics, and engineering, to strengthen cooperation and communication with universities, research institutions, etc., and clinical settings regarding evaluation methods for innovative pharmaceuticals, medical devices, and regenerative medical products, and to make approaches to advanced technology products more adequately, for example, by utilizing Pharmaceutical Affairs Consultation on R&D Strategy.
2. Enhance regulatory science research
   - Establish a system in PMDA to enable electronic submission of clinical study data for new pharmaceuticals that are to be submitted after FY 2016.
     Conduct PMDA-initiated cross-sectional analyses on cross-sectional clinical study data, etc., using advanced methods of analysis and prediction evaluation, and consider a system that increases the efficiency of pharmaceutical development through establishment of guidelines, etc.
   - As a part of RS research aimed at improving the quality of PMDA's services, a system and environment shall be developed by cooperating with external organizations (NIHS, academia, etc.) when necessary, so PMDA can take initiative in reaching solutions for issues that become evident through its services and issues of making practical use of the latest technologies.
   - Develop an environment to easily engage in RS research, to promote and enhance designated research.
   - Promote RS research, and encourage those results to be presented at conferences or to be submitted to scientific journals. Through RS research, train human resources to be experts in it.
   - As for cross-sectional activities, establish the concept of developing and evaluating pharmaceuticals to enable exchange of opinions between industry, government, and academia, and to establish guidelines and GRP, etc.
3. Enhance staff training
   - Besides improving the quality of review, etc., and post-marketing safety measures, from the perspective of developing experts in RS research, status of the current training programs shall be evaluated for their implementation status, and their content shall be improved and conducted steadily.
   - Enhance staff training to raise staff members with abilities to take the initiative in discussions at global negotiations and conferences, and to cooperate with foreign countries in establishing standards and guidelines, etc.
   - Enhance on-site training at clinical settings and at manufacturing sites of companies, etc., as it is necessary, when conducting reviews, etc., and post-marketing safety measures, to have experience in clinical settings and increase in knowledge of manufacturing processes and quality controls for pharmaceuticals and medical devices.
4. Promote Interaction and investigative research with external researchers
   - Proactively accept personnel from universities and research institutions in the field to facilitate practical use of innovative pharmaceuticals, medical devices, and regenerative medical products conducted by MHLW, while also dispatching staff from PMDA in order to help promote the development of innovative seed-stage resources and to establish guidelines.

- Develop and enhance education and research guidance systems that are conducted by directors and staff members at joint graduate school program, including regulations for those systems. These approaches will target increasing staff members who have a doctoral degree, etc.

2) Response to Globalization

1. Reinforce partnerships with the United States, Europe, Asian countries, and global organizations, etc.
   - Cooperation with the United States FDA, the European Commission, EMA, and Swissmedic, etc., in promoting bilateral conferences based on confidentiality agreement and promoting exchange of information.
   - Establish partnerships with other countries in America, Europe, and Asia, and global organizations.
   - Continue dispatching liaison personnel to the United States, Europe, and Switzerland as much as possible, while promoting further dispatches to other countries in America, Europe, and Asia, etc., and global organizations, etc., as well.
   - Utilize the liaison personnel dispatched to foreign countries to proactively collect information from their dispatched country, and to strengthen cooperation with those countries.
   - Regarding GLP, GCP, GMP, and QMS inspections, further strengthen cooperation with foreign countries by proactively exchanging information on inspection notifications and investigation reports, etc.
   - Respond to globalization of pharmaceutical distribution by enhancing globalization measures, for example, by promoting support in issuing an English version of the Japanese Pharmacopoeia as soon as possible, by disseminating information in English, and by promoting partnerships with the pharmacopoeias of Europe, the United States and Asia, etc.
   - Reinforce partnerships with regulatory agencies in the United States and Europe in order to conduct accurate reviews and consultations based on the latest science and technology, and to take post-marketing safety measures based on the latest information.
   - Promote cooperation necessary to deepen mutual understanding regarding pharmaceutical regulations with the regulatory agencies in Asian countries, which are becoming increasingly important as sites of clinical development and manufacturing of pharmaceuticals, etc.
   - Make necessary efforts for the pharmaceuticals and medical devices approved in Japan to be accepted by regulatory agencies in foreign countries, by enhancing information dissemination regarding review and post-marketing safety measures in Japan, etc.
2. Enhance approaches toward global harmonization
   - Contribute to the establishment of global standards and provide cooperation at global conferences regarding establishment of standards, such as at ICH and International Medical Device Regulators Forum (hereinafter referred to as “IMDRF”), etc., by proposing new topics, taking the initiative in establishing global standards, and proactively stating opinion on topics initiated by other countries. Promote harmonization with other global standards, such as standards for establishing application data that were defined in these conferences, and the ISO and others.
   - For medical devices, continue promoting activities of the Harmonization by Doing (HBD) conducted with the United States and promote exchange of information.
   - Promote globalization of the Japanese Pharmacopoeia through global harmonization of pharmacopoeia, etc., at the Pharmacopoeial Discussion Group (PDG).
   - Participate in discussions at IGDRP, where global collaboration is held for generic drugs, and promote cooperation with foreign countries regarding reviews for generic drugs.

- Cooperate with MHLW in discussions at the International Cooperation on Cosmetics Regulation (ICCR) in order to promote cooperation with foreign countries.
- Participate in and contribute to global cooperation activities such as WHO and OECD.
- Consider accepting a wider range of submission data for new pharmaceutical applications that are in English.

3. Promote interaction of personnel
   - In order to promote establishment of networks with foreign regulatory agencies, have staff members proactively participate in global academic meetings and conferences, and increase opportunities to dispatch staff to organizations other than FDA, EMA, and Swissmedic.
   - Promote personnel interactions through PMDA training seminars with Asian countries, etc., and global organizations, etc., and accepting trainees, etc., in order to establish a system to regularly exchange information related to reviews and post-marketing safety measures. Also have Asian countries, etc., increase their understanding of Japanese regulations, etc., and standards regarding pharmaceutical applications, etc., through symposiums co-hosted by multiple countries, etc.
4. Train and enhance human resources to acquire global perspectives and communication skills
   - In order to train human resources to be globally involved in establishing guidelines such as ICH and IMDRF, staff training programs shall be established and conducted, including attendance at meetings and global conferences where guidelines are established, and research opportunities at foreign institutions and graduate schools, etc.
   - Improve linguistic ability by continuing and enhancing English training for executives and staff members, etc.

5. Enhance and improve global public relations and information dissemination
   - Enhance system to improve ability of disseminating information globally.
   - Enhance and improve the content of PMDA's website in English to promote exchange of opinions and information with foreign countries. To be more specific, proactively release English versions of pharmaceutical regulations, details of services, review reports, and safety information, etc. Make certain that review reports are translated into English especially for products having significance in disseminating information, such as products that are the first in the world to be approved. (Forty products per year by the end of FY 2014. Thereafter, targets will be set in each fiscal year plan, with consideration of the utilization status of relevant people and the application status of pharmaceuticals and medical devices, etc.)
   - Continuously conduct lectures and present booth exhibits, etc., at global conferences.

3) Measures for Intractable Diseases and Orphan Diseases, etc.
- Develop review guidelines and enhance consultation services regarding pharmaceuticals for intractable diseases and orphan diseases.
- Take necessary measures to operate notifications and guidance regarding companion diagnostics pharmaceuticals, etc., smoothly.
- Take necessary measures through discussions with foreign regulatory agencies regarding points to be considered in developments, etc., using biomarkers.
- In order to promote utilization of pharmacogenomics in pharmaceutical development, PMDA shall take initiative in establishing evaluation guidelines at ICH, cooperate and share information with foreign regulatory agencies to establish a system that enables the 3 regions, including FDA and EMA, to make recommendations together, and thereby contributing to the development of global methods.

4) Provide Information Including Review Reports, etc.
   - In order to promote transparency of the services, PMDA shall proactively promote efforts to enhance disclosure of information by cooperating with MHLW to promptly provide information related to review reports, including results of priority reviews, and other review services, in an easily accessible manner for the public and healthcare professionals, and by enhancing the content of information related to review.
   - Both the regulatory authority and the applicants shall make efforts to reveal in public review reports of new pharmaceuticals and new medical devices under the concept of rational use on the website immediately after approval, and also take appropriate measures to release re-examination reports of pharmaceuticals, etc. The outlines of the documents related to new pharmaceuticals and new medical devices shall also be released on the website within three months after approval.
   - In addition to the integration of the services of releasing information, such as the service of information disclosure based on the Act on Access to Information Held by Independent Administrative Agencies, and the service of revealing in public review reports, so that PMDA can cope with the yearly increasing disclosure requests of documents, PMDA shall further improve efficiency of the services with the cooperation of relevant divisions.

5) Ensuring Fairness when Utilizing External Experts
   - Utilize external experts with relevant knowledge. When utilizing external experts, PMDA shall ensure neutrality and fairness in both the review, etc., and post-marketing safety measures services based on fair rules, and shall review those rules when necessary.

6) Improving the Quality of Review and Safety Services by Enhancing the Information System
   - Improve the quality of services by enhancing the function of information system to cope with the changes in review and post-marketing safety measures services where increase of the amount of information to be handled and deepening of the correlation and accuracy of information are expected.
   - Consider Enhancing computerization of review procedures, including eCTD, and improving the IT literacy of the staff.

Part 3
Budget, Income and Expenditure Plan and Cash Flows Plan

1. Budget: see Attachment 1

2. Income and expenditure plan: see Attachment 2

3. Cash flows plan: see Attachment 3

Part 4
Limit of Short-term Borrowing

1) Limit of Borrowing
   2.2 billion yen

2) Expected Reasons for Short-term Borrowing
   a) Shortage of funds due to delayed receipt of administrative subsidies, subvention, and agent service fees, etc.
   b) Unexpected retirement payments.
   c) Shortage of funds due to other unexpected situations.

Part 5
Plans for Transferring or Mortgaging Important Property if Applicable

None

Part 6
Use of Surplus Funds

Surplus funds can be allocated to the review account for the following purposes.
- Resources for expenditure related to operational improvement.
- Financial resources for training and research, etc., to improve personnel qualifications and service quality.
  Regarding the ADR relief account and the infection relief account, surplus funds shall be adjusted as reserve funds, as specified in the provision of Article 31, Paragraph 4 of the Act on the Pharmaceuticals and Medical Devices Agency (Act No. 192, 2002).

Part 7
Other Matters Regarding Operation Management Specified in the Ordinance of the Competent Ministry, etc.
The following measures shall be taken for matters regarding operation management, etc., specified in Article 4 of the Ministerial Ordinance Regarding Operation Management, Finance, and Accounting of the Pharmaceuticals and Medical Devices Agency (MHLW Ministerial Ordinance No. 55, 2004), etc.

1) Matters Regarding Personnel Affairs
   a) Plans regarding personnel affairs of staff members
      - In order to increase regular staff, PMDA shall employ highly specialized and capable human resources, mainly through open recruitment based on the Act for Partial Revision of the Pharmaceutical Affairs Act that reflects the final proposals of the Japan Revitalization Strategy, the Healthcare and Medical Strategy, and the Committee for Investigation of Pharmaceutical-induced Hepatitis Cases and Appropriate Regulatory Administration to Prevent Similar Sufferings.

        Note: Standards regarding personnel affairs
        The number of regular staff at the end of the term shall not exceed 141.9% of that at the beginning of the term.

        Reference 1) Number of regular staff members at the beginning of the term: 751
        Number of regular staff members at the end of the term: 1,065

        Reference 2) Total personnel expenses for effective period for the Mid-term Targets:
        36,535 million yen (estimate)
        Note that the above amount is equivalent to the expenses for the executive compensation and basic pay, miscellaneous allowances, and overtime work pay for staff members.
      - Improve qualification and capacity of the staff members by interacting with the government, research institutions, and universities with a consideration of a mobilization of human resources, and reduce proportion of transferees from the government with a consideration of appropriate balance.

Therefore, PMDA shall strive to make reductions in accordance with the Basic Policy for Review of System/Organization of Incorporated Administrative Agencies (adopted by the Cabinet) established on December 7, 2010, and shall disclose those statuses every year.
PMDA shall also systematically make approaches to steadily increase staff members, including specialized technical employees, etc., as specified in Part 7-1). Employment terms shall also be revised systematically to make a more attractive work environment.
To ensure employment of highly specialized human resources, PMDA shall determine strategic methods, including an increase in number of fixed-term staff and introduce an annual salary system.

- In order to avoid any suspicion of inappropriate relationships with pharmaceutical companies, etc., PMDA shall appropriately manage personnel by establishing certain restrictions in employment, allocation, and post-retirement reemployment, etc., for executives and employees.

b) Develop a comfortable working environment

- Consider developing a comfortable working environment for employees by improving working environment such as a promotion of work-life balance. Make approaches that enable a good balance between family life and career and that allows especially the women staff members, accounting for about half of the total employees, to keep fulfilling their abilities.

1.1.c) Adjust salary standards

- Based on the Basic Policy Regarding Reform of Incorporated Administrative Agency (adopted by the Cabinet on December 24, 2013), PMDA shall take necessary measures to adjust the salary standards of the employees to achieve an appropriate and efficient level, taking into consideration the salary standards of national government employees as well as its competitiveness to stably securing distinguished human resources.
  PMDA shall also inspect its state of approaches for adjusting salary standards every year from the following perspectives and shall disclose those results.
  1) Appropriateness in salary standards of the employees when compared to the national government employees in view of factors such as their office locations and academic backgrounds, etc.
  2) Room to improve the causes of high salary standards, for example, high proportion of employees dispatched form the government.
  3) Ability to thoroughly explain the appropriateness of the current salary standards when the large government spending, the accumulated losses, and the salary standards of private companies engaged in similar services are pointed out.
  4) Competitive salary standards of PMDA's staff members compared to the standards in the relevant fields, such as pharmaceutical companies and research institutes at universities, etc., when we need to secure human resources with highly specialized knowledge and experience in technical matters.
  5) Other explanations for the salary levels must be rational to gain sufficient public consent.

d) Improve qualifications of the staff members

- In order to improve the quality of the services, PMDA shall improve qualification of the staff members by systematically providing opportunities for training according to targets of the services, etc., by enhancing training conducted with the cooperation of companies, and by interacting with MHLW, as well as domestic and foreign universities and research institutions, etc.
- Training for new staff members shall especially be enhanced in order to ensure effectiveness of enhancing system by increasing staff numbers.

- Enhance staff training programs for administrative staff members who are on main career tracks, so as to improve the quality of staff members at clerical positions supporting the organizational management.
- Implement a personnel evaluation system that allows motivation of the staff members to increase, and appropriately reflect those evaluations and the status of achieving their goals on their salary, pay raise, and promotion.
- Strategically allocate the staff members in view of their future career development to maintain their specialization as well as the continuity of operations.

2) Ensure Security
- Continue enhancing the internal control system for security and confidentiality reasons by thoroughly controlling entrances and exits 24 hours a day, using the entrance and exit control system at the office.
- Continue ensuring security of information related to the information system.
- Continue ensuring the document control system based on the property of the stored documents.

3) Matters Regarding Facilities and Equipment

None

4) Matters Regarding Disposition of the Reserve Funds Specified in Article 31, Paragraph 1 of the Act on the Pharmaceuticals and Medical Devices Agency

In cases where there are still reserve funds for the review account even after adjusting profit and loss according to Article 44 of the Act on General Rules at the end of the last fiscal-year of the effective period for the Second Mid-term Targets, the amount approved by the MHLW out of those reserve funds can be applied to the financial resources of the review service and post-marketing safety measures service, as specified in Article 15 of the Act on Pharmaceuticals and Medical Devices Agency.

5) Other Matters

Steadily conduct approaches based on the government policy indicated in past Cabinet decisions, etc.

Budget

Budgets for Mid-term Plan (FY 2014 - FY 2018)

(Unit: million yen)

Classification	Amount						
	Adverse drug reactions relief account	Infection relief account	Review account	Specified relief account	Commission and loan account	Commission payment account	Total
Income							
Administrative subsidies			6,350				6,350
Governmental subsidies	883	707	1,854				3,444
Contributions	20,322	553	16,043	18,390			55,308
User fees			60,151				60,151
Commissioned operations			926		5,410	3,262	9,598
Management income	1,671	312					1,983
Miscellaneous income	7	1	146		8	5	167
Total	22,883	1,572	85,471	18,390	5,418	3,268	137,001
Expenditure							
Operating expenses	16,501	1,300	81,659	18,585	5,380	3,243	126,667
Personnel expenses	1,254	130	38,056	85	188	99	39,813
Administrative expenses	15,247	1,170		18,500	5,192	3,143	43,252
Expenses for reviews and related services			29,533				29,533
Expenses for safety measures, etc.			14,069				14,069
General administrative expenses	541	74	10,526	12	38	25	11,216
Personnel expenses	270		3,626				3,897
Non-personnel expenses	271	74	6,899	12	38	25	7,319
Total	17,043	1,374	92,184	18,597	5,418	3,268	137,883

<Note 1> Personnel expenses were calculated as expenses based on self-financial resources for increases in and after FY 2015.

<Note 2> In principle, all figures have been rounded off; therefore, individual totals shown may not coincide with the actual totals.

Income and Expenditure Plan

Income and Expenditure Plan for the Mid-term Plan (FY 2014 - FY 2018)

(Unit: million yen)

Classification	Amount						
	Adverse drug reactions relief account	Infection relief account	Review account	Specified relief account	Commission and loan account	Commission payment account	Total
Expenditure							
Ordinary expenses	24,163	1,495	93,471	18,600	5,422	3,269	146,420
Operating expenses	16,346	1,233	75,708	18,585	5,383	3,243	120,498
Relief benefits	12,270	155					12,425
Operating expenses for health and welfare	197	621					818
Operating expenses for reviews			29,719				29,719
Operating expenses for safety measures			11,317				11,317
Specified relief benefits				18,390			18,390
Benefits (healthcare allowances, etc.)					5,118		5,118
Benefits (special allowances, etc.)						1,294	1,294
Operating expenses for research and study						1,768	1,768
Administrative expenses	2,619	331		117	93	88	3,249
Personnel expenses	1,260	126	34,673	78	172	92	36,399
General administrative expenses	542	78	10,520	12	38	25	11,214
Personnel expenses	272		3,306				3,577
Non-personnel expenses	270	78	7,214	12	38	25	7,636
Depreciation expenses	241	16	7,243	4	1	1	7,507
Provision for liability reserve	7,030	163					7,192
Miscellaneous losses	5	5					10
Income							
Ordinary income	22,876	1,572	85,713	18,600	5,418	3,268	137,447
Governmental subsidies	883	707	1,854	207			3,651
Contributions	20,322	553	16,043				36,918
User fees			60,151				60,151
Commissioned operations					5,410	3,262	8,672
Other governmental grants			926				926
Administrative subsidies			6,350				6,350
Reversal of asset offset subsidies			89	4			92
Reversal of asset offset administrative subsidies			207				207
Reversal of asset offset gifts received							
Financial income (no operating income)	1,671	312					1,983
Gain on reversal of specified relief fund deposit received				18,390			18,390
Miscellaneous income		1	92		8	5	107
Net income (△net loss)	△ 1,287	77	△ 7,759	0	△ 4	△ 1	△ 8,974
Reversal of appropriated surplus							
Gross income (△gross loss)	△ 1,287	77	△ 7,759	0	△ 4	△ 1	△ 8,974

<Note 1> Administrative subsidies are assumed to be the financial resource for retirement allowances for staff members in charge of operations financed by administrative subsidies under the review account.
However, this excludes the amount arranged through administrative subsidies as retirement allowances equivalent to tenure, as provided for in Article 8-2 of the supplementary provisions in the Act for Pharmaceuticals and Medical Devices Agency.

<Note 2> In principle, all figures have been rounded off; therefore, individual totals shown may not coincide with the actual totals.

Cash Flows Plan

Cash Flows Plan for the Mid-term Plan (FY 2014 - FY 2018)

(Unit: million yen)

Classification	Amount						
	Adverse drug reactions relief account	Infection relief account	Review account	Specified relief account	Commission and loan account	Commission payment account	Total
Cash Outflows							
Cash outflows from operating activities	16,462	1,210	86,230	18,599	5,430	3,304	131,234
Relief benefits	12,251	155					12,406
Operating expenses for health and welfare	197	621					818
Operating expenses for reviews			29,012				29,012
Operating expenses for safety measures			10,811				10,811
Specified relief benefits				18,390			18,390
Benefits (healthcare allowances, etc.)					5,131		5,131
Benefits (special allowances, etc.)						1,294	1,294
Operating expenses for research and study						1,768	1,768
Administrative expenses	2,275	243		114	86	119	2,837
General administrative expenses	266	69	6,882	12	31	25	7,286
Personnel expenses	1,472	121	39,525	83	183	97	41,480
Cash outflows from investing activities	20,532	2,664	5,357				28,552
Payments for purchases of investment in securities	20,000	2,500					22,500
Payments for purchases of intangible fixed assets	532	164	5,357				6,052
Cash outflows from financial activities							
Amount carried forward to the next mid-term plan period	438	422	9,440	123	40	96	10,559
Total	37,431	4,296	101,026	18,721	5,471	3,400	170,345
Cash Inflows							
Cash inflows from operating activities	22,906	1,575	86,332	18,423	5,433	3,268	137,937
Governmental subsidies	885	708	1,854				3,447
Administrative subsidies			6,350				6,350
Contributions	20,322	553	16,043	18,422			55,340
User fees			60,975				60,975
Commissioned operations			382		5,423	3,262	9,067
Miscellaneous income	1,698	315	728	1	10	6	2,757
Cash inflows from investing activities	14,100	2,500					16,600
Cash inflows from financial activities							
Amount brought forward at the beginning of the mid-term plan period	426	221	14,694	299	37	132	15,808
Total	37,431	4,296	101,026	18,721	5,471	3,400	170,345

<Note> In principle, all figures have been rounded off; therefore, individual totals shown may not coincide with the actual totals.

Overview of the Act for Partial Revision of the Pharmaceutical Affairs Act (Act No. 84 of 2013)

Overview of the Act for Partial Revision of the Pharmaceutical Affairs Act (Act No. 84 of 2013)

In the view of securing the early access to safe and effective drugs, medical devices, etc., the following actions will be taken:
1. Strengthen safety measures regarding drugs, medical devices, etc.
2. Establish the regulation based on the characteristics of medical devices.
3. Establish the regulation based on the characteristics of regenerative medical products.

Ⅰ Overview

1. Strengthen safety measures regarding drugs, medical devices, etc.

i. Specify the necessity of regulations to prevent health hazards from occurring or expanding in the "Purpose" of the revised Pharmaceutical Affairs Act (PAA).
ii. Specify relevant parties' obligation to ensure the quality, safety, and efficacy of drugs, medical devices, etc.
iii. Specify Marketing Authorization Holder (MAH)'s obligation to notify the Minister of Health, Labour and Welfare of a package insert that includes the latest findings.

2. Establish the regulation based on the characteristics of medical devices

i. Provide an independent chapter for the regulations for medical devices separately from those for drugs, etc.
ii. Expand the scope of third-party medical device certification to include "specially controlled medical devices" by newly establishing certification standards for them.
iii. Classify stand-alone programs for diagnosis as medical devices, which are subject to product approval/certification.
iv. Change from the licensing system to the registration system for manufacturers of medical devices.
v. Rationalize the QMS inspection regarding manufacturing and quality control of medical devices.

3. Establish the regulation based on the characteristics of regenerative medical products

i. Define "regenerative medical products" newly and establish regulatory framework including safety measures based on their characteristics.
ii. Grant time-limited conditional approval for a non-homogeneous regenerative medical product if its safety is confirmed and its efficacy is predicted.

4. Others

The official name of the revised act is **the "Act on Securing Quality, Efficacy and Safety of Pharmaceuticals, Medical Devices, Regenerative and Cellular Therapy Products, Gene Therapy Products, and Cosmetics**"

Ⅱ The date of enforcement

The revised act will come into force as from the date specified by a Cabinet Order within 1 year from the day of promulgation (November 27, 2013).

1. Strengthen safety measures regarding drugs and medical devices, etc.

Background

- It is required to strengthen safety measures to facilitate practical application of drugs and medical devices.
- A package insert of drugs and medical devices is essential to convey the instructions and directions for use of such products in clinical settings. As a result of the investigation of drug-induced hepatitis cases, it is pointed out that the definition of package insert needs to be revised. In addition, package inserts should include the latest findings in a timely manner, but it is not stated clearly in the PAA.
- For the reasons mentioned above, it is important to strengthen safety measures for medical products through the re-definition of package insert and other relevant actions.

【Re-definition of package insert】

(1) MAHs of drugs, etc. are required to notify the Minister of Health, Labour and Welfare of a package insert that includes the latest findings. At the same time, the package insert should be posted on the website promptly with a view to providing information in a timely manner.

【Other amendments】

(2) Specify the necessity of regulations to prevent health hazards from occurring or expanding in the "Purpose" of the revised Pharmaceutical Affairs Act (PAA).
(3) Specify the roles of industries, medical professionals and other relevant parties to secure the quality, efficacy and safety of drugs, etc.
(4) Have medical institutions as well as MAHs submit the Adverse Drug Reaction Reports to the Pharmaceuticals and Medical Devices Agency (PMDA), which enables the government to request PMDA to analyze the information and take necessary post-marketing safety measures.

2. Establish the regulation based on the characteristics of medical devices

Background

- The characteristics of medical devices* are different from those of drugs since considerable numbers of medical devices are improved and upgraded frequently as with other mechanical products such as personal computers.
- The development and practical application of new medical devices are expected to promote economic growth in Japan as well as to improve the quality of medical care. On the other hand, it is pointed that the time from the development of products to their approval and launch may be prolonged.
- The international regulatory harmonization should be considered in order to expand the market of medical devices originated from Japan.
- To this end, the early access to medical devices and rationalization of regulatory framework should be realized through the regulatory reform based on the characteristics of medical devices.
  - Major characteristics of medical devices
    i. Being developed through practical use at clinical setting.
    ii. Having a short life span due to frequent improvement and upgrade.
    iii. The efficacy and safety of medical devices largely depends on skills of individual medical professionals, and diversified small quantity devices are used in clinical settings

【Provide an independent chapter / Specify medical devices in the official title of the revised act】

(1) Provide an independent chapter for the regulations for marketing and manufacturing medical devices separately from those for drugs.

(2) Specify medical devices in the official title of the revised PAA.
- The title of the revised PAA is "the Act on Securing Quality, Efficacy and Safety of Pharmaceuticals, Medical Devices, Regenerative and Cellular Therapy Products, Gene Therapy Products, and Cosmetics" (hereinafter referred to as the "Pharmaceuticals and Medical Devices Act" or "PMD Act").

【Rationalization of regulatory system for providing early access to new products】

(3) Expand the scope of third-party medical device certification to include "specially controlled medical devices (*)" by newly establishing certification standards, which allows PMDA reviewers to focus on and accelerate the review of new medical devices.
- Examples: contact lenses and dental implants

  - The PMD Act also specify the succession of the status of a MAH with certification for medical devices; the government approval for the operating rules prepared by registered certification bodies; the issuance of the order of the Minister of Health, Labour and Welfare to revoke certification for medical devices; and other matters necessary to address the expansion of the scope of third-party certification.

【Clarify the positioning of stand-alone programs】

(4) Classify stand-alone programs as medical devices which is subject to approval/certification for marketing in view of the fact that stand-alone programs are classified as medical devices in the U.S. and the EU.
Examples: programs for MRI systems to display, save, analyze the imaging data.

【Other amendments】

(5) Change from the licensing system from the registration system for manufacturers of medical devices to reduce regulatory requirements.

(6) Rationalize the procedures for product-based QMS inspection to allow for product family-based QMS inspection (which is conducted for a group of medical devices categorized depending on their characteristics).
- If at least one product of the same product family has been in compliance with QMS requirements, the rest of the product family will be exempted from the QMS inspection. QMS inspections conducted by prefectural governments is to be abolished and all QMS inspections will be conducted by registered certification bodies and/or PMDA.

(7) The efficacy and safety of medical devices* designated by the Minister of Health, Labour and Welfare are to be confirmed by use-results surveys which is conducted for the period determined by the product characteristics, instead of re-evaluation and/or re-examination.
* e.g. medical devices such as an artificial heart implanted in the human body for a long time.

(8) Approval/registration is to be required for the person who leases "specially controlled medical devices" even if the leasing status is non-profitable.

(9) When a medical device is sold to medical institutions etc., the attachment of a package insert to the device can be omitted on conditions that the package insert is posted on the MAH's website and relevant consent is obtained from medical institutions.

3. Implementation of regulatory system considering the characteristics of regenerative medical products

Background

- Practical application of regenerative medical product using iPS cells, etc., as innovative medicines, is highly expected by the nation. On the other hand, several issues including safety are still remained.
- It is necessary to develop regulatory system for regenerative medical products by considering their characteristics in order to accelerate their practical application while ensuring the safety.
  * Major characteristics of regenerative medical products
    Non-homogeneity in product quality due to the individual variability in human cells

【Independent definition of regenerative medical products】

(1) Define "regenerative medical products" in a new chapter of the PMD Act independently from those for drugs and medical devices.

The scope of regenerative medical products

- The products produced from cultured and/or processed human cells and/or tissues for the following purposes:
  i. To reconstruct, restore or reproduce the structure or functions of human body.
  ii. To treat or prevent human diseases.
- The products used for gene transfer and expression in human cells for the treatment of human diseases.

  * Since those products are produced using human cells, etc., they are characterized by non-homogenous quality and it may be difficult to predict the efficacy of products. The exact scope is to be defined by a Cabinet Order.

【Introduction of time-limited conditional approval system】

(2) Grant time-limited conditional approval for a non-homogeneous regenerative medical product in the earlier stage of regulatory process than usual if its safety is confirmed and its efficacy is predicted. In that case, the efficacy and safety of the approved product will be reviewed for a specified post-marketing period.

- Expected conditions and periods: Medical devices only sold to specialized clinics/hospitals with appropriate facilities; the duration of time-limited conditional approval does not exceed 7 years in principal. Also, the MAH is required to re-submit the application with the data obtained during the specified time period.

【Improvement of safety measures】

(3) Medical professionals such as physicians should make efforts to provide the patients with appropriate explanation and obtain his/her consent before the use of the products.

(4) MAHs should take post-market safety measures such as use-results surveys, periodic infection reports, and record and storage of information on product users.

- With regard to regenerative medical products designated by the Minister of Health, Labour and Welfare, their MAHs are required to store all the data obtained from medical institutions for an extended period of time. The medical institutions is also required to record/store the data of users.

(5) Any health damage caused by regenerative medical products is to be eligible for the Relief System for Adverse Drug Reactions and the Relief System for Infections Acquired through Biological Products. (Act on the Pharmaceuticals and Medical Devices Agency)

【Other amendments】

(6) Ensure the quality and safety of products through setting standards for manufacturing control and quality control at manufacturing sites.

(7) As a principle, collecting human blood is prohibited as a business. However, manufacturing of products from human blood collected by MAHs and/or medical institutions is permitted. (Revision of the Act on Securing a Stable Supply of Safe Blood Products [Act No. 160 of 1956])

4. The date of enforcement

The revised act will come into force as from the date specified by a Cabinet Order within 1 year from the day of promulgation.